HUBUNGAN ANTARA ANEMIA PADA IBU HAMIL DENGAN KEJADIAN BERAT BADAN LAHIR RENDAH

LITERATURE REVIEW

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PROGRAM STUDI ILMU KEPERAWATAN
FAKULTAS ILMU KESEHATAN
UNIVERSITAS dr. SOEBANDI
JEMBER
2022

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Untuk Memenuhi Persyaratan
Memperoleh Gelar Sarjana Ilmu Keperawatan (S.Kep)

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LEMBAR PERSETUJUAN

Skripsi ini telah diperiksa oleh pembimbing dan telah disetujui untuk mengikuti seminar hasil pada Program Studi Ilmu Keperawatan
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PERNYATAAN KEASLIAN PENELITIAN

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Menyatakan dengan sebenar-benarnya bahwa *literature review* ini adalah asli dan belum pernah diajukan sebagai syarat penelitian, baik di Universitas dr. Soebandi Jember maupun di perguruan tinggi lain. *literature review* ini murni gagasan dan rumusan saya sendiri tanpa bantuan pihak lain, kecuali arahan Tim Pembimbing. Dalam perumusan *literature review* ini tidak terdapat karya atau pendapat orang lain yang telah ditulis serta dipublikasikan, kecuali secara tertulis dengan jelas dicantumkan dalam daftar pustaka. Apabila dikemudian hari terdapat penyimpangan dan ketidakbenaran dalam pernyataan ini, maka saya bersedia menerima sanksi akademik dan atau sanksi lainnya, sesuai dengan norma yang berlaku dalam perguruan tinggi ini.

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LEMBAR PENGESAHAN

Proposal *Literature Review* yang berjudul **Hubungan Antara Anemia Pada Ibu Hamil Dengan Kejadian Berat Badan Lahir Rendah** telah diuji dan disahkan oleh Program Studi Ilmu Keperawatan pada:

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PERSEMBAHAN

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MOTTO

Sesungguhnya hanya orang- orang yang bersabarlah yang
dicukupkan pahala mereka tanpa batas
(QS. Az- Zumar: 10)

ABSTRAK

Andariyanti, Novie * Rohmah, Nikmatur** Wulansari, Yunita Wahyu ***.2022. **Hubungan Antara Anemia Pada Ibu Hamil Dengan Kejadian Berat Badan Lahir Rendah**. Skripsi. Program Studi Ilmu Keperawatan Universitas dr. Soebandi Jember

Pendahuluan: berat badan lahir rendah telah dipelajari secara luas dan merupakan faktor risiko penting untuk morbiditas dan mortalitas pada bayi. beberapa faktor ibu seperti usia, anemia dapat mempengaruhi berat badan lahir rendah pada bayi. oleh karenanya, anemia selama kehamilan dapat dianggap sebagai salah satu penyebab utama bayi berat badan lahir rendah. Tinjauan ini bertujuan untuk menjelaskan hubungan antara anemia pada ibu hamil dengan kejadian berat badan lahir rendah. **Metode:** Desain penelitian adalah *Literatur review*. Database menggunakan *google scholar*, *PubMed,* dan *Elsevier* dengan pendekatan PEOS *framework.* Tujuh artikel publikasi 2017-2022 teridentifikasi sesuai kriteria. **Hasil:** kejadian anemia maternal mencapai 24,9% - 52,5% yang yang pada umumnya pada derajad ringan (*mild*) dengan rata-rata kadar hemoglobin ibu selama masa kehamilan rata- rata adalah 10,6 g/dl sampai 11,7 g/dl dan bayi berat lahir rendah mencapai 23,9% - 51,53% dengan rerata berat badan lahir adalah 1850 – 2431 gram. **Analisis**: tujuh artikel mengungkap adanya korelasi anemia maternal dengan kejadian berat lahir rendah, anemia pada ibu hamil meningkatkan risiko kejadian berat lahir rendah sebesar 0,53 – 9,5 kali. **Diskusi:** Disarankan untuk meningkatkan dukungan pada suplementasi, fortifikasi makanan dengan vitamin dan mineral esensial dalam mencegah anemia.

Kata Kunci : **Anemia, Ibu Hamil, Berat Badan Lahir Rendah**

*Peneliti
** Pembimbing 1
***Pembimbing 2

ABSTRACT

Andariyanti, Novie * Rohmah, Nikmatur** Wulansari, Yunita Wahyu***.2022. **The Relationship Between Maternal Anemia and Incident of Low Birth Weight**. *Undergraduated Thesis. Nursing Science Study Program, dr. Soebandi University*

Introduction*: Low birth weight has been studied extensively and is an important risk factor for infant morbidity and mortality. Several maternal factors such as age, anemia can affect low birth weight in infants. therefore, anemia during pregnancy can be considered as one of the main causes of low birth weight babies. This review aims to explain the relationship between anemia in pregnant women and the incidence of low birth weight.* ***Methods****: The research design is a literature review. The database uses Google Scholar, PubMed, and Elsevier with the PEOS framework approach. Seven articles published in 2017-2022 were identified according to the criteria.* ***Results****: the incidence of maternal anemia reached 24.9% - 52.5%, most of which were mild with an average maternal hemoglobin level during pregnancy of 10.6 g/dl to 11.7 g/dl. dl and low birth weight babies reached 23.9% - 51.53% with an average birth weight of 1850 – 2431 grams.* ***Analysis****: seven articles revealed a correlation between maternal anemia and the incidence of low birth weight, anemia in pregnant women increased the risk of low birth weight by 0.53 – 9.5 times.* ***Discussion****: recommendation to increase support for supplementation, food fortification with essential vitamins and minerals in preventing anemia.*

Keywords : Maternal Anemia, Low Birth Weight

* *Researcher*
** *Advicer 1st*
*** *Advicer 2nd*

KATA PENGANTAR

Puji Syukur Kepada Tuhan Yang Maha Esa yang telah melimpahkan rahmat dan hidayah-Nya sehingga penyusunan *literature review* ini dapat terselesaikan. *literature review* ini disusun untuk memenuhi salah satu persyaratan menyelesaikan pendidikan pada Program Studi Ilmu Keperawatan Universitas dr. Soebandi dengan judul **Hubungan Antara Anemia Pada Ibu Hamil Dengan Kejadian Berat Badan Lahir Rendah** Selama proses penyusunan *literature review* ini peneliti dibimbing dan dibantu oleh berbagai pihak, oleh karena itu peneliti mengucapkan terima kasih kepada:

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Dalam penyusunan *literature review* ini peneliti menyadari masih jauh dari kesempurnaan, untuk itu peneliti sangat mengharapkan kritik dan saran untuk perbaikan di masa mendatang.

Jember, 24 Agustus 2022

Peneliti

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DAFTAR BAGAN

DAFTAR LAMPIRAN

DAFTAR SINGKATAN DAN SIMBOL

ANC	:	*Antenatal Care*
AIDS	:	Acquired Immunodeficiency Syndrome
BBLR	:	Bayi Berat Lahir Rendah
BBLSR	:	Bayi Berat Lahir Sangat Rendah
BBLER	:	Bayi Berat Lahir Ekstrem Rendah
dl	:	Desiliter (Satuan)
gr	:	Gram (Satuan)
Hb	:	*Haemoglobin*
HR	:	*Heart Rate*
HIV	:	*Human Immunodeficiency Virus*
Hct	:	*Hematokrit*
IUFD	:	*Intrauterine Deaths*
IUGR	:	*Intrauterine Growth Restriction*
IUGR	:	*Intrauterine Growth Restriction*
KIA	:	Kesehatan Ibu Dan Anak
KEK	:	Kurang Energi Kronis
KJDK	:	Kematian Janin Di Dalam Kandungan
LILA	:	Lingkar Lengan Atas
mmHg	:	*Milimeter Hidragirum* (Satuan Tekanan Berdasarkan Raksa)
MCV	:	*Mean Corpuscular Volume*
MCH	:	*Mean Corpuscular Hemoglobin*

RoP	:	*Retinopathy Of Prematurity*
SSP	:	Susunan Saraf Pusat
TTD	:	Tablet Tambah Darah
WHO	:	*World Health Organization*
WUS	:	Wanita Usia Subur

BAB 1

PENDAHULUAN

1.1 Latar Belakang

Berat badan lahir rendah (BBLR) merupakan masalah utama di berbagai masyarakat. Bayi dengan berat lahir kurang dari 2500 gr dikenal sebagai bayi BBLR, tanpa memandang usia kehamilan. Beberapa faktor ibu seperti usia, anemia dapat mempengaruhi BBLR pada bayi. Oleh karena itu, anemia selama kehamilan dapat dianggap sebagai salah satu penyebab utama bayi BBLR (Rahmati *et al*., 2017). Anemia selama kehamilan merupakan masalah kesehatan masyarakat terutama di negara berkembang dan berhubungan dengan luaran yang merugikan pada kehamilan (Stephen & Mgongo, 2018). Anemia selama kehamilan dilaporkan memiliki efek negatif kesehatan ibu dan anak dan meningkatkan risiko kematian ibu dan perinatal. Efek kesehatan negatif bagi ibu antara lain kelelahan, kapasitas kerja yang buruk, gangguan fungsi kekebalan tubuh, peningkatan risiko penyakit jantung, dan kematian serta penyebab tidak langsung kematian ibu dan anak di negara berkembang (Figueiredo & Suzart, 2019). Berat badan lahir rendah memberikan kontribusi yang signifikan terhadap beban perawatan kesehatan ibu dan anak sehingga membutuhkan perhatian lebih dengan melakukan identifikasi faktor risiko serta memulai pengobatan khusus untuk ibu berisiko tinggi (Madendag & Mefkure, 2019).

*World Health Organization (*WHO) mendefinisikan anemia pada kehamilan sebagai konsentrasi hemoglobin (Hb) kurang dari 11 g/dl. Menurut WHO, anemia dianggap sebagai masalah atau masalah kesehatan masyarakat jika studi populasi menemukan prevalensi anemia sebesar 5,0% atau lebih tinggi. Prevalensi anemia sebesar 40% pada suatu populasi tergolong sebagai masalah kesehatan masyarakat yang berat.

*World Health Organization (*WHO) melaporkan bahwa prevalensi anemia di antara wanita hamil dan tidak hamil berusia 15 hingga 49 tahun meningkat dari 2012 ke 2016 di seluruh dunia. Sebanyak 40,05% wanita hamil di seluruh dunia telah anemia selama kehamilan pada tahun 2016 dengan prevalensi tertinggi di Asia Tenggara yang mencapai 48,15% (Huifeng & Chen, 2022). Salah satu dampak anamia maternal adalah berat lahir rendah. Tinjauan oleh Marete & Ekhguere (2020) mengunkapkan bahwa dalam lima tahun terakhir prevalensi kejadian berat badan lahir rendah pada negara negara dengan pendapatan rendah mencapai 36,51% dan di negara berkembang mencapai 15,6%, sedangkan di negara dengan pendapatan yang tinggi menjadi 8,7%.

Anemia selama kehamilan telah dihubungkan dengan risiko kelahiran prematur dan bayi berat lahir rendah (BBLR). Ini juga telah dikaitkan dengan peningkatan risiko kematian intrauterin atau *intrauterine deaths* (IUFD), skor APGAR yang rendah pada 5 menit, dan pembatasan pertumbuhan intrauterine atau *intrauterine growth restriction* (IUGR) yang merupakan risiko bayi berat lahir rendah serta pengerdilan (*stunting*) pada anak-anak di bawah dua tahun (Stephen, 2018). Berat badan lahir rendah telah dipelajari secara luas dan merupakan faktor risiko penting untuk morbiditas dan mortalitas pada bayi (Kumari & Garg, 2019). Mekanisme yang mendasari asosiasi antara anemia dengan kejadian berat badan lahir rendah belum jelas. Namun diduga anemia selama kehamilan terutama disebabkan oleh penurunan hemoglobin dan sintesis eritrosit karena bioavailabilitas nutrisi hematopoietik yang tidak mencukupi dan peningkatan volume plasma yang lebih besar dibandingkan dengan massa sel darah merah (Osol, 2019). Penurunan kadar hemoglobin yang relatif rendah selama kehamilan kemungkinan mencerminkan ekspansi volume plasma yang mengurangi viskositas darah, meningkatkan aliran darah uteroplasenta dan perfusi uteroplasenta, dan sering disertai dengan perubahan kardiovaskular, termasuk peningkatan curah jantung dan penurunan

resistensi perifer yang merupakan mekanisme adaptasi. Adaptasi ini dapat menguntungkan kelangsungan hidup ibu namun kompensasi fisiologis yang demikian dapat dikaitkan dengan hasil yang merugikan pada janin (Smith, 2019).

Meskipun determinan berat badan lahir rendah serupa dengan mekanisme yang menghubungkan anemia ibu dengan berat badan lahir rendah belum sepenuhnya diketahui. Beberapa studi korelatif telah menganalisis hubungan antara anemia ibu dan berat badan lahir rendah namun belum ada kajian yang sifatnya menyeluruh terhadap hasil studi tersebut. Berdasarkan penelitian yang dilakukan sebelumnya menunjukkan bahwa berat badan lahir rendah berdampak pada risiko dan komplikasi perinatal. Berat badan lahir rendah dapat diakibatkan oleh berbagai faktor penyebab yang salah satunya adalah anemia pada masa kehamilan, maka dari itu penting untuk dilakukan studi lebih lanjut menggunakan kajian *literature review* berupa hubungan antara anemia pada ibu hamil dengan kejadian berat badan lahir rendah

1.2 Rumusan Masalah

Berdasarkan uraian diatas maka rumusan masalah pada *literature review* ini adalah bagaimanakah hubungan antara anemia pada ibu hamil dengan kejadian berat badan lahir rendah?

1.3 Tujuan

1.3.1 Tujuan Umum

Berdasarkan pendekatan *literature review* maka tujuan umum dari penelitian ini yaitu untuk menjelaskan hubungan antara anemia pada ibu hamil dengan kejadian berat badan lahir rendah.

1.3.2 Tujuan Khusus

a. Mengidentifikasi anemia pada ibu hamil berdasarkan *literature review*
b. Mengidentifikasi kejadian berat badan lahir rendah berdasarkan *literature review*
c. Menjelaskan hubungan antara anemia pada ibu hamil dengan kejadian berat badan lahir rendah berdasarkan *literature review*

1.4 Manfaat Penelitian

1.4.1 Teoritis

a. Penelitian ini diharapkan dapat memberikan landasan teoritis pada penelitian terkait anemia pada ibu hamil dengan kejadian berat badan lahir rendah
b. Memberikan refrensi tambahan bagi perkembangan ilmu keperawatan dalam mengembangkan intervensi keperawatan utamanya pada departemen keperawatan anak terkait faktor yang memengaruhi kejadian berat badan lahir rendah pada bayi baru lahir

1.4.2 Praktis

a. Bagi ibu hamil dapat digunakan sebagai bahan informasi guna mencegah kejadian anemia yang berdampak pada permasalahan perinatal berupa kejadian berat badan lahir rendah
b. Bagi pengampu kebijakan diharapkan penelitian ini dapat menjadi bahan masukan dalam menyusun pedoman maupun intervensi dalam menurunkan angka kejadian anemia pada ibu hamil sehingga komplikasinya dapat dicegah
c. Bagi para tanaga kesehatan hasil penelitian ini diharapkan dapat menjadi acuan dalam memberikan edukasi kesehatan kepada ibu hamil untuk mencegah kejadian anemia melalui berbagai intervensi

BAB 2

TINJAUAN PUSTAKA

2.1 Konsep Anemia pada Ibu Hamil

2.1.1 Definisi

Anemia merupakan keadaan tubuh dengan konsentrasi hemoglobin (Hb) yang rendah di dalam darah. Perempuan dikatakan anemia saat memiliki Hb lebih rendah dari 12,0 gram/ 100 ml. Anemia dapat menyebabkan masalah kesehatan karena hemoglobin merupakan bagian darisel darah merah dan memiliki peran untukmengikat oksigen serta mendistribusikannya ke semua jaringan tubuh. Dampak dari kurangnya oksigen pada jaringan otak serta otot dapat menimbulkan gejala seperti menurunnya konsentrasi dan menurunnya kebugaran untuk melaksanakan kegiatan (Bobak, 2018).

Penyebab anemia selama kehamilan khususnya di negara berkembang karena kekurangan asupan gizi, khususnya defisiensi zat besi, defisiensi folat, defisiensi vitamin lainnya yang dapat mengakibatkan kejadian anemia contohnya kekurangan vitamin A. Penyebab lain anemia yang paling sering di negara berkembang ialah infeksi oleh parasit, contohnya disentri yang disebabkan amuba, kecacingan, malaria, ketidaknormalan hemoglobin serta penyakit demam keong. Anemia dalam kehamilan dapat diartikan wanita sedang hamil mengalami kekurangan zat besi pada dalam darah. Selain itu, anemia dalam kehamilan dapat dikatakan juga sebagai suatu situasi dimana ibu memiliki hemoglobin (Hb) <11 gr% (Lewis, 2018).

2.1.2 Penyebab Umum

Terdapat banyak hal yang bisa mengakibatkan anemia, tetapi ada tiga hal utama dalam tubuh yang menjadi penyebab ialah (Smeltzer & Bare, 2017):

a. Berlebihnya sel darah merah yang dihancurkan

   Sumsum tulang akan menghasilkan sel-sel darah normal yang kemudian akan didistribusikan ke seluruh tubuh melalui darah. Sel-sel darah yang akan disekresi dalam darah juga dapat berupa sel darah muda. Biasanya, selama darah muda ini mudah terbelah menjadi beberapa bagian. Hal ini yang dapat menyebabkan anemia karena adanya peningkatan sel darah yang pecah dan rusak secara berlebihan (Smeltzer & Bare, 2017).

b. Kehilangan darah

   Salah satu penyebab anemia ialah kehilangan darah yang bisa disebabkan oleh pendarahan atau penyakit. Pendarahan disini dimaksudkan saat menstruasi dan persalinan yang memiliki kemungkinan untuk mengalami kehilangan darah. Penyakit yang dimaksud seperti malaria, kanker, colitis ulserativa, rheumatoid arthritis, borok lambung, dan lainnya. Contohnya adalah kanke ryang telah menjalar ke sumsum tulang/berasal dari sumsum tulang yang dapat mengakibatkan produksi sel darah merah dari sumsum tulang belum mencukupi kebutuhan tubuh sehingga terjadi anemia. Contoh lainnya ialah kemoterapi dapat mengakibatkan penurunan jumlah sel darah merah karena terjadi gangguan di sumsum tulang dan dapat menyebabkan anemia (Smeltzer & Bare, 2017).

c. Rendahnya sel darah merah yang diproduksi

Rendahnya sel darah merah yang diproduksi terjadi saat ada gangguan di daerah sumsum tulang atau tidak adanya bahan dasar untuk diproduksi. Hal ini diakibatkan oleh konsumsi obat-obatan, racun, alkohol, usaha menurunkan berat badandengan ketat, gagal ginjal, kelainan genetic (talasemia), serta masa kehamilan (Smeltzer & Bare, 2017).

2.1.3 Patofisiologis

Perubahan hematologik sehubungan dengan kehamilan adalah karena perubahan sirkulasi yang semakin naik terhadap plasenta dan pertumbuhan payudara.Volume plasma meningkat 45-65% dimulai pada trimester II kehamilan dan maksimum terjadi pada bulan ke-9. Selama kehamilan kebutuhan terhadap zat besi meningkat sekitar 800-1000 mg untuk mencukupi kebutuhan peningkatan sel darah merah. Sel darah merah membutuhkan 300-400 mg zat besi dan sampai puncak pada usia kehamilan 32 minggu, janin membutuhkan zat besi sekitar 100-200 mg. Absorbsi zat besi dan gangguan percernaan boleh menyebabkan seseorang mengalami anemia defisiensi besi (Brunner & Suddarth, 2016)

Walaupun zat besi di dalam tubuh mencukupi dan zat besi yang adekuat tetapi apabila pasien mengalami gangguan pencernaan maka zat besi tersebut tidak boleh diabsorbsi dan dipergunakan oleh tubuh. Berkembangnya anemia dapat melalui empat tingkatan yang berkaitan dengan ketidak normalan indikator hematologis tertentu. Tingkatan pertama disebut dengan kurang besi laten yaitu suatu keadaan dimana banyaknya

cadangan besi yang berkurang di bawah kadar normal namun besi di dalam sel darah merah dari jaringan tetap masih dalam kadar normal. Tingkatan kedua disebut anemia kurang besi dini yaitu penurunan besi cadangan terus berlangsung sampai atau hampir habis tetapi besi di dalam sel darah merah dan jaringan belum berkurang. Tingkatan ketiga disebut dengan anemia kurang besi lanjut yaitu besi di dalam sel darah sudah mengalami penurunan namun besi dan jaringan belum berkurang.Tingkatan keempat disebut dengan kurang besi dalam jaringan yaitu besi dalam jaringan sudah berkurang atau tidak ada sama sekali (Kumar *et al.*, 2015).

2.1.4 Diagnosis

Secara garis besar anemia dapat didiagnosis melalui pemeriksaan fisik, tes laboratorium, dan pemeriksaan lain (Barrett *et al.*, 2018):

a. Pemeriksaan fisik

Pemeriksaan fisik menjadi salah satu cara dalam mendiagnosis anemia seperti pertanyaan tentang sejarah keluarga, sejarah pribadi, obat, warna tinja, urin, dan pendarahan. Selain itu, pemeriksaan fisik dapat difokuskan untuk kondisi umum yaitu kelelahan, pucat, kulit kuning, mata kuning, *spenomegaly*, *hepatomegaly*, dan detak jantung.

b. Tes Laboratorium

Tes laboratorium yang terdiri dari:

1. Perhitungan darah umum

Digunakan untuk mengklasifikasi derajat kegawatan anemia, macam anemia, serta informasi terkait leukosit dan trombosit. Tes ini dapat

melihat kapasitas darah dengan satuan ukur yaitu jumlah sel/ millimeter kubik (mm3).

2. Tes hemoglobin pada feses

   Digunakan untuk mendeteksi pendarahan dari perut atau usus

3. Pemeriksaan darah tepi

   Digunakan untuk menentukan ukuran, bentuk, jumlah, dan warna dalam darah.

4. Pemeriksaan kadar besi, transferrin, ferritin, asam folat, vitamin B12, bilirubin, dan logam berat.

   Digunakan untuk mengevaluasi kadar zat tersebut di dalam tubuh jika mungkin menyebabkan anemia. Terkait dengan kadar logam berat, umumnya timbal merupakan salah satu indikator penyebab anemia pada anak-anak

5. Elektroforesis hemoglobin

   Digunakan untuk mengetahui apakah seseorang memiliki sejarah anemia berbentuk sel sabit atau talasemia dalam silsilah keluarga.

6. Jumlah retikulosit

   Digunakan untuk mengukur eritrosit yang telah dihasilkan dari sumsum tulang.

7. Uji kegunaan ginjal dan hati

   Digunakan agar mengetahui kerja ginjal serta hati, kemudian mengabarkan informasi jika terdapat disfungsi hati dan ginjal

c. Pemeriksaan lain

Pemeriksaan lain yang dapat dilakukan selain tes-tes diatas untuk mengidentifikasi penyebab anemia seperti pengukuran *hematokrit* (Hct) yang menunjukkan volume darah lengkap, *Mean Corpuscular Hemoglobin* (MCH) yang menunjukan kepadatan hemoglobin dalam satu sel eritrosit, dan *Mean Corpuscular Volume* (MCV) yang menunjukan pengukuran besarnya sel darah merah (Davidson *et al.*, 2012)

2.1.5 Derajad Keparahan

Klasifikasi anemia berdasarkan derajat keparahan sebagai berikut, yaitu (Tjokroprawiro, 2015):

a. Anemia ringan

Anemia ringan saat pemeriksaan kadar hemoglobin sebesar 10,0 gr/dl–10,9 gr/dl. Anemia ringan biasanya belum memiliki gejala atau tanda-tanda yang signifikan berupa keluhan lelah, lemah, dan kulit yang sedikit pucat (Tjokroprawiro, 2015)

b. Anemia sedang

Anemia sedang saat pemeriksaan kadar hemoglobin sebesar 7,0 gr/dl–9,9 gr/dl. Pada saat ini, anemia sudah semakin memburuk dengan gejala yang lebih berat seperti pingsan, pusing, rasa haus berlebih, berkeringan, meningkatnya denyut nadi, dan meningkatnya laju pernafasan (Tjokroprawiro, 2015).

c. Anemia berat

Anemia berat saat pemeriksaan kadar hemoglobin <7 gr/dl. Anemia berat memiliki gejala berat seperti kram pada kaki, sesak nafas, kerusakan bagian otak, serta jantung harus memompa lebih kencang agar darah kaya oksigen dapat disalurkan ke seluruh tubuh. Dalam fase ini, ibu hamil sudah harus mendapatkan transfusi darah(Tjokroprawiro, 2015).

2.1.6 Faktor Risiko Anemia pada Ibu Hamil

Faktor risiko kejadian anemia ibu hamil ialah sebagai berikut:

a. Usia ibu

Ibu hamil yang berada pada umur <20 tahun dan >35 tahun merupakan faktor risiko penyebab kejadian anemia. Hal ini dikarenakan saat umur <20 tahun dan >35 tahun, ibu berisiko untuk hamil. Sebab, kesehatan janin dan kesehatan ibu berada dalam risiko tinggi seperti dapat mengakibatkan pendarahan yang berujung pada anemia.

b. Pendidikan ibu

Adanya peningkatan pendidikan masyarakat membuat penerimaan informasi lebih simpel. Dengan mengetahui banyak informasi, maka masyarakat akan mengaplikasikan pengetahuannya dalam kehamilan untuk mencegah anemia

c. Jumlah paritas ibu

Jumlah paritas ibu dengan kejadian anemia dalamkehamilan dimana wanita hamil yang memiliki paritas tinggi beresiko 11 kali lebih tinggi untuk mengalami anemia. Wanita dengan riwayat paritas tinggi

(melahirkan ≥4 kali) lebih mudah merasakan komplikasi selama hamildandapat berdampak sampai akhir masa kehamilan.

d. Frekuensi kunjungan *Antenatal Care* (ANC) ibu

Salah satu upaya pencegahan agar memiliki kehamilan yang baik ialah melakukan kunjungan ANC seperti melakukan observasi fisik, distribusi suplemen, dan edukasi kesehatan kepada ibu hamil.Dengan melakukan kunjungan ANC, diharapkan dapat dengan lebih cepat mengetahui beberapa faktor risiko yang dapat timbul dalam kehamilan seperti anemia. Pelayanan ANC lengkap dalam kehamilan ialah paling sedikit 4 kali yang dibagi menjadi sekali pada trimester I, sekali pada trimester II, dan 2 kali pada trimester III. Sesuai pedoman, pelayanan ANC dikerjakan oleh tenaga kesehatan dan dicatatkan di dalam buku KIA (Kesehatan Ibu dan Anak)

e. Kepatuhan konsumsi tablet besi ibu

Kepatuhan konsumsi tablet besi dengan anemia dimana dengan meningkatnya kepatuhan dalam mengonsumsi tablet besi, maka akan menurunkan probabilitas kehamilan dengan anemia

f. Jarak kelahiran ibu

Jarak kelahiran dengan kejadian anemia pada wanita hamil dimana kehamilan dengan jarak kelahiran dengan risiko tinggi berisiko 15,5 kali lebih tinggi untuk mengalami anemia. Jarak kelahiran beresiko tinggi ialah jarak kelahiranyang sangat rapat yaitu <2 tahun. Hal ini dikarenakan sistem reproduksi ibu belum pulih layaknya keadaan awal sebelum hamil. Seorang ibu hendaknyamemilki jarak kelahiran diatas 2 tahun karena

kondisi yang belum pulih dapat mengakibatkan terjadinya penyulit dalam kehamilan (Rochjati, 2003).

g. Status gizi ibu

Untuk mengetahui status gizi dapat menggunakan indikator pengukuran Lingkar Lengan Atas (LILA) dimana jika ukuran LILA < 23,5 cm, maka berisiko Kurang Energi Kronis (KEK). Hubungan status gizi ibu hamil berisiko KEK dengan anemia. Wanita hamil menderita KEK berisiko 3 kali lebih tinggi untuk menderita anemia daripada wanita hamiltidak menderita KEK

h. Konsumsi vitamin ibu

Kurangnya vitamin dalam tubuh khususnya vitamin asam folat dan vitamin B12. Asam folat merupakan vitamin B yang bertugas menghindari bayi dari kecacatan berat dan mempengaruhi tulang belakang. Disampingitu, asam folat juga dipercaya dapat mengatasi masalah kesehatan tertentu

2.1.7 Upaya Pencegahan

Upaya yang bisa dilakukan untuk mencegah anemia dalam kehamilan, sebagai berikut: Pencegahan primer. Upaya preventif kejadian anemia dalam kehamilan bisa berupa promosi kesehatan dan perlindungan spesifik, seperti (Robert *et al.*, 2016):

a. Promosi Kesehatan

Promosi kesehatan dalam upaya pencegahan kejadian anemia dilakukan dengan memberikan edukasi tentang konsumsi makanan yang sehat dan bernutrisi sesuai dengan kebutuhan masing-masing

individu. Promosi kesehatan juga memberikan pendidikan di tingkat rumah tangga dalam hal menyiapkan asupan yang mempercepat absorbsi zat besi seperti jenis asupan makanan yang terdiri dari asam askorbat serta vitamin C (Cunningham *et al.*, 2014)

b. Meningkatkan asupan makanan sumber zat besi

Pemenuhan nutrisi dengan lengkap ialah pencegahan yang tepat untuk menghalangi kejadian anemia dalam kehamilan. Konsumsi asupan yangbanyak mengandung zat besi contohnya sayur berdaun hijau, daging berwarna merah, sereal, kacang tanah, serta telur. Makanan ini dapat membuat jumlah besi yang dibutuhkan tubuh tersedia sehingga dapat berproses dengan optimal (Fatkhiyah, 2016).

c. Penambahan zat besi kedalam pangan

Adanya penambahan minimal 1 zat gizi yang dimasukkan ke bahanmakanan agar kadar gizibahan makanan meningkat. Adapun contoh bahan pangan di Indonesia yang telah dilakukan penambahan yaitu tepung terigu, minyak goreng, beras, mentega, serta makanan ringan. Selain itu, ada juga penambahan zat besi, vitamin, serta mineral pada bahan pangan yang tersedia dalam skala rumahan yang menggunakan bubuk tabur gizi dan biasa disebut dengan *Multiple Micronutrient Powder* (Cunningham *et al.*, 2014)

d. Suplementasi zat besi

Saat tidak terpenuhinya kebutuhan akan zat besi yang berasal dari makanan,maka dibutuhkan tambahan zat besi. Pendistribusian zat besi tambahan secara berkaladan dengan waktu yang teratur akan dengan

cepat menambah jumlah hemoglobin serta untuk menambah penyimpanan zat besi dalam tubuh. Upaya yang telah dilaksanakan oleh pemerintah Indonesia untuk mencukupi kebutuhan zat besi ialah dengan pemberian Tablet Tambah Darah (TTD) untuk remaja putri serta WUS (Lowdermilk *et al.*, 2016)

Pendistribusian TTD dengan cara yang sesuai dapat menambah ketersediaan zat besi dalam tubuh serta mencegah timbulnya anemia. Skrining Skrining atau deteksi dini anemia perlu dilakukan pada kelompok risiko tinggi seperti remaja putri, ibu hamil, ibu menyusui, dan wanita dewasa. Skrining sebaiknya dilakukan satu tahun sekali untuk wanita dewasa dan dilakukan saat kunjungan ANC pertama untuk ibu hamil. Deteksi dini anemia diperlukan untuk mengetahui lebih awal status anemia seseorang sehingga dapat diupayakan tindakan pencegahan maupun Tindakan pengobatan Skrining anemia pada ibu hamil telah dilaksanakan di puskesmas yang telah memiliki program pemeriksaan kadar Hb darah untuk mengevaluasi wanita hamil dengan status anemia. Selain wanita hamil, masyarakat juga bisa memanfaatkan program tersebut untuk mengetahui status anemia masing- masing Pemeriksaan darah Anemia biasanya terdeteksi dengan menghitung sel darah lengkap yang digunakan untuk memeriksa berbagai jenis sel dalam darah. Komponen tes yang mirip dengan pemeriksaan anemia ialah tes hitung eritrosit, hematokrit, dan kadar kemoglobin. Jika kadar hemoglobin rendah biasanya volume eritrosit dan hematokrit rendah juga sehingga dapat terindikasi anemia (Lewis, 2018).

Suplementasi zat besi Dalam pengobatan anemia, zat besi yang digunakan biasanya adalah ferrous sulfat karena penyerapan garamnya lebih tinggi daripada garam ferolainnya. Dosis zat besi yang digunakan ialah sebesar 200 mg per hari atau2-3 mg/kg dengan penyerapan sebesar 18%. Hal ini menyebabkan waktu yang dibutuhkan untuk mencapai nilai Hb normal sekitar 1 hingga 2 bulan dan waktu yang dibutuhkan untuk mengembalikan simpanan zat besi dalam tubuh sekitar lebih dari 2 bulan (Lewis, 2018)

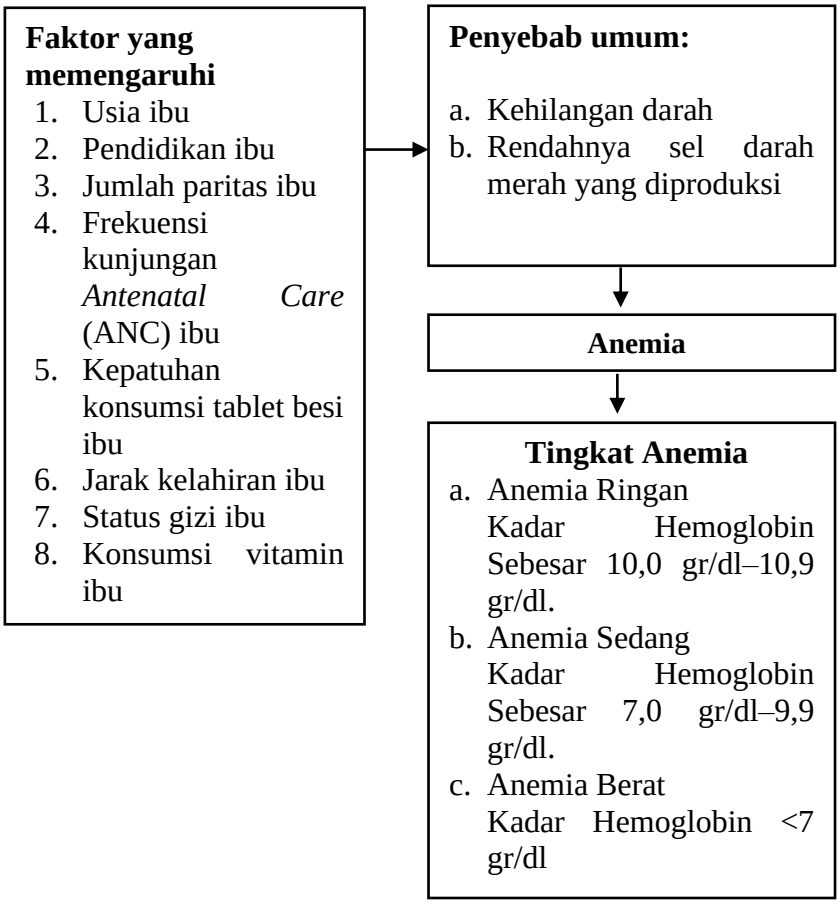
2.1.8 Komplikasi

Komplikasi Anemia pada wanita hamil sangat berkaitan dengan angka kematian ibu. Anemia pada wanita hamil patut berjaga-jaga. Komplikasi yang dialami wanita yang sedang hamil boleh berakibat fatal, baik pada ibu maupun janinnya. Anemia pada wanita hamil boleh mengakibatkan pertumbuhan bayi yang terhambat, kelahiran bayi secara prematur, bayi menjadi lebih senang terseranginfeksi sewaktu lahir dan bayi boleh mati dalam kandungan jika anemianya parah (Smith, 2019).

2.1.9 Prognosis

Prognosis anemia kekurangan besi dalam kehamilan umumnya baik bagi ibu dan anak jika persalian berlaku seperti normal tanpa banyak perdarahan atau komplikasi lain. Morbiditas dan mortalitas wanita hamil meningkat dalam anemia berat. Penampakan anemia infantum pada beberapa bulan kemudian berlaku dengan cadangan besi kurang, walaupun bayi yang dilahirkan dari ibu yang menderita anemia defisiensi besi tidak mempaparkan haemoglobin (Hb) yang rendah (Saifuddin, 2015).

2.1.10 Kerangka Teoritis Kejadian Anemia pada Ibu Hamil



Bagan 2.1 Kerangka Teoritis Anemia
Sumber: (Lewis, 2018); (Smeltzer & Bare, 2017); (Brunner & Suddarth, 2016); (Barrett *et al.*, 2018); (Robert *et al.*, 2016)

2.2. Konsep Kejadian Berat Badan Lahir Rendah

2.2.1 Definisi

Berat badan merupakan salah satu indicator kesehatan bayi baru lahir. Rerata berat bayi normal (usia gestasi 37-41 minggu) adalah 3200 gram (7lbs) secara umum, bayi berat lahir rendah dan bayi berat lahir berlebih (≥ 3800 gram) lebih besar risikonya untuk mengalami masalah. Masa gestasi juga merupakan indikasi kesejahteraan bayi baru lahir karena semakin cukup masa gestasi semakin baik kesejahteraan bayi. Konsep bayi berat

lahir rendah tidak sinonim dengan prematuritas telah diterima secara luas pada akhir tahun 1960 an. Tidak semua Berat Badan Lahir Rendah yang memiliki berat lahir kurang dari 2500 gram lahir Bayi Kurang Bulan (BKB). Demikian pula tidak semua Berat Badan Lahir Rendah dengan berat lahir lebih dari 2500 gram lahir aterm (Paul & Bagga, 2018).

Bayi dengan berat badan lahir rendah adalah neonatus yang dilahirkan kecil. Berat badan lahir rendah mengacu pada kelahiran dengan berat 500-2500 gram; berat badan lahir sangat rendah mengacu untuk kelahiran dengan berat 500-1500 gram; berat badan lahir ekstrem rendah mengacu untuk kelahiran dengan berat 500-1000 gram. Bayi berat lahir rendah berarti bayi berbobot 2,5 kg atau kurang saat lahir. Penyebabnya bisa berupa persalinan prematur atau kegagalan untuk berkembang. Definisi berat badan lahir rendah adalah neonatus yang dilahirkan terlalu kecil, kelahiran kurang bulan atau prematur adalah istilah yang digunakan untuk mendefinisikan neonatus yang dilahirkan terlalu dini. Berdasarkan usia kehamilan bayi baru lahir mungkin kurang bulan, aterm, atau lebih bulan (Marcdante & Kliegman, 2019).

Bayi berat lahir (BBL) adalah berat badan bayi yang di timbang dalam waktu 1 jam pertama setelah lahir. Hubungan antara waktu kelahiran dengan umur kehamilan dan kelahiran bayi dapat dikelompokan menjadi: bayi kurang bulan (prematur), yaitu bayi yang dilahirkan dengan masa gestasi (kehamilan) <37 minggu (<259 hari). Bayi cukup bulan, bayi yang dilahirkan dengan masa gestasi antara 37-42 minggu (259 - 293 hari); dan bayi lebih bulan, bayi yang dilahirkan dengan masa gestasi > 42 minggu

(>294 hari). Berkaitan dengan berat badan bayi lahir, bayi dapat dikelompokkan berdasarkan berat lahirnya yaitu: bayi berat lahir rendah (BBLR), yaitu berat lahir <2500 gram, bayi berat lahir sedang, yaitu berat lahir antara 2500-3999 gram, dan berat badan lebih, yaitu berat lahir ≥4000 gram (Kliegman, 2016)

2.2.2 Klasifikasi Bayi Berat Lahir Rendah

Pada Kongres *Europan Perinatal Medicine* ke II di London (1970) diusulkan definisi untuk mendapatkan keseragaman yaitu bayi kurang bulan (bayi dengan masa kehamilan kurang dari 37 minggu), bayi cukup bulan (bayi dengan masa kehamilan 37-42 minggu), bayi lebih bulan (bayi dengan masa kehamilan 42 minggu atau lebih (Cowen & Bindler, 2018).

Klasifikasi bayi menurut ukuran yaitu bayi berat lahir rendah (BBLR, bayi yang berat badannya <2500 gram tanpa memperhatikan usia gestasi), bayi berat lahir sangat rendah (BBLSR, bayi yang berat badannya <1500 gram), bayi berat lahir ekstrem rendah (BBLER, bayi yang berat badannya <1000 gram), bayi berat badan lahir moderat (BBLM, bayi yang berat badannya 1501 gram sampai 2500 gram), bayi berat badan sesuai usia gestasinya (bayi yang berat badannya antara persentil ke 10 sampai ke 90 padakurva pertumbuhan intrauterin), bayi berat badan kecil untuk usianya atau kecil untuk usia gestasinya, retardasi pertumbuhan intrauterin (IUGR), dan bayi besar untuk usia gestasinya (bayi dengan berat badan lairnya di atas persentil ke 90 pada kurva pertumbuhan intrauterin) (Wong, 2012).

Secara umum, gambaran klinis dari bayi BBLR adalah berat kurang dari 2500 gram, panjang kurang dari 45 cm, lingkar dada kurang dari 30

cm,lingkar kepala kurang dari 3 cm, umur kehamilan kurang dari 37 minggu, kepala lebih besar, kulit transparan, tipis, rambut lanugo banyak; pernafasan tidak teratur sehingga dapat terjadi apnea paha abduksi, sendi lutut/kaki fleksi-lurus, kepala tidak mampu tegak, pernafasan 40-50 kali/menit,nadi 100-140 kali/menit. Pada setelah bayi lahir dijumpai bayi dengan retardasi pertumbuhan intrauterin, secara klinik tampak seperti bayi yang kelaparan, bayi prematur, jaringan lemak bawah kulit sedikit, menangis lemah, vernik caseosa ada, kulit tipis, kulit merah dan transparan (Duncan & Baumle, 2011).

2.2.3 Etiologi Berat Badan Lahir Rendah

Etiologi dari BBLR dapat dilihat dari faktor maternal dan faktor fetus. Etiologi dari maternal dapat dibagi menjadi dua yaitu prematur dan IUGR (*Intrauterine Growth Restriction*). Yang termasuk prematur dari faktor maternal yaitu Preeklamsia, penyakit kronis, infeksi, penggunaan obat, KPD, polihidramnion, iatrogenic, disfungsi plasenta, plasenta previa, solusio plasenta, inkompeten serviks, atau malformasi uterin. Sedangkan yang termasuk IUGR (*Intrauterine Growth Restriction*) dari faktor maternal yaitu Anemia, hipertensi, penyakit ginjal, penyakit kronis, atau pecandu alcohol atau narkortika. Selain etiologi dari faktor maternal juga ada etiologi dari faktor fetus. Yang termasuk prematur dari faktor fetus yaitu Gestasi multipel atau malformasi. Sedangkan, yang termasuk IUGR (*Intrauterine Growth Restriction*) dari faktor fetus yaitu Gangguan kromosom, infeksi intrauterin (TORCH), kongenital anomali, atau gestasi multipel (Fauziah & Sutejo, 2017).

2.2.4 Patofosiologi Berat Badan Lahir Rendah

Bayi dengan BBLR secara umum berhubungan dengan umur kehamilan ibu yang belum mencapai 9 bulan atau umur janin belum cukup untuk dilahirkan (prematur) di samping juga dikarenakan faktor belum matang (dismaturitas). Hal tersebut berarti bahwa bayi lahir cukup bulan (umur kehamilan ibu yaitu 38 minggu), tapi BB lahir bayi lebih kecil dari umur kehamilannya,dalam kata lain berat badan bayi tidak sampai 2.500 gram (Saadoon, 2018).

Gangguan tersebut terjadi oleh karena terdapatnya masalah pertumbuhan dan perkembangan bayi pada saat bayi dalam rahim yang dikarenakan penyakit ibu pada saat hamil seperti terdapatnya masalah gangguan pada plasenta, terjadinya infeksi, ibu hamil mengalami hipertensi dan kondisi lain yang mengakibatkan berkurangnya suplai nutrisi ke janin.Seorang ibu hamil memerlukan gizi yang baik supaya pertumbuhan dan perkembangan janin dalam rahim tidak mengalami retardasi atau hambatan, dan seterusnya ibu akan melahirkan bayi dengan BB yang normal pada saat dilahirkan. Keadaan kesehatan yang adekuat, sistem reproduksi ibu hamil yang normal, ibu hamil tidak menderita suatu penyakit atau sedang sakit saat hamil, dan tidak ada terjadi masalah gizi pada waktu sebelum hamil ataupun pada waktu ibu sedang masa kehamilan, ibu akan melahirkan bayi dengan ukuran BB lebih besar dan bayi juga akan tumbuh dan berkembang menjadi lebih sehat dari pada ibu hamil yang mempunyai keadaan sebaliknya (Paul & Bagga, 2018).

Ibu yang hamil dengan keadaan gizi kronis (KEK) sering kali mempunyai bayi dengan berat badan lahir rendah pada saat dilahirkan, vitalitas ibu hamil yang rendah dan kematian ibu dan bayi yang masih tinggi, terlebih jika ibu pada saat kehamilan mengalami kurang darah atau anemia. Pada saat hamil, ibu biasanya juga mengalami penyusutan zat besi dalam tubuhnya sehingga janin hanya mendapatkan sedikit zat besi yang diperlukan bayi untuk metabolisme besi dalam tubuh janin secara normal. Kekurangan zat besi (Fe) yang dialami oleh seorang ibu pada saat hamil dapat mengakibatkan hambatan pada pertumbuhan dan perkembangan janin dalam rahim baik sel otak maupun sel tubuh (Marcdante & Kliegman, 2019b)

Anemia gizi yang dialami oleh ibu pada masa kehamilan dapat menyebabkan kematian janin di dalam kandungan (KJDK), keguguran atau abortus, bayi mengalami kelainan kongenital atau cacat bawaan, dan bayi berpeluang untuk mengalami BBLR. Hal ini menyebabkan angka kesakitan danangka kematian ibu serta kematian bayi pada masa perinatal secara bermakna lebih meningkat, sehingga probabilitas ibu untuk melahirkan bayi premature dengan kondisi bayi BBLR menjadi lebih besar pula (Kyle & Carman, 2018).

2.2.5 Faktor Yang Memengaruhi Berat Badan Lahir Rendah

Sulit untuk menentukan secara pasti penyebab BBLR, namun ada beberapa faktor risiko yang erat hubungannya dengan kejadian BBLR. Adapun faktor-faktor risiko tersebut adalah:

a. Penyakit yang diderita Ibu

Penyakit kronik adalah penyakit yang sangat lama terjadi dan biasanya kejadiannya bisa penyakit berat yang dialami ibu pada saat ibu hamil ataupun pada saat melahirkan. Penyakit kronik pada ibu yang dapat menyebabkan terjadinya BBLR adalah hipertensi kronik, Preeklampsia, diabetes melitus dan jantung . Adanya komplkasi - komplikasi kehamilan, seperti anemia, perdarahan antepartum, preekelamsi berat, eklamsia, infeksi kandung kemih. Menderita penyakit seperti malaria, infeksi menular seksual, hipertensi atau darah tinggi, HIV/AIDS, TORCH, penyakit jantung. Salah guna obat, merokok, konsumsi alkohol (Saifuddin, 2015)

b. Sosial Ekonomi Keluarga

Kejadian yang paling sering terjadi yaitu pada keadaan sosial ekonomi yang kurang. Karena pengawasan dan perawatan kehamilan yang sangat kurang. Aktivitas fisik yang berlebihan dapat juga mempengaruhi keadaan bayi. diusahakan apabila sedang hamil tidak melakukan aktivitas yang ekstrim. Perkawinan yang tidak sah juga dapat mempengaruhi fisik serta mental (Triana *et al.*, 2015)

c. Faktor Janin dan Plasenta

Faktor janin juga bisa menjadi salah satu faktor bayi BBLR disebabkan oleh kelainan kromosom, infeksi janin kronik (inklusi sitomegali, rubella bawaan, gawat janin, dan kehamilan kembar). Faktor plasenta yang dapat menyebabkan bayi BBLR juga dapat menjadi salah satu faktor. Kelainan plasenta dapat disebabkan oleh hidramnion, plasenta previa, solutio plasenta, sindrom tranfusi bayi kembar (sindrom parabiotik), ketuban pecah dini (Lowdermilk et al., 2016).

d. Umur saat Melahirkan

Secara umum ibu yang umurnya lebih muda akan mempunyai bayi yang lebih kecil dibandingkan dengan ibu yang lebih tua. Faktor usia pada wanita hamil di negara berkembang perlu diperhatikan, hal ini dikarenakan perkawinan pada masyarakat di pedesaan sering terjadi pada usia muda, yaitu sekitar usia menarche. Di usia ini resiko untuk melahirkan BBLR sekitar 2 kali lipat dari yang hamil pada usia 2 tahun setelah *menarche* (Damayanti *et al.,* 2017). Disisi lain pada umur yang tua akan banyak merugikan perkembangan janin selama periode dalam kandungan, hal ini disebabkan oleh karena penu runan fungsi fisiologik dan reproduksinya. Kejadian BBLR berdasarkan umur ibu paling tinggi terjadi pada ibu yang melahirkan di bawah usia 20 tahun (Milah, 2019)

e. Usia Kehamilan

Saat Melahirkan Kehamilan yang kurang dari 37 minggu merupakan penyebab utama terjadinya BBLR. Semakin pendek usia keham ilan maka pertumbuhan janin semakin belum sempurna, baik itu organ reproduksi

dan organ pernafasan oleh karena itu ia mengalami kesulitan untuk hidup diluar uterus ibunya (Damayanti *et al.,* 2017)

f. Tingkat Pendidikan

Tingkat pendidikan merupakan faktor yang bepengaruh secara tidak langsung terhadap kejadian BBLR namun bisa dijelaskan secara sederhana bahwa semakin tinggi tingkat pendidikan seseorang maka semakin banyak pula informasi yang bisa dia dapatkan mengenai BBLR sehingga secara otomatis semakin banyak pula pengetahuannya mengenai langkah-langkah dalam pencegahan BBLR. Secara konsisten penelitian menunjukan bahwa tingkat pendidikan yang dimiliki ibu mempunyai pengaruh kuat pada perilaku reproduksi, kelahiran, kematian anak dan bayi, kesakitan, dan sikap serta kesadaran atas kesehatan keluarga (Cunningham et al., 2014)

Latar belakang pendidikan ibu mempengaruhi sikapnya dalam memilih pelayanan kesehatan dan pola konsumsi makan yang berhu bungan juga dengan peningkatan berat badan ibu semasa hamil yang pada saatnya akan mempengaruhi kejadian BBLR. Ibu yang berpendidi kan rendah sulit untuk menerima inovasi dan sebagian besar kurang mengetahui pentingnya perawatan pra kelahiran. Disamping itu juga mempunyai keterbatasan mendapatkan pelayanan antenatal yang adekuat, keterbatasan mengkonsumsi makanan yang bergizi selama hamil. Kesemuanya iniakan mengganggu kesehatan ibu dan janin, bahkan sering mengalami keguguran atau lahir mati (Cunningham et al., 2014)

g. Jenis Kelamin Bayi

Bayi laki-laki saat lahir memiliki rata-rata berat lahir 150 gram lebih berat daripada bayi perempuan, perb edaan ini paling nyata pada umur kehamilan 28 minggu. Diduga hal ini akibat stimulasi hormone androgenik atau karena kromosom Y memuat materi genetik yang dapat meningkatkan pertumbuhan janin laki-laki. Pada umur kehamilan yang sama, janin dengan jenis kelamin laki-laki lebih berat 5% dan lebih panjang 1% dibanding dengan janin jenis kelamin perempuan dan yang mempengaruhi keadaan ini adalah hormon seks laki-laki dan kromosom Y yang dimiliki laki-laki. Hal ini mulai tampak pada kehamilan 24 minggu (Rahmati *et al.*, 2017).

2.2.6 Masalah Kesehatan pada Berat Badan Lahir Rendah

Ketidakmatangan sistem organ pada bayi menjadi masalah yang dapat terjadi pada bayi dengan berat badan lahir rendah (BBLR) terutama pada bayi yang dilahirkan secara prematur. Masalah yang sering terjadi pada BBLR yaitu susunan saraf pusat, hematologi, gangguan pada sistem pernafasan, gastrointerstinal, ginjal, kardiovaskular, termoregulasi (Marcdante & Kliegman, 2019b).

a. Sistem Pernafasan

Bayi dengan BBLR umumnya mengalami kesulitan untuk bernafas segera setelah lahir oleh karena jumlah alveoli yang berfungsi masih sedikit, kekurangan surfaktan (zat di dalam paru dan yang diproduksi dalam paru serta melapisi bagian alveoli, sehingga alveoli tidak kolaps pada saat ekspirasi). Luman sistem pernafasan yang kecil, kolaps atau

obstruksi jalan nafas, insufisiensi klasifikasi dari tulang thorax, dan pembuluh darah paru yang imatur. Kondisi inilah yang mengganggu usaha bayi untuk bernafas dan sering mengakibatkan gawat nafas, distress pernafasan (Marcdante & Kliegman, 2019b).

b. Sistem Neurologi (Susunan Saraf Pusat)

Bayi lahir dengan berat badan lahir rendah umumnya mudah sekali terjadi trauma susunan saraf pusat. Kondisi ini disebabkan antara lain: perdarahan intracranial karena pembuluh darah yang rapuh, trauma lahir, perubahan proses koagulasi, hipoksia dan hipoglikemia. Sementara itu asfiksia berat yang terjadi pada BBLR juga sangat berpengaruh pada sistem Susunan Saraf Pusat (SSP), yang diakibatkan karena kekurangan oksigen dan kekurangan perfusi (Marcdante & Kligman, 2014).

c. Sistem Kardio vaskuler

Gangguan atau kelainan janin paling sering dialami bayi dengan BBLR yaitu paten ductus arteriosus, yang merupakan dampak dari intrauterine kehidupan ekstrauterine seperti terlambatnya penutupan *ductus arteriosus* (Marcdante & Kligman, 2014)

d. Sistem Gastrointestinal

Saluran pencernaan bayi dengan BBLR belum berfungsi secara optimal seperti yang terjadi pada bayi yang cukup bulan. kondisi ini dikarenakan tidak adanya kemampuan bayi untuk mengisap dan menelan sampai usia gestasi 33 sampai dengan 34 minggu sehingga mengakibatkan kurangnya cadangan gizi seperti kurang dapat

menyerap atau menghisap lemak dan juga kemampuan untuk mencerna protein (Cowen & Bindler, 2018).

e. Sistem Termoregulasi

Bayi dengan BBLR sering mengalami temperatur yang tidak stabil, yang disebabkan antara lain: Kehilangan panas karena perbandingan luas permukaan kulit dengan berat badan lebih besar (permukaan tubuh bayi relatif luas). Kurangnya lemak subkutan (brown fat / lemak cokelat). Jaringan lemak di bawah kulit lebih sedikit. Tidak adanya refleks kontrol dari pembuluh darah kapiler kulit (Marcdante & Kliegman, 2019)

f. Sistem Hematologi

Bayi dengan BBLR lebih cenderung mengalami masalah hematologi bila dibandingkan dengan bayi yang cukup bulan. Penyebabnya antara lain adalah Usia sel darah merahnya lebih pendek. Pembuluh darah kapilernya mudah rapuh. Hemolisis dan berkurangnya darah akibat dari pemeriksaan laboratorium yang sering (Ball et al., 2014).

g. Sistem Imunologi

Bayi dengan BBLR mempunyai sistem kekebalan tubuh yang terbatas, sering kali memungkinkan bayi tersebut lebih rentan terhadap infeksi (Ball et al., 2014).

h. Sistem Perkemihan

Sistem perkemihan pada bayi dengan BBLR juga mempunyai masalah. Belum matangnya ginjal bayi tersebut sehingga tidak memiliki kemampuan untukmengelola elektrolit, air, asam/basa, bayi

juga tidak memiliki kemampuan untuk mengeluarkan hasil metabolisme dan obat-obatan secara memadai serta tidak memiliki kemampuan untuk membuat pekat urin (Ball et al., 2014).

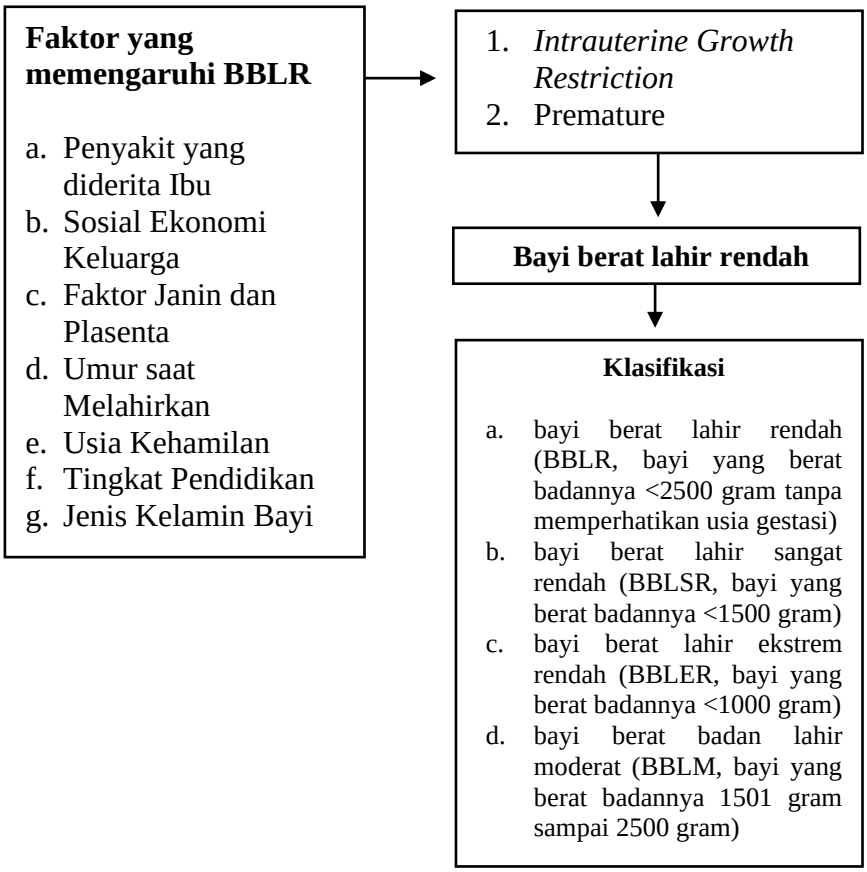
i. Sistem Integumen

Struktur kulit bayi dengan BBLR yang transparan dan sangat tipismenyebabkan terjadi gangguan integritas kulit dengan mudah (Ball et al., 2014).

j. Sistem Penglihatan

Bayi dengan BBLR dapat mengalami Kejadian *retinopathy of prematurity* (RoP) dapat dialami oleh bayi dengan BBLR yang diakibatkan ketidakmatangan organ retina (Nelson & Olitsky, 2015).

2.2.7 Kerangka Teoritis Kejadian Berat Badan Lahir Rendah



Bagan 2.2 Kerangka Teoritis Kejadian Bayi Berat Lahir Rendah (BBLR)
Sumber: (Wong, 2012); (Cowen & Bindler, 2018);
(Duncan & Baumle, 2011); (Fauziah & Sutejo, 2017);
(Saadoon, 2018).

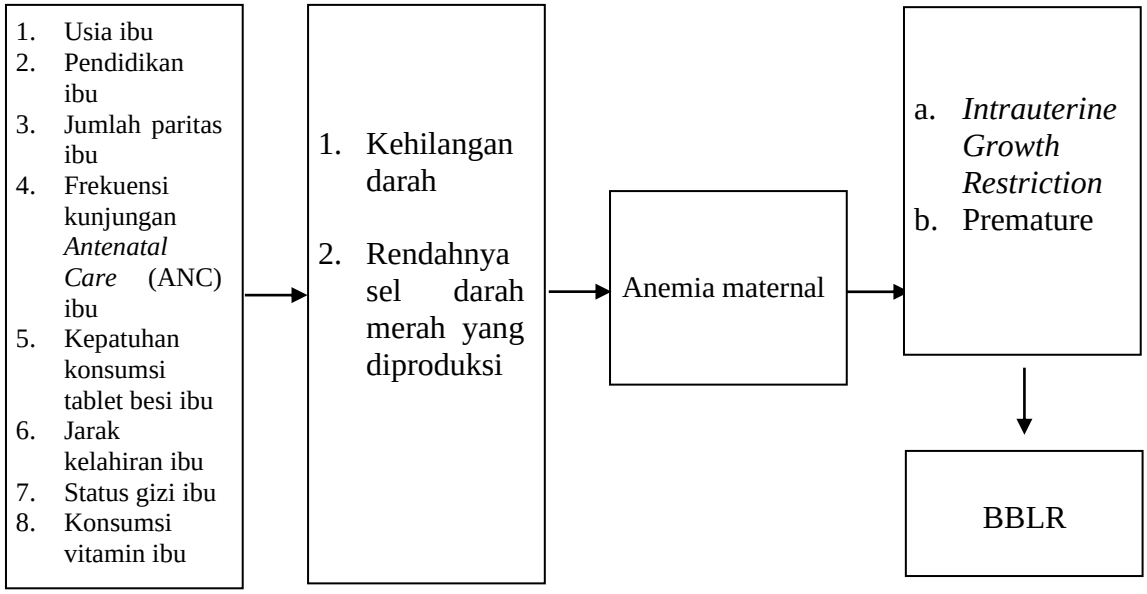
2.3 Konsep Hubungan Anemia dengan Kejadian Berat Badan Lahir Rendah

Anemia ibu mempengaruhi janin untuk pembatasan pertumbuhan intrauterin dan akibatnya dapat mempengaruhi berat badan lahir. Secara fisiologis, dimulai pada pertengahan trimester kedua kehamilan, wanita menghasilkan rata-rata 30 sampai 40 ml plasma per kilogram, sesuai dengan hipervolemia. Namun, ketika jumlah sel hematologi tidak meningkat secara paralel dengan proses ini, terjadi hemodilusi, dan anemia ibu dapat berkembang. Dengan demikian, kadar hemoglobin yang rendah dapat

merangsang perubahan angiogenesis plasenta dan mendukung hipoksia janin (White et al., 2011).

Menurut teori ini, pengurangan nutrisi dan oksigen ke janin karena defisit transportasi plasenta dapat terjadi akibat penipisan hemoglobin. Kerangka potensial restriksi pertumbuhan uterus dimulai dengan penurunan perfusi darah di uterus, peningkatan resistensi vaskular dan restriksi pertumbuhan permukaan trofoblas, yang bertanggung jawab untuk mengeluarkan darah arteri ibu ke dalam plasenta. Peristiwa ini dapat mengakibatkan pembatasan pertukaran gas dalam kompleks ibu-janin dan, akibatnya, berat lahir rendah/tidak mencukupi. Oleh karena itu, jika terjadi berat badan lahir rendah, pemantauan hemoglobin sejak antenatal dan konsumsi suplemen harus dipantau secara cermat (Silwal, 2020).

2.4 Kerangka Teori Hubungan Anemia pada Ibu Hamil dengan Kejadian Berat Badan Lahir Rendah



Bagan 2.1 Kerangka Teori Hubungan Antara Anemia Pada Ibu Hamil Dengan Kejadian Berat Badan Lahir Rendah.

BAB 3

METODE PENELITIAN

3.1 Desain Penelitian

Sugiyono (2017) menjelaskan bahwa desain penelitian adalah strategi yang dipilih oleh peneliti untuk mengintegrasikan secara menyeluruh komponen riset dengan cara logis dan sistematis untuk membahas dan menganalisis apa yang menjadi fokus penelitian. Penelitian ini menggunakan desain *literature review.* Nursalam (2020) menjelaskan bahwa *Literature review* adalah analisis terintegrasi tulisan ilmiah yang terkait langsung dengan pertanyaan penelitian. *Literature review* dapat menjelaskan latar belakang penelitian tentang suatu topik, menunjukkan mengapa suatu topik penting untuk diteliti, menemukan hubungan antara studi/ide penelitian, mengidentifikasi tema, konsep, dan peneliti utama pada suatu topik, identifikasi kesenjangan utama dan membahas pertanyaan penelitian lebih lanjut berdasarkan studi sebelumnya. Studi literatur pada penelitian ini bertujuan untuk mengetahui hubungan antara anemia pada ibu hamil dengan kejadian berat badan lahir rendah.

3.2 Strategi Pencarian Literatur

3.2.1 Protokol dan Registrasi

Studi ini merupakan kajian literatur (*literature review, literature research*) atau penelitian kepustakaan (*library research*) yaitu serangkaian penelitian yang berkenaan dengan metode pengumpulan data pustaka, atau

penelitian yang obyek penelitiannya digali melalui beragam informasi kepustakaan (buku, ensiklopedi, jurnal ilmiah, koran, majalah, dan dokumen). Studi ini berisi rangkuman menyeluruh dalam bentuk *literature review* mengenai hubungan anemia pada ibu hamil dengan kejadian berat badan lahir rendah. Metode registrasi dalam pencarian literatur meliputi *framework* yang digunakan, kata kunci, database atau *search engine*

3.2.2 Database Pencarian

Literature review ini merupakan kajian dari beberapa hasil studi penelitian yang ditentukan berdasarkan tema penelitian. Tema utama pada penelitian ini adalah terkait dengan anemia pada ibu hamil dan kejadian berat badan lahir rendah. Pencarian literatur dilakukan pada 1 - 29 April 2022. Data yang digunakan dalam penelitian ini adalah data sekunder yang diperoleh bukan dari pengamatan langsung, akan tetapi diperoleh dari hasil penelitian yang telah dilakukan oleh peneliti- peneliti terdahulu. Sumber data sekunder yang didapatkan berupa artikel dari jurnal ilmiah yang bereputasi baik sesuai dengan tema yang ditentukan. Pencarian literatur dalam *literature review* ini menggunakan *database* yaitu *Google Scholar, Pubmed, Elsevier*.

3.2.3 Kata Kunci

Pencarian artikel atau jurnal menggunakan *keyword* dan *boolean operator* (dan, dan atau, *and, or, and not*) yang digunakan untuk memperluas atau menspesifikkan pencarian, sehingga mempermudah dalam penentuan artikel atau jurnal yang digunakan sebagai berikut:

Tabel 3.1 Kata Kunci Pencarian

Anemia pada ibu hamil	**Berat badan lahir rendah**
Atau	Atau
Anemia kehamilan	BBLR
OR	*OR*
Maternal anemia	*Insufficient weight at birth*
Anemia during pregnancy	*Insufficient weight at birth*

3.3 Kriteria Inklusi dan Eksklusi

3.3.1 Seleksi Studi dan Penilaian Kualitas

Setelah dilakukan penetapan topik *review* maka seluruh kata kunci dimasukkan dalam database yaitu *google scholar, PubMed, Elsevier* setelah itu dilakukan pembatasan pencarian dengan membatasi tahun yaitu artikel bertahun 2017-2022. Setelah mendapatkan artikel sesuai topik dilakukan identifikasi abstrak dan selanjutnya di telaah naskah lengkapnya (*fulltext*) selanjutnya dilakukan matrik sebagai bagian untuk melakukan analisis. Setelah dilakukan matrix dari artikel maka dilakukan sintesis berupa menyusun hasil matrix dalam bentuk narartif.

Strategi yang digunakan untuk mencari artikel menggunakan PEOS *framework* yaitu:

a. *Population/problem*

   Populasi atau masalah yang akan di analisis. Pada *literature review* ini masalah yang diangkat atau menjadi topik utama adalah kejadian berat badan lahir rendah

b. *Exposure*

   Merupakan variabel yang diduga sebagai variabel penyebab atau variabel pajanan terhadap variabel *out come*. Pada *literature review* ini variabel *exposure* adalah anemia pada ibu hamil

c. *Outcome*

   Hasil atau luaran yang diperolah pada penelitian. Pada *literature review* ini *outcome* artikel dengan hasil analisis adanya hubungan antara anemia pada ibu hamil dengan kejadian berat badan lahir rendah

d. *Study design*

   Desain penelitian yang digunakan oleh jurnal yang akan di *review*. Desain dari *literature review* ini seluruhnya berjenis kuantitatif.

Artikel yang digunakan pada penelitian ini di screening melalui PEOS *framework* dengan kriteria sebagai berikut:

Tabel 3.2 Tabel PEOS

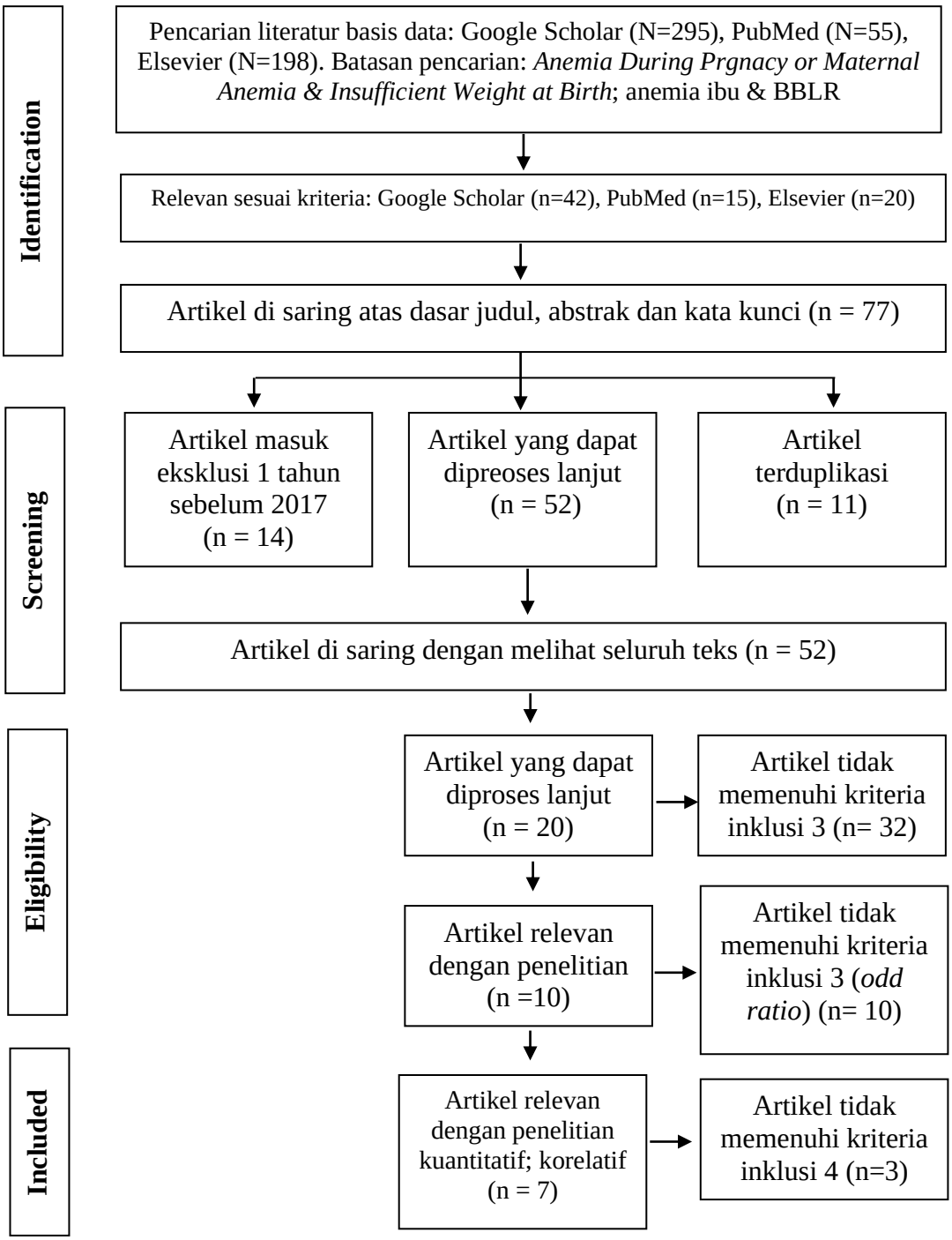
Kriteria	Inklusi	Eksklusi
Population/ Problem	Kejadian berat badan lahir rendah(1)	BBLR pada persalinan premature, BBLR dengan kelainan bawaan (anomaly) yang mencakup disabilitas fisik, *ductus arteriosus persisten*, penyakit jantung bawaan
Exposure	anemia pada ibu hamil(2)	Artikel tidak dapat diakses seluruhnya
Outcome	Adanya hubungan anemia pada ibu hamil dengan kejadian berat badan lahir rendah (3)	Tidak terdapat nilai *Odd ratio*
Study design	*Korelatif: crossectional, retrospektif; Prospective* (4)	*Literature review, Systematic Review, qualittive study, mixstudy, eksperiment*

(1)Kriteria inklusi 1;(2)Kriteria inklusi 2;(3)Kriteria inklusi 3;(4)Kriteria inklusi 4

3.3.2 Hasil Pencarian dan Seleksi Studi

Berdasarkan hasil pencarian literatur melalui publikasi dalam database dan menggunakan katakunci sesuai dengan *boolean operator* didapatkan melalui database *google scholar* sebanyak 295 artikel terkait dengan bayi berat lahir rendah dan berdasarkan identifikasi awal hanya terdapat 42 artikel yang relevan dengan tema. Melalui *PubMed* sebanyak 55 artikel terkait dengan *anemia during prgnacy or maternal anemia and Insufficient weight at birth* namun hany 15 artikel yang relevan dengan tema. Melalui *Elsevier* sebanyak 198 artikel terkait dengan *maternal anemia and Insufficient weight at birth* namun, berdasarkan identifikasi awal hanya terdapat 20 artikel yang relevan dengan tema. Selanjutnya berdasarkan

identifikasi abstrak pada hasil pencarian artikel melalui database *google scholar*, *PubMed*, dan *Elsevier* diperoleh sebanyak 77 artikel. Hasil seleksi artikel studi dapat digambarkan dalam diagram *flow* dibawah ini:



Bagan 3.1 Diagram *Flow* Penelitian *Literature Review* Hubungan Perilaku Merokok Dengan Kejadian Hipertensi

BAB 4

HASIL DAN ANALISIS

Bab ini menguraikan tentang hasil dan analisis penelitian. Hasil diuraikan secara berurutan dengan memaparkan karakteristik artikel yang menjadi sumber emperis utama juga temuan sesuai dengan tujuan penelitian.

4.1 Hasil Identifikasi Studi Berdasarkan Karakteristik Artikel

4.1.1 Tahun Publikasi

Tabel 4.1 Karakteristik Artikel Hasil Penyeleksian Studi Berdasarkan Tahun Publikasi (n=7)

Kategori (Tahun)	n	%
2018	0	0
2019	3	42,8
2020	0	0
2021	3	42,8
2022	1	14,2
Total	7	100

Tabel 4.1 menunjukkan bahwa sumber emperis utama terbanyak pada *literature review* ini adalah artikel dengan tahun publikasi 2019 dan 2021

4.1.2 Jenis Publikasi

Tabel 4.2 Karakteristik Artikel Hasil Penyeleksian Studi Berdasarkan Jenis Publikasi (n=7)

Kategori	n	%
Internasional	7	100
Lokal/Nasional	0	0
Total	7	100

Tabel 4.2 menunjukkan bahwa sumber emperis utama pada *literature review* ini seluruhnya merupakan publikasi internasional

4.1.3 Jenis Bahasa yang Digunakan

Tabel 4.3 Karakteristik Artikel Hasil Penyeleksian Studi Berdasarkan Bahasa yang Digunakan (n=7)

Kategori	**N**	**%**
Indonesia	0	0
Inggris	7	100
Total	7	100

Tabel 4.3 menunjukkan bahwa sumber emperis utama pada *literature review* ini seluruhnya menggunakan bahasa Inggris

4.1.4 Jumlah Sampel

Tabel 4.4 Karakteristik Artikel Hasil Penyeleksian Studi Berdasarkan Jumlah Sampel yang Digunakan (n=7)

Sumber Empiris Utama	**Jumlah Sampel**
Figueiredo & Gomes, (2019)	622
Srour & Samah, (2018)	300
Rebecca & Carpenter, (2022)	1665
Gomaa & Mohamed, (2021)	500
Deriba & Jemal, (2021)	555
Syafiqoh & Ghrahani, (2021)	379
Lumbanraja & Yaznil, (2019)	200

Tabel 4.4 menunjukkan bahwa sumber emperis utama pada *literature review* ini seluruhnya telah menggunakan sampel diatas jumlah minimal sampel untuk penelitian berjenis kuantitatif yakni telah diatas 30 sampel penelitian.

4.2 Hasil Identifikasi Studi Berdasarkan Karakteristik Partisipan

4.2.1 Karakteristik Usia Ibu

Tabel 4.5 Karakteristik Partisipan Berdasarkan Usia Yang Termuat dalam Artikel Ilmiah (n=7)

Sumber Empiris Utama	Rerata Usia Ibu (Tahun)
Figueiredo & Gomes, (2019)	
<18	24
18-35	33,9
>35	23,3
Srour & Samah, (2018)	26,3±5,9
Rebecca & Carpenter, (2022)	
<20	4,7
21-35	91,4
>35	3,6
Gomaa & Mohamed, (2021)	30,1±5,7
Deriba & Jemal, (2021)	
<20	8,6
21-35	81,6
>35	9,8
Syafiqoh & Ghrahani, (2021)	
<20	15,8
21-35	69,9
>35	14,2
Lumbanraja & Yaznil, (2019)	29±5,5

Tabel 4.5 menunjukkan bahwa berdasarkan sumber emperis utama diketahui sebagian besar ibu berada pada rentang usia dewasa awal hingga pertengahan (26-30 tahun).

4.2.2 Karakteristik Tingkat Pendidikan

Tabel 4.6 Karakteristik Partisipan Berdasarkan Tingkat Pendidikan Yang Termuat dalam Artikel Ilmiah (n=7)

Sumber Empiris Utama	**Tingkat Pendidikan**
Figueiredo & Gomes, (2019)	
Low	0
Middle	26,7
High	24,2
Srour & Samah, (2018)	11,6±3,2
Rebecca & Carpenter, (2022)	
Low	34
Middle	53,8
High	6,2
Gomaa & Mohamed, (2021)	n/a
Deriba & Jemal, (2021)	
Formal	67,6
Non formal	32,4
Syafiqoh & Ghrahani, (2021)	n/a
Lumbanraja & Yaznil, (2019)	
Low	13,8
Middle	58
High	24,5

Tabel 4.6 menunjukkan bahwa berdasarkan sumber emperis utama diketahui lima dari tujuh artikel menyatakan sebagian besar menyelesaikan pendidikan formal pada tingkat menengah.

4.2.3 Karakteristik Besar Pendapatan Keluarga

Tabel 4.7 Karakteristik Partisipan Berdasarkan Besar Pendapatan keluarga Yang Termuat dalam Artikel Ilmiah (n=7)

Sumber Empiris Utama	**Proporsi Pendapatan Keluarga (%)**
Figueiredo & Gomes, (2019)	
Low	23,9
High	27,4
Srour & Samah, (2018)	
Low	100
Rebecca & Carpenter, (2022)	
Low	87,1
High	12,9
Gomaa & Mohamed, (2021)	n/a
Deriba & Jemal, (2021)	
Low	77,8
High	22,2
Syafiqoh & Ghrahani, (2021)	n/a
Lumbanraja & Yaznil, (2019)	
Low	77,3
High	22,7

Tabel 4.7 menunjukkan bahwa berdasarkan sumber emperis utama diketahui lima dari tujuh artikel mengungkapkan bahwa sebagian besar partisipan memiliki pendapatan rendah atau berada pada tingkat sosial ekonomi rendah

4.2.4 Karakteristik Paritas

Tabel 4.8 Karakteristik Partisipan Berdasarkan Paritas Yang Termuat dalam Artikel Ilmiah (n=7)

Sumber Empiris Utama	Proporsi Paritas (%)
Figueiredo & Gomes, (2019)	
Primipara	23
Multypara	26,6
Srour & Samah, (2018)	n/a
Rebecca & Carpenter, (2022)	
Primipara	42,7
Multypara	57,3
Gomaa & Mohamed, (2021)	
Primipara	26,4
Multypara	73,6
Deriba & Jemal, (2021)	
Primipara	34,1
Multypara	65,9
Syafiqoh & Ghrahani, (2021)	
Primipara	44,1
Multypara	49,6
Lumbanraja & Yaznil, (2019)	n/a

Tabel 4.8 menunjukkan bahwa berdasarkan sumber emperis utama diketahui lima dari tujuh artikel mengungkapkan sebagian besar partisipan merupakan ibu primipara

4.2.5 Karakteristik Jenis Kelamin Anak

Tabel 4.9 Karakteristik Partisipan Berdasarkan Jenis Kelamin Anak Yang Termuat dalam Artikel Ilmiah (n=7)

Sumber Empiris Utama	Proporsi Jenis Kelamin Anak (%)
Figueiredo & Gomes, (2019)	
Laki	22,9
Perempuan	26,9
Srour & Samah, (2018)	n/a
Rebecca & Carpenter, (2022)	
Laki	48,4
Perempuan	49,4
Gomaa & Mohamed, (2021)	n/a
Laki	
Perempuan	
Deriba & Jemal, (2021)	n/a
Syafiqoh & Ghrahani, (2021)	
Laki	22,4
Perempuan	23,5
Lumbanraja & Yaznil, (2019)	n/a

Tabel 4.9 menunjukkan bahwa berdasarkan sumber emperis utama diketahui bahwa tiga dari tujuh artikel mengungkapkan bahwa sebagian besar jenis kelamin anak yang mengalami berat lahir rendah (*low birth weigh*) adalah anak perempuan

4.3 Hasil Identifikasi Variabel Utama

4.3.1 Hasil Identifikasi Anemia Pada Ibu Hamil

a. Karakter Anemia Maternal

Tabel 4.10 Hasil Identifikasi Karakter Anemia dalam Artikel Ilmiah (n=7)

Sumber Empiris Utama	Proporsi Karakteristik Anemia (%)
Figueiredo & Gomes, (2019)	
Anemia	24,9
Non anemia	75,1
Srour & Samah, (2018)	
Anemia	25,7
Non anemia	74,3
Rebecca & Carpenter, (2022)	
Anemia	48,3
Non anemia	51,7
Gomaa & Mohamed, (2021)	
Anemia	100
Deriba & Jemal, (2021)	
Anemia	41,1
Non anemia	58,9
Syafiqoh & Ghrahani, (2021)	
Anemia	34,6
Non anemia	65,4
Lumbanraja & Yaznil, (2019)	
Anemia	52,5
Non anemia	47,5

Tabel 4.10 menunjukkan bahwa berdasarkan sumber emperis utama diketahui bahwa enam dari tujuh artikel mengunkapkan bahwa proporsi kejadian anemia maternal rata- rata antara 24,9% sampai 52,5%

b. Derajad Anemia Maternal

Tabel 4.11 Hasil Identifikasi Derajad Anemia Maternal dalam Artikel Ilmiah (n=7)

Sumber Empiris Utama	**Frekuensi**	**Proporsi (%)**
Figueiredo & Gomes, (2019)		n/a
Srour & Samah, (2018)		
Mild	51	17
Moderate	26	8,7
Severe	0	0
Rebecca & Carpenter, (2022)		
Severe	11	0,66
Moderate	423	25,4
Mild	370	22,2
Normal	823	49,42
High	38	2,2
Gomaa & Mohamed, (2021)		
Mild	162	32
Moderate	225	45
Severe	113	22,6
Deriba & Jemal, (2021)		
<11 gram/dl	64	34,6
>11 gram/dl	121	65,4
Syafiqoh & Ghrahani, (2021)		
Mild	110	79,7
Moderate	28	20,3
Lumbanraja & Yaznil, (2019)	n/a	n/a

Tabel 4.11 menunjukkan bahwa berdasarkan sumber emperis utama diketahui empat dari tujuh artikel mengungkapkan bahwa sebagian besar ibu mengalami anemia ringan (*mild anemia*).

c. Kadar Hemoglobin Rata-rata selama kehamilan

Tabel 4.12 Hasil Identifikasi Rerata Kadar Haemoglobin Maternal dalam Artikel Ilmiah (n=7)

Sumber Empiris Utama	Karakter Hemoglobin Maternal (g/dl)
Figueiredo & Gomes, (2019)	11,6±1,1
Srour & Samah, (2018)	11,7±1,4
Rebecca & Carpenter, (2022)	10,6±2,0
Gomaa & Mohamed, (2021)	n/a
Deriba & Jemal, (2021)	11,6±1,1
Syafiqoh & Ghrahani, (2021)	n/a
Lumbanraja & Yaznil, (2019)	10,73±2,0

Tabel 4.12 menunjukkan bahwa berdasarkan sumber emperis utama diketahui bahwa rata-rata kadar hemoglobin ibu selama masa kehamilan rata- rata adalah 10,6 g/dl sampai 11,7 g/dl

d. Identifikasi Faktor yang Memengaruhi Anemia Maternal

Tabel 4.13 Hasil Identifikasi Faktor Yang Memengaruhi Anemia Maternal dalam Artikel Ilmiah (n=7)

Sumber Empiris Utama	Proporsi (%) / Nilai rerata
Figueiredo & Gomes, (2019)	n/a
Srour & Samah, (2018)	
HCt	34,1±3,2 g/dl
Serum Feritin	34,1±2,32 mg/dl
Abortus	0,6%
Rebecca & Carpenter, (2022)	
Riwayat persalinan preterm	13,1%
Gomaa & Mohamed, (2021)	
Antenatal visite <4	11,4%
Supplementation iron (no)	17,6%
Deriba & Jemal, (2021)	
Antenatal visite <4	27%
Syafiqoh & Ghrahani, (2021)	n/a
Lumbanraja & Yaznil, (2019)	n/a

Tabel 4.13 menunjukkan bahwa berdasarkan sumber emperis utama diketahui bahwa empat dari tujuh artikel menyatakan bahwa kejadian anemia maternal dikaitkan dengan ketidakpatuhan kunjungan selama *antenatal care* dan rendahnya suplementasi zat besi yang

dibuktikan dengan rendahnya serum ferritin dan rendahnya kadar serum hematokrit.

4.3.2 Hasil Identifikasi Berat Bayi Lahir Rendah (*Low Birth Weigh*)

a. Proporsi Kejadian Bayi Berat Lahir Rendah

Tabel 4.14 Hasil Identifikasi Kejadian Hipertensi Berdasarkan Diagnosis Profesional dalam Artikel Ilmiah (n=7)

Sumber Empiris Utama	**Proporsi Kejadian BBLR (%)**
Figueiredo & Gomes, (2019)	
Berat Normal	72,4
BBLR	27,6
Srour & Samah, (2018)	
Berat Normal	76,1
BBLR	23,9
Rebecca & Carpenter, (2022)	
Berat Normal	75
BBLR	25
Gomaa & Mohamed, (2021)	
Berat Normal	64
BBLR	36
Deriba & Jemal, (2021)	
Berat Normal	65,9
BBLR	34,1
Syafiqoh & Ghrahani, (2021)	
Berat Normal	54,08
BBLR	45,92
Lumbanraja & Yaznil, (2019)	
Berat Normal	48,46
BBLR	51,53

Tabel 4.14 menunjukkan bahwa berdasarkan sumber emperis utama diketahui prevalensi kejadian berat lahir rendah (*Low Birth Weigh*) mencapai 23,9% hingga 51,53%.

b. Rerata Berat Bayi Yang Mengalami Lahir Rendah

Tabel 4.15 Hasil Identifikasi Kejadian Hipertensi Berdasarkan Diagnosis Profesional dalam Artikel Ilmiah (n=7)

Sumber Empiris Utama	Rerata Berat Badan (gram)
Figueiredo & Gomes, (2019)	3000±439 (2049-3272)
Srour & Samah, (2018)	3022±585 (1900-4350)
Rebecca & Carpenter, (2022)	n/a
Gomaa & Mohamed, (2021)	2593,19±420 (1850-3500)
Deriba & Jemal, (2021)	n/a
Syafiqoh & Ghrahani, (2021)	n/a
Lumbanraja & Yaznil, (2019)	3015±584 (2431-3500)

Tabel 4.15 menunjukkan bahwa berdasarkan sumber emperis utama diketahui rerata bayi yang mengalami berat lahir rendah memiliki berat lahir rata-rata 1850-2431 gram.

4.3.3 Hasil Identifikasi Anemia pada Ibu Hamil dengan Berat Bayi Lahir Rendah

Tabel 4.16 Hasil Identifikasi Anemia pada Ibu Hamil dengan Berat Bayi Lahir Rendah dalam Artikel Ilmiah (n=7)

Sumber Emperis Utama	Hasil	Statistik
Figueiredo & Gomes, (2019)		*p-value*: 0,003
Anemia		OR:1,38
Normal weight	63,4	
Low weight	36,8	
Non- Anemia		
Normal weight	73	
Low weight	23	
Srour & Samah, (2018)		*p-value*: 0,009
Low weight on:		OR: 0,53
Mild	9,8	
Moderate	5,5	
Severe	8,6	
Rebecca & Carpenter, (2022)		*p-value*: 0,038
Low weight on:		OR: 2,73
Mild	20,4	
Moderate	23,1	
Severe	1,2	
Gomaa & Mohamed, (2021)		*p-value*:0,001
Low weight on:		OR:9,5
Mild	11,1	
Moderate	35,1	
Severe	73,5	
Deriba & Jemal, (2021)		*p-value*:0,001
Low weight on anemia	34,6	OR:2,34

Syafiqoh & Ghrahani, (2021)		*p-value*:0,047
Low weight on anemia	15,8	OR: 0,79
Normal weight on anemia	20,6	
Lumbanraja & Yaznil, (2019)		*p-value*:0,045
Low weight on anemia	19	OR: 0,84

Tabel 4.16 menunjukkan bahwa berdasarkan sumber emperis utama diketahui seluruh artikel mengungkapkan korelasi anemia maternal dengan kejadian berat lahir rendah. Ketujuh artikel juga menyebutkan bahwa anemia pada ibu hamil meningkatkan risiko kejadian berat lahir rendah sebesar 0,53 – 9,5 kali. Juga diketahui bahwa derajad anemia meningkatkan proporsi kejadian berat lahir rendah.

BAB 5

PEMBAHASAN

Bab ini membahas mengenai interpretasi hasil penelitian yang disajikan secara berurutan berdasarkan tujuan dengan merujuk pada hasil *review*, konsep teori, dan opini dengan membandingkan kajian terdahulu serta menyampaikan keterbatasan.

5.1 Interpretasi Hasil *Review*

5.1.1 Anemia pada Ibu Hamil

Hasil studi menunjukkan bahwa prevalensi kejadian anemia maternal atau anemia pada ibu hamil mencapai 24,5% hingga 52,5% yang umumnya adalah derajad ringan (*mild anemia*).

Bobak, (2018) menjelaskan bahwa anemia merupakan keadaan tubuh dengan konsentrasi hemoglobin (Hb) yang rendah di dalam darah. Perempuan dikatakan anemia saat memiliki Hb lebih rendah dari 12,0 gram/ 100 ml. Anemia dapat menyebabkan masalah kesehatan karena hemoglobin merupakan bagian darisel darah merah dan memiliki peran untukmengikat oksigen serta mendistribusikannya ke semua jaringan tubuh. Dampak dari kurangnya oksigen pada jaringan otak serta otot dapat menimbulkan gejala seperti menurunnya konsentrasi dan menurunnya kebugaran untuk melaksanakan kegiatan.

Temuan menarik dalam studi ini adalah sebagian besar artikel tidak menyebutkan satu faktor tunggal yang berpotensi terhadap kejadian anemia namun lebih cenderung pada multifactor. Faktor dominan secara umum

yang mengakibatkan anemia maternal diantaranya ketidakpatuhan kunjungan selama *antenatal care* dan rendahnya suplementasi zat besi yang dibuktikan dengan rendahnya serum ferritin dan rendahnya kadar serum hematokrit. Konsisten dengan temuan ini, studi oleh James & Andra (2021) mengungkap bahwa sebagian besar ibu hamil yang mengalami anemia berada pada derajad sedang yang dikaitkan dengan kekurangan zat besi selama periode trimester awal. Hal serupa diungkapkan oleh Anuradha *et al.,* (2021) yang mengungkapkan bahwa rendahnya suplementasi zat besi selama periode maternal akan berimplikasi terhadap kejadian anemia selama kehamilan.

Hasil identifikasi juga menunjukkan bahwa anemia maternal telah dikaitkan dengan ketidaklengkapan kunjungan antenatal care atau ketidakpatuhan terhadap kunjungan *antenatal care* dimana sekurang-kurangnya kunjungan antenatal care lebih dari empat kali selama trimester 1-3. Konsisten dengan studi ini, studi oleh Ngimbudzi *et al.,* (2021) mengungkapkan bahwa anemia selama kehamilan berkaitan erat dengan kunjungan pemeriksaan selama periode *antenatal care* (ANC). Alasamnya, anemia lebih banyak terjadi pada wanita yang memulai kunjungan ANC mereka pada trimester kedua atau ketiga. Wanita-wanita ini cenderung mendapatkan suplementasi zat besi dan asam folat untuk durasi yang lebih pendek selama kehamilan dibandingkan dengan mereka yang mulai menghadiri ANC lebih awal.

Berdasarkan usia diketahui bahwa ibu hamil yang mengalami anemia adalah berada pada rentang usia dewasa awal hingga dewasa pertengahan.

Hasil penelitian ini konsisten dengan *systematic review* oleh Rahman et al., (2022) bahwa anemia selama kehamilan mayoritas terjadi pada usia dewasa awal hingga pertengahan yang erat kaitanya dengan kejadian kekurangan zat besi atau rendahnya suplementasi. Menurut Chreg (2018) rendahnya suplementasi asam folat dan zat besi yang terjadi pada ibu hamil usia dewasa awal hingga pertengahan merupakan dampak dari ketidakpatuhan yang tinggi selama periode usia tersebut. Hal tersebut merupakan efek modukasi persepsi terkait usia masih mudah dan tidak perlu untuk mengkonsumsi suplementasi zat besi, vitamin maupun asam folat.

Berdasarkan tingkat pendidikan pada ibu sebagian besar ibu yang mengalami anemia memiliki pendidikan setingkat sekolah menengah. Secara konsisten, temuan ini sejalan dengan studi oleh Yadav & Ghimire, (2021) bahwa tingkat pendidikan berkorelasi secara positif dengan anemia selama masa kehamilan. Kajian ini mengkonfirmasi kajian terdahulu bahwa telah dibahas dalam banyak penelitian bahwa tingkat pendidikan yang rendah dapat meningkatkan kemungkinan seseorang terkena anemia karena fakta bahwa wanita berpendidikan memiliki kesempatan lebih besar untuk mendapatkan informasi yang tepat terkait dengan masalah kesehatan seperti anemia. Pendidikan juga dapat mempengaruhi seseorang untuk memahami informasi yang diberikan di ANC.

Berdasarkan besar pendapatan keluarga diketahui sebagian besar ibu yang mengalami anemia adalah tinggal dalam keluarga dengan penghasilan rendah. konsisten dengan temuan oleh Mekonnen, (2018) bahwa pendapatan keluarga merupakan faktor determinan yang berkontribusi terhadap kejadian

anemia selama kehamilan. Ini memperkuat kajian bahwa status sosial ekonomi juga dianggap sebagai salah satu prediktor anemia pada kehamilan, karena ibu hamil dengan indeks kekayaan rendah sampai menengah dianggap tidak bisa mendapatkan porsi makan yang adekuat selama periode kehamilannya.

Berdasarkan status paritas diketahui bahwa mayoritas ibu yang mengalami anemia maternal adalah ibu multipara. Menurut Imai, (2020) ibu primipara umumnya memiliki kadar hemoglobin yang lebih tinggi dibandingkan dengan ibu multipara.

Temuan ini membuktikan bahwa anemia pada kehamilan masih merupakan masalah kesehatan utama secara global yang terjadi pada ibu hamil. Alasan berbasis bukti emperis menyebutkan bahwa status sosial ekonomi rendah, asupan makanan yang kurang zat besi dan asam folat sebagai faktor predictor yang berkontribusi dalam meningkatkan prevalensi anemia diantara ibu hamil. Memperkuat pandangan bahwa kajian ini menemukan rendahnya serum ferritin dan hematocrit merupakan predictor kuat anemia pada ibu hamil terjadi akibat defisiensi besi. Hal ini memberikan suatu gagasan bahwa kekurangan zat gizi mikro dapat terjadi selama kehamilan, yang mempengaruhi produksi darah melalui jalur ferinitn. Oleh karena itu, suplementasi zat besi yang merupakan bagian dari suplementasi mikronutrien pada ibu hamil perlu ditingkatkan

5.1.2 Kejadian Bayi Berat Lahir Rendah

Hasil studi menunjukkan bahwa kejadian berat badan lahir rendah mencapai 23,9% hingga 51,53%. Juga ditemukan bahwa berat lahir rata-

rata adalah 1900 – 2500 gram. Hal ini menunjukkan bahwa berat badan lahir rendah yang terjadi pada tingkat ringan.

Marcdante & Kliegman, (2019) menjelaskan bahwa bayi dengan berat badan lahir rendah adalah neonatus yang dilahirkan kecil. Berat badan lahir rendah mengacu pada kelahiran dengan berat 500-2500 gram; berat badan lahir sangat rendah mengacu untuk kelahiran dengan berat 500-1500 gram; berat badan lahir ekstrem rendah mengacu untuk kelahiran dengan berat 500-1000 gram. Bayi berat lahir rendah berarti bayi berbobot 2,5 kg atau kurang saat lahir.

Penelitian ini menemukan bahwa sebagian besar bayi yang mengalami berat lahir rendah adalah berjenis kelamin perempuan. Hasil studi ini konsisten dengan temuan oleh Vliet & Liu, (2019) bahwa kejadian bayi berat lahir rendah terjadi pada bayi perempuan. Kajian ini juga sejalan dengan temuan oleh Fernando & Machinn, (2017) bahwa potensi kejadian bayi berat lahir rendah lebih tinggi 1,58 kali pada perempuan dibandingkan pada laki- laki.

Berdasarkan besar pendapatan keluarga diketahui bahwa mayoritas bayi yang mengalami berat lahir rendah adalah yang tinggal dalam keluarga dengan pendapatan rendah. Konsisten dengan temuan ini, studi oleh Tessema & Tamirat (2021) proporsi terbesar bayi berat lahir rendah adalah pada keluarga dengan pendapatan yang rendah. Menurut Supadmi & Kusrini, (2020) pada keluarga dengan pendapatan rendah atau dengan sosial ekonomi rendah memiliki prefrensi kehadiran yang rendah selama periode *antenatal care*. Rendahnya kehadiran dalam kunjungan selama periode

antenatal care ini berimplikasi terhadap kejadian bayi berat lahir rendah. Menariknya, berkaitan dengan tingkat pendidikan studi ini menemukan bahwa mayoritas ibu berpendidikan menengah, ini memperkuat asumsi bahwa ketidakhadiran selama periode *antenatal* dapat diakibatkan oleh rendahnya pemahaman ibu akan pentingnya pemeriksaan selama kehamilan. Secara konsisten, Kaur, (2019) mengungkapkan hal serupa bahwa rendahnya kunjungan selama periode antenatal care berkorelasi terhadap kejadian berat lahi rendah yang dimediasi oleh rendahnya pemahaman ibu akan nutrisi yang harus dikonsumsi selama periode kehamilan.

Bukti ini menunjukkan bahwa status sosial ekonomi individu berimplikasi terhadap pemberdayaan dan pemanfaatan pemeriksaan kehamilan yang melemahkan pemeriksaan status kesehatan sehingga menghasilkan *outcome* berupa bayi berat lahir rendah (*low birth weight*). Kajian ini menemukan bahwa sebagian parameter status sosial ekonomi seperti pendapatan, pendidikan ibu, secara langsung atau tidak langsung mempengaruhi berat badan lahir. Dengan demikian, pendapatan keluarga memegang peranan penting dalam berat badan lahir. Hal ini memberikan suatu gagasan bahwa ANC sangat penting untuk mendeteksi kelainan bayi selama masa penting perkembangan neonatal. Hal ini terutama berlaku bagi ibu yang tinggal di daerah dengan sumber daya terbatas seperti sosial ekonomi yang rendah. Melalui pemeriksaan selama kunjungan ANC maka deteksi dini dapat dilakukan secara optimal sehingga diagnosis tepat waktu dan intervensi terapeutik akhirnya berkontribusi untuk mencegah BBLR

5.1.3 Hubungan Antara Anemia Pada Ibu Hamil Dengan Kejadian Berat Badan Lahir Rendah

Hasil studi mengungkapkan bahwa seluruh artikel menyatakan adanya korelasi antara anemia maternal dengan kejadian berat badan lahir rendah dimana, semakin berat derajad anemia maka potensi kejadian berat lahir rendah semakin tinggi dengan risiko sebesar 0,53 – 9,5 kali

Silwal, (2020) menjelaskan bahwa berdasarkan konsep teori *intrauterine growth restriction* salah satu faktor maternal yang mengakibatkan bayi berat lahir rendah (BBLR) adalah anemia, yang terjadi akibat pengurangan nutrisi dan oksigen ke janin karena defisit transportasi plasenta dapat terjadi akibat penipisan hemoglobin. Kerangka potensial restriksi pertumbuhan uterus dimulai dengan penurunan perfusi darah di uterus, peningkatan resistensi vaskular dan restriksi pertumbuhan permukaan trofoblas, yang bertanggung jawab untuk mengeluarkan darah arteri ibu ke dalam plasenta. Peristiwa ini dapat mengakibatkan pembatasan pertukaran gas dalam kompleks ibu-janin dan, akibatnya, berat lahir rendah/tidak mencukupi. Oleh karena itu, jika terjadi berat badan lahir rendah, pemantauan hemoglobin sejak antenatal dan konsumsi suplemen harus dipantau secara cermat.

Kajian ini sejalan dengan studi oleh Rahmati & Delpishe (2017) yang mengungkapkan keterkaitan antara anemie dengan berat bayi lahir rendah. Hal serupa dinyatakan oleh Gnanasekaran & Jakanattane, (2019) bahwa anemia maternal sering kali ditemukan pada ibu hamil dengan sosial

ekonomi rendah, hal ini berdampak pada hasil maternal berupa bayi berat lahir rendah (*low birth weight*).

Kajian ini menemukan hal menarik bahwa baik anemia selama periode maternal, dan kejadian bayi berat lahir rendah diasosiasikan dengan lemahanya kunjungan selama periode *antenatal care*. Pertama bahwa kejadian anemia pada ibu hamil berkaitan dengan lemahnya kunjungan selama periode *antenatal care* sebagai akibatnya ibu hamil tidak mendapatkan dukungan suplementasi zat besi dan asal folat secara adekuat. Kedua, berat badan lahir rendah yang seharusnya telah terditeksi selama periode pemeriksaan antenatal care, karena rendahnya kunjungan maka tidak terpantau secara adekuat. Ketiga, keterkaitan antara kejadian anemia maternal dengan bayi berat lahir rendah merupakan hubungan kausalitas yang dimodulasi oleh berbagai faktor selama periode *antenatal care*. Terakhir, kajian ini mengkonfirmasi hasil studi terdahulu bahwa faktor risiko klasik untuk bayi berat lahir rendah (BBLR) terkait dengan anemia maternal dihubungkan melalui jalur kondisi biologis, sosial dan lingkungan yang tidak adekuat yang mungkin terjadi pada ibu hamil selama periode antenatal care. Hal ini memperkuat asumsi bahwa tidak adekuatnya pemantauan selama periode antenatal akan berdampak pada minimnya pengetahuan dan pemahaman ibu tentang kondisi dan keharusan yang dilakukan seperti pengaturan yang berkaitan dengan nutrisi, seperti berat badan sebelum hamil dan penambahan berat badan selama kehamilan. Sebagai akibatnya asupan kalori ibu yang tidak memadai, yang disebabkan oleh pola makan yang buruk dan rendahnya penyerapan zat gizi mikro

esensial, seperti vitamin B12 dan zat besi sehingga berdampak pada anemia yang pada akhirnya berdampak pada pertumbuhan janin.

5.2 Keterbatasan Penelitian

5.2.1 Studi ini hanya terbatas pada hasil kajian *literatur review* dan tidak menjangkau hingga dilakukan metanalisis sehingga diperlukan kajian lanjutan untuk memperkuat hasil kedepan. Hal ini karena metanalisis hanya dilakukan terhadap kajian yang sudah dilakukan review

5.2.2 Penelitian ini tidak mempertimbangkan lokasi dari artikel yang di *review* apakah artikel tersebut mengevaluasi pada populasi urban ataupun non-urban, karena berdasarkan teori lokasi dapat memengaruhi apakah indvidu tersebut mengalami anemia atau tidak, yang berarti dalam artikel ini kami tidak meninjau apakah ibu dengan anemia itu berada di wilayah rural (desa) atau wilayah urban (perkotaan)

5.2.3 Penelitian ini tidak mengevaluasi apakah artikel tersebut dilakukan di negara dengan *income* rendah ataupun tinggi. Sebagai pengetahuan umum negara dengan income rendah memiliki potensi masalah gizi dalam masyarakat yang berimplikasi terhadap anemia maternal.

BAB 6

KESIMPULAN

6.1 Kesimpulan

Berdasarkan hasil *review* telah teridentifikasi hasil sesuai dengan tujuan penelitian, sehingga dapat disimpulkan beberapa hal sebagai berikut:

6.1.1 Kejadian anemia pada ibu hamil mayoritas berada pada derajad ringan - sedang (*moderate*)

6.1.2 Kejadian bayi berat lahir rendah mencapai 23,9-51,53% dengan rata- rata berat lahir adalah 1950 – 2431 gram.

6.1.3 Anemia pada ibu hamil terbukti berkorelasi dengan kejadian bayi berat lahir rendah dengan risiko sebesar 0,53 – 9,5 kali

6.2 Saran

Berdasarkan hasil *literatur review* dapat disarankan beberapa hal sebagai berikut:

1. Bagi Pengampu Kebijakan

   Disarankan kepada pengampu kebijakan untuk mengoptimalkan program kesadaran masyarakat melalui edukasi atau promosi kesehatan harus dibangkitkan agar masyarakat mengetahui tentang anemia, komplikasinya, dan cara pencegahannya

2. Bagi Wanita Usia Subur

   Wanita usia subur harus dimotivasi untuk mengambil suplemen penambah darah, suplemen vitamin yang diperlukan sebelum hamil dan melanjutkannya sampai menyusui bayinya.

3. Bagi Pasangan

   Edukasi pasangan pria mengenai komplikasi penyakit dan kegunaan makanan tambahan selama kehamilan dapat banyak membantu ibu hamil untuk melaksanakan kebijakan ini dalam kehidupan sehari-hari.

4. Bagi Fasilitas pelayanan kesehatan dan Pemegang Program

   Menambah dukungan pada suplementasi, fortifikasi makanan dengan vitamin dan mineral esensial dapat membantu tujuan tersebut. Fortifikasi besi dapat digunakan dalam makanan yang biasa digunakan seperti garam dan gula untuk menyediakan akses yang mudah dan terjangkau oleh masyarakat utamanya populasi dengan status sosial ekonomi rendah.

5. Bagi Tenaga Kesehatan

   Melaksanakan giat promosi kesehatan dan mempermudah jalur pemeriksaan *antenatal care* secara mudah, murah dan menyenangkan bagi ibu hamil

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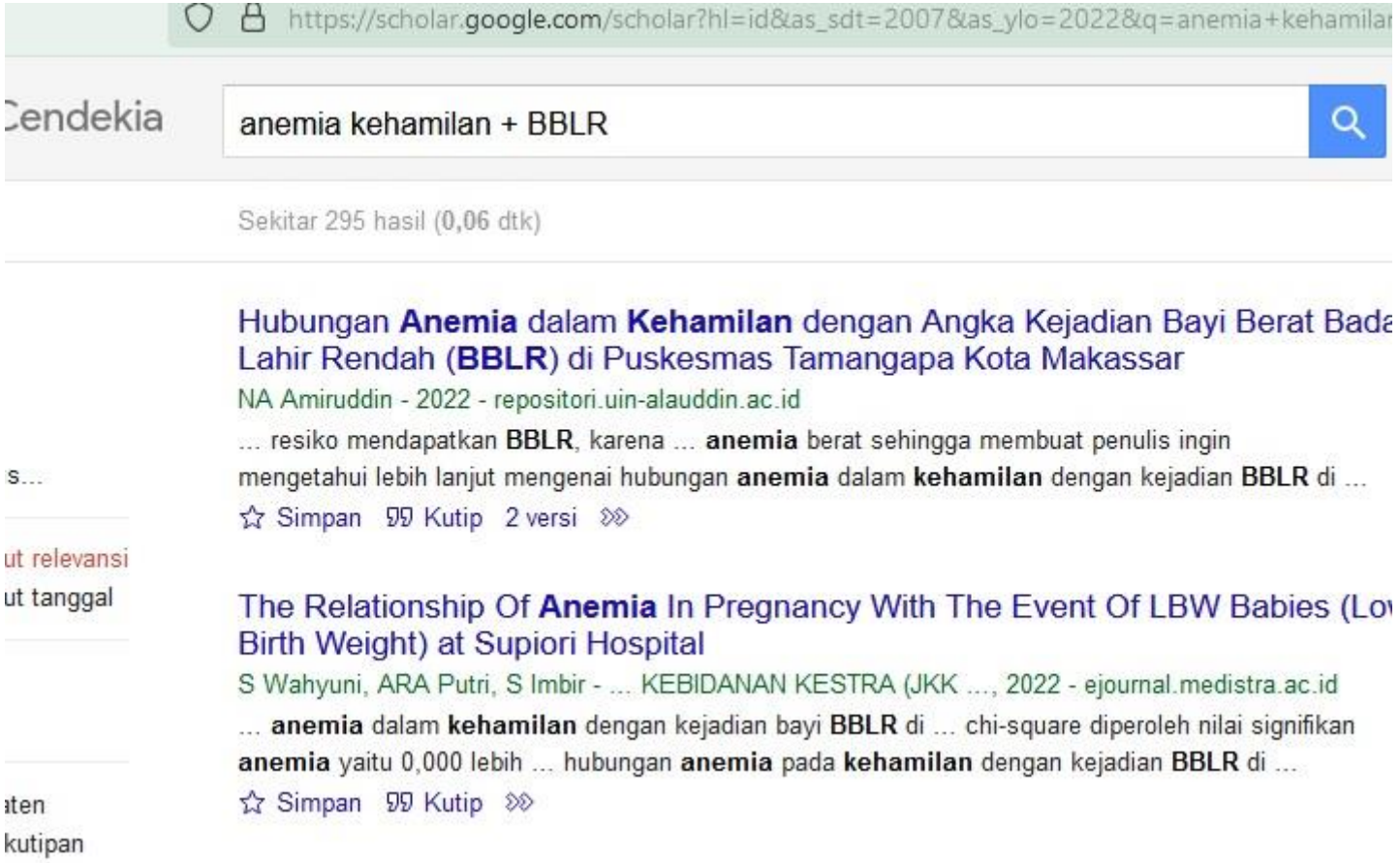
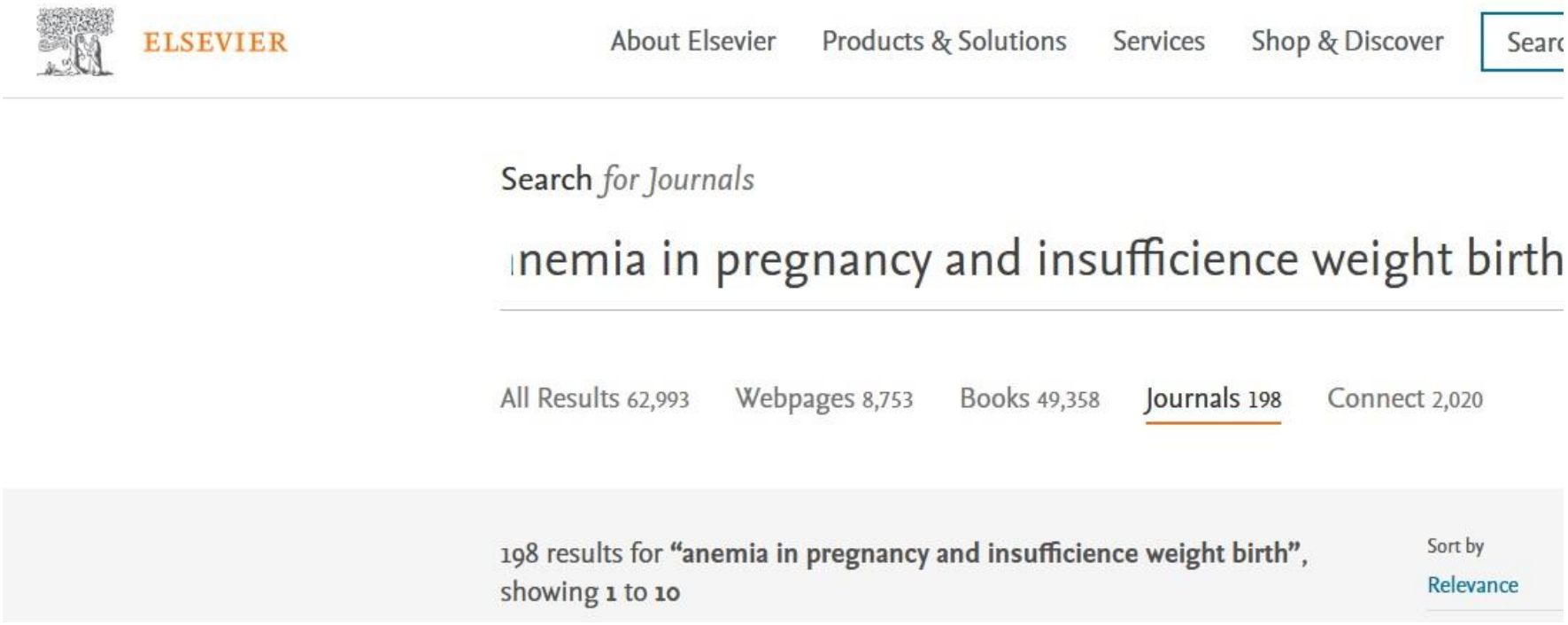
Lampiran 1: Pencarian Data Base

a. Google Scholar = 295 Jurnal



b. Elsevier = 55 jurnal

c. PubMed = 198 Jurnal



Lampiran 2: Matrix

No	Penulis & Tahun	Database	Metode penelitian	Ringkasan Hasil
1	(Figueiredo & Gomes, 2019)		**Desain** : *Prospective cohort study* **Sampel** : 622 responden **Teknik sampling** : *Random sampling* **Instrument** : *Epi Info (StatCalc)* **Analisis** : *Regresi logistic; odd ratio*	Ditemukan wanita hamil sebanyak 24,9% dengan anemia dan 75,1% tanpa anemia. Mengenai beratnya anemia ibu, 20,1% dari ibu hamil didiagnosis dengan anemia ringan, dan 4,8% didiagnosis dengan anemia sedang; tidak ada catatan anemia ibu berat. Frekuensi anemia defisiensi besi mencapai 6,0%, frekuensi anemia penyakit kronis adalah 18,9%. Kekurangan zat besi terjadi pada 16,4% wanita hamil. Mengenai berat lahir, 29,4% memiliki anak dengan berat lahir kurang dari 3000 g, dengan 3,4% dari kelahiran hidup diklasifikasikan sebagai berat badan lahir rendah dan 26% diklasifikasikan sebagai berat lahir tidak mencukupi. **Wanita yang didiagnosis dengan anemia menunjukkan insiden anak dengan berat lahir <3000 g secara signifikan lebih tinggi daripada wanita yang tidak mengalami anemia selama kehamilan (OR = 1,36; 95% CI: 1,06 hingga 1,76).** Wanita hamil dengan anemia memiliki risiko 38% lebih tinggi untuk memiliki anak dengan berat lahir rendah/tidak mencukupi dibandingkan wanita tanpa anemia (OR = 1,38; 95% CI: 1,07 hingga 1,77).
2	(Srour & Samah, 2018)		**Desain** : *Cross sectional study* **Sampel** : 300 responden	Menemukan bahwa anemia pada ibu hamil sebanyak 25,7% dan 52% diantaranya mengalami *depleted iron store*. SAda

		Teknik sampling **Instrument** **Analisis**	: : :	*Structured random sampling* *Anthropometric; questionnaire* *ANOVA; Chi square*	hubungan yang signifikan antara feritin serum ibu dan frekuensi berat badan lahir rendah (P= 0,001). Analisis kadar feritin serum menunjukkan bahwa 156 ibu hamil (52%) memiliki kadar feritin serum di bawah 15 ng/mL yang mengindikasikan depleted iron store (defisiensi besi) berdasarkan rekomendasi WHO. **Tujuh puluh tujuh wanita hamil (25,7%) ditemukan memenuhi kriteria klinis (Hb < 110 g/L dan feritin serum < 15 ng/mL) (OR; 0,53)**
3	(Rebecca & Carpenter, 2022)	**Desain** **Sampel** **Teknik sampling** **Instrument** **Analisis**	: : : : :	*Prospective Multycenter* 1.665 responden *Structured random sampling* *the National Institute of Child Health Global Network Maternal Newborn Health Registry (MNHR)* *Chi Square; Fisher exact; Odd Ratio*	Menggunakan *cutoff* khusus trimester untuk anemia, 48,3% wanita mengalami anemia dengan kadar Hb rata-rata adalah 10,6 (61,24) g/dL. **Risiko BBLR tertinggi terlihat pada kadar Hb sangat rendah (<7.0 g/dL, OR=2.00, 95% CI=0.43-7.01, P=0.031).** Mekanisme yang mendasari hubungan ini mungkin termasuk penurunan ekspansi plasma selama kehamilan dan/atau disregulasi besi yang mengakibatkan penyakit plasenta.
4	(Gomaa & Mohamed, 2021)	**Desain** **Sampel** **Teknik sampling**	: : :	*Cross sectional* 500 responden *Random sampling*	Menemukan berat lahir berkisar antara 1850 sampai 3500 gram dengan rata-rata 2593,192 gram. Tiga puluh enam persen (36%) memiliki bayi lahir berat rendah dengan kadar

		Instrument **Analisis**	: :	Nigel Formula Che square	hemoglobin berkisar antara 6,5-10,9 g/dL dengan rerata 9,258 g/dL. Empat puluh lima (45%) mengalami anemia sedang, sedangkan 22,6% mengalami anemia berat. **ada hubungan antara kadar hemoglobin darah pada ibu hail dengan berat lahir pada bayi (p-0,001) dimana ibu dengan kadar hemoglobin darah sangat rendah berpotensi 10,95 kali memiliki bayi dengan berat lahir rendah.**
5	(Deriba & Jemal, 2021)	**Desain** **Sampel** **Teknik sampling** **Instrument** **Analisis**	: : : : :	*Unmatched case control* 180 casus; 380 kontrol *Systematic random sampling* *Questionnaire; Epi Info* Regresi logisitic; che square	Analisis regresi logistik bivariat dan multivariat dilakukan untuk melihat hubungan, dan rasio odds yang disesuaikan dengan interval kepercayaan 95% (CI) dan nilai P < 0,05 dianggap menyatakan signifikansi statistik. Kurangnya konseling gizi (rasio odds yang disesuaikan [AOR] = 2,14; 95% CI = [1,13, 4,04]), tidak dapat mengonsumsi suplemen zat besi-folat (AOR = 2,3,78; 95% CI = [2,1, 6,85]), asupan makanan tambahan yang tidak mencukupi (AOR = 6,93; 95% CI = [3,92, 12,26]), pembatasan makanan (AOR = 2,29; 95% CI = [1,81, 4,09]), lingkar lengan atas ibu (MUAC) < 23 cm (AOR=2,85; 95% CI = [1,68, 4,85]), tinggi badan ibu 155 cm (AOR=3,58; 95% CI = [1,92, 6,7]), **anemia (AOR = 2,34; 95% CI = [1,21 , 4,53]),**

					komplikasi terkait kehamilan (AOR = 3,39; 95% CI = [2,02, 5,68]), dan minum alkohol selama kehamilan (AOR = 2,25; 95% CI = [1,24, 4,08]) **secara signifikan terkait dengan BBLR**
6	(Syafiqoh & Ghrahani, 2021)	**Desain** **Sampel** **Teknik sampling** **Instrument** **Analisis**	: : : : :	*Cross sectional study* 379 responden *Total sampling* *Medical record* Chi square; multivariate binariy logistic	Dari 379 ibu hamil, 138 (36,4%) mengalami anemia dan 60 (15,8%) ibu hamil diantaranya melahirkan bayi BBLR. Ibu hamil yang tidak anemia berjumlah 241 ibu hamil (63,6%), dimana 114 (30,1%) diantaranya melahirkan bayi BBLR (p=0,047). Dari analisis multivariat, variabel **anemia pada kehamilan berhubungan dengan BBLR [p=0,039, AOR 1,91 (95% CI 1,03-3,54)]**
7	(Lumbanraja & Yaznil, 2019)	**Desain** **Sampel** **Teknik sampling** **Instrument** **Analisis**	: : : : :	*Cross sectional study* 200 responden *Simple random sampling* *Medical record* Chi square	Hasil penelitian ini menunjukkan antara luaran maternal, hanya kadar hemoglobin antepartum yang memiliki korelasi bermakna secara statistik dengan kadar hemoglobin selama kehamilan (p <0,05), pada luaran neonatus. BBLR adalah **satu-satunya faktor yang secara statistik berkorelasi signifikan dengan konsentrasi hemoglobin selama kehamilan (OR= 0,84 p <0,05).**

Lampiran 3: Critical Appraisal

		Apraisal Checklist Item									
	Sumber	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**total**	**%**
1	Figueiredo & Gomes, (2019)	1	1	1	1	1	1	1	1	**8**	**100**
2	Srour & Samah, (2018)	1	1	1	1	1	1	1	1	**8**	**100**
3	Rebecca & Carpenter, (2022)	1	1	1	1	1	1	1	1	**8**	**100**
4	Gomaa & Mohamed, (2021)	1	1	1	1	1	0	1	1	**7**	**87,5**
5	Deriba & Jemal, (2021)	1	1	1	1	1	1	1	1	**8**	**100**
6	Syafiqoh & Ghrahani, (2021)	1	1	1	1	1	1	1	1	**8**	**100**
7	Lumbanraja & Yaznil, (2019)	1	1	1	1	1	1	1	1	**8**	**100**

1. Apakah kriteria inklusi dalam sampel sudah jelas didefinisikan?
2. Apakah subyek penelitian dan latarnya dijelaskan dengan detail?
3. Apakah paparan diukur secara valid dan reliabel?
4. Apakah digunakan kriteria standar (objektif) untuk pengukuran kondisi?
5. Apakah faktor perancu (*confounding factor*) diidentifikasi?
6. Apakah strategi untuk mengatasi factor perancu dijelaskan?
7. Apakah hasil diukur secara valid dan reliabel?
8. Apakah analisis statistik yang digunakan sesuai?

PLOS ONE

RESEARCH ARTICLE

Maternal anemia and birth weight: A prospective cohort study

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Abstract

Objective

To investigate the association between maternal anemia and low/insufficient birth weight.

Design

A prospective cohort study of pregnant women who underwent prenatal care at the health-care units in a municipality of northeast Brazil together with their newborn infants was carried out. The pregnant women were classified as having anemia when the hemoglobin level was below 11 g/dl. Infants who were born full term weighing less than 2500 grams were classified as low birth weight, and those weighing between 2500 and 2999 grams were classified as insufficient weight. The occurrence of maternal anemia and its association with birth weight was verified using crude and adjusted Relative Risk (RR) estimates with their corresponding 95% confidence intervals (95%CIs).

Results

The final sample was comprised of 622 women. Maternal anemia was considered a risk factor for low/insufficient birth weight, after adjusting the effect measurement for maternal age, family income, urinary infection, parity, alcoholic beverage consumption during pregnancy and gestational body mass index: $RR_{adjusted}$ = 1.38 [95% CI: 1.07 to 1.77].

Conclusions

Maternal anemia was associated with low/insufficient birth weight, representing a risk factor for the gestational outcomes studied.

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Competing interests: The authors have declared that no competing interests exist.

Introduction

Low birth weight has been widely studied and is an important risk factor for infant morbidity and mortality [1–4]. However, insufficient weight has received little attention [5–8], even though three decades ago, children with birth weights less than 3000 grams were considered to have a risk of mortality that was three times higher during the first year of life than that of children whose weights were above or equal to this cutoff point [9,10]. In Brazil, 2017, 8.49% of the newborn infants had weight <2500g. In this same year, the frequency of children with insufficient weight, that is ≥ 2500g and <3000g, was almost three times more 22.41%, increasing the necessity to investigate this weight special group [7].

The classic risk factors for low birth weight are associated with unfavorable biological, social and environmental conditions that may occur before or during the pregnancy period [4, 11–13]. Nutritional determinants, such as pre-gestational weight and weight gain during pregnancy, influence birth weight. Thus, inadequate maternal caloric intake, which may be the result of a diet that is nutritionally poor, leads to lower absorption of essential micronutrients, such as vitamin B12 and iron, for fetal growth [14].

Although the determinants of both low and insufficient weight at birth are similar, the mechanism that links maternal anemia to insufficient birth weight is not fully known. Few prospective cohort studies have analyzed the association between maternal anemia and low birth weight [15–25]. Indeed, after a rigorous search of previous investigations on the topic, only two retrospective cohort studies, from Colombia and Finland, that addressed the relationship between nutritional exposure and insufficient birth weight were identified [5, 6].

Given the relevance of the theme, the high frequency of insufficient birth weight in the studied group, and the knowledge that the association between maternal anemia and birth weight is affected by demographic and socioeconomic factors, an investigation of this relationship in diverse populations is necessary to identify the groups at greatest risk. The objective of this study was to verify the frequency of maternal anemia and its association with low/insufficient birth weight in users of the public health service from a population in northeastern Brazil.

Materials and methods

Study design/population

A prospective analytical cohort study was carried out with pregnant women, who underwent prenatal follow-up at healthcare units in the urban area of Santo Antônio de Jesus, Bahia, Brazil, and their newborns. The data collection period was from January 2013 to March 2017.

Sample size

To calculate the sample size, the following parameters were used: an Odds Ratio of 2.36 [26], the frequency of the rarest outcome, a low-birth-weight incidence of 8.29% in the group of pregnant women without anemia [26] and a ratio of exposed *versus* not exposed to anemia of 1:3. A study power of 80%, alpha error of 5% and the 95% confidence interval were also considered. Thus, the minimum estimated sample size was 141 pregnant women in the group diagnosed with anemia and 421 in the non-anemic group. In addition, 10% was added to the sample size to correct for possible losses, with a minimum sample calculation of 618 pregnant women. The sample size was calculated using Epi Info (StatCalc), version 7 [27].

The present study was approved by the Research Ethics Committee of Feira de Santana State University. All pregnant women voluntarily participated in the study and signed the Free Consent Form.

Eligibility criteria

Inclusion criteria. The pregnant women in this study had the following: pregnancy with fetal gestational ages between 8 and 32 weeks, assistance from the public health system, prenatal care from the selected healthcare units, live births, and children available for the study.

Exclusion criteria. Women were excluded from the study if they had a twin pregnancy, preterm birth or a history of bleeding that required hospital treatment for at least 24 hours.

Data collection procedures

Information concerning the pregnant women was first obtained through interviews. Then, trained researchers performed blood collections, and oral examinations of all teeth were performed by a dentist according criteria defined previously [28, 29].

The data that could not be obtained during the interview were acquired from the patient's chart and/or pregnancy card. During the postpartum period, information on birth weight was collected from the birth registration document (Declaration of Live Births).

Data collection tools

The questionnaire form was divided into six sections: 1) identification, socioeconomic-demographic data and environmental data; 2) nutritional information; 3) gynecological-obstetric history; 4) drug information; 5) variables related to the anthropometry of the pregnant woman; and 6) information concerning childbirth.

Blood collection for laboratory tests

The blood collection followed the standard criteria of collection and storage [30] to obtain the complete blood count and ferritin dosage.

Birth weight

Birth weight was measured immediately after delivery on a precise scale and subsequently recorded in the Declaration of Live Birth by a health professional who participated in the birth [31].

Criteria for the definitions of exposure and outcome

Exposure: Maternal anemia. Study participants were diagnosed as having maternal anemia when the hemoglobin level was below 11 g/dl or when the hematocrit was less than 33% (32). Additionally, the participants were diagnosed with iron deficiency anemia when the reference value for serum ferritin was less than 15 femtoliters and the mean corpuscular volume (MCV) was less than 80 femtoliters [32]. Participants were diagnosed with anemia of chronic disease when the MCV was normal, from 80 to 96 femtoliters, and when they had the aforementioned hemoglobin level [32]. In addition, hemoglobin levels were evaluated in their continuous form.

Outcome: Low/Insufficient birth weight. The classification of birth weight was defined according to the criteria of the World Health Organization [2]. Children born with weights above or equal to 3000 grams were allocated to the group of newborns with satisfactory weights. Newborns with birth weights less than 2500 grams were classified as low birth weight, and those weighing between 2500 and 2999 grams were classified as insufficient weight. In addition, the birth weight was evaluated in its continuous form.

Procedure for analyzing the data

Descriptive analysis for all selected variables was performed, according to the relative and absolute frequency. The Kolmogorov-Smirnov test [33] was applied, and histogram inspection was performed to verify the normality of the continuous variables. Student's t-test [34] or the Mann-Whitney U test [35] was used, according to the normality test of the variable, employing the mean, median and standard deviation to verify the differences between the groups. Categorical covariables were also evaluated for distribution, the presence of maternal anemia and weight less than 3000 grams using the chi-square test [36] or Fisher's exact test [37], with a significance level of 5%.

The investigation of the association between maternal anemia and low/insufficient birth weight was performed using logistic regression analysis by estimating the crude and adjusted odds ratio (OR) with their 95% confidence intervals and a significance level of 5%. Poisson model was used to convert the association measurement in relative risk (RR) with it 95% confidence interval.

Initially, a conceptual framework was adopted to select the following covariables involved in the multicausality of the association between maternal anemia and low/insufficient birth weight: maternal age, family income, urinary infection, parity, alcoholic beverage consumption during pregnancy and gestational BMI.

Subsequently, potential confounding factors and effect modification were selected by stratified analysis. The interaction identification was performed using the maximum likelihood ratio test, according to the definition of the saturated and reduced models for each of the possible effect modifier variables. A covariable was considered confounding when, after being eliminated from the saturated model, the covariable promoted a variation in the effect measurement that was greater than 10%compared to the main association measurement. In addition, the criterion of epidemiological importance for the selection of confounding covariables was adopted during modeling. The diagnosis of the model was performed using the Hosmer-Lemeshow test [38].

To evaluate the relationship between hemoglobin levels and the outcome, the multicollinearity test was performed, followed by univariate and multiple linear regression analysis using the common minimum squares technique [39], after confirming the linearity between the main variables by means of the F test [40]. For the adjusted model, the covariables that were considered to be confounders were used. These covariables included those that altered the parameters of the null model based on the statistical criteria ($p < 0.20$) and those of epidemiological relevance. Stata software, version 15, was used for data processing and analysis [41].

Results

The sample consisted of 622 pregnant (Fig 1) women who utilized the public health service of the municipality of Santo Antônio de Jesus, BA. The mean age of the participants was 25.5 years (± 6.5 SD), with a median of 25 years and a range of 13 to 46 years. The refusal rate was 2%.

The pregnant women were classified into two groups per the maternal anemia diagnostic criteria: 24.9% (n = 155) with anemia and 75.1% (n = 467) without anemia. Regarding the severity of maternal anemia, 20.1% of the pregnant women were diagnosed with mild anemia, and 4.8% were diagnosed with moderate anemia; there was no record of severe maternal anemia. The frequency of iron deficiency anemia was 6.0% among the participants, whereas the frequency of anemia of chronic disease was 18.9%. Iron deficiency was present in 16.4% of the pregnant women.

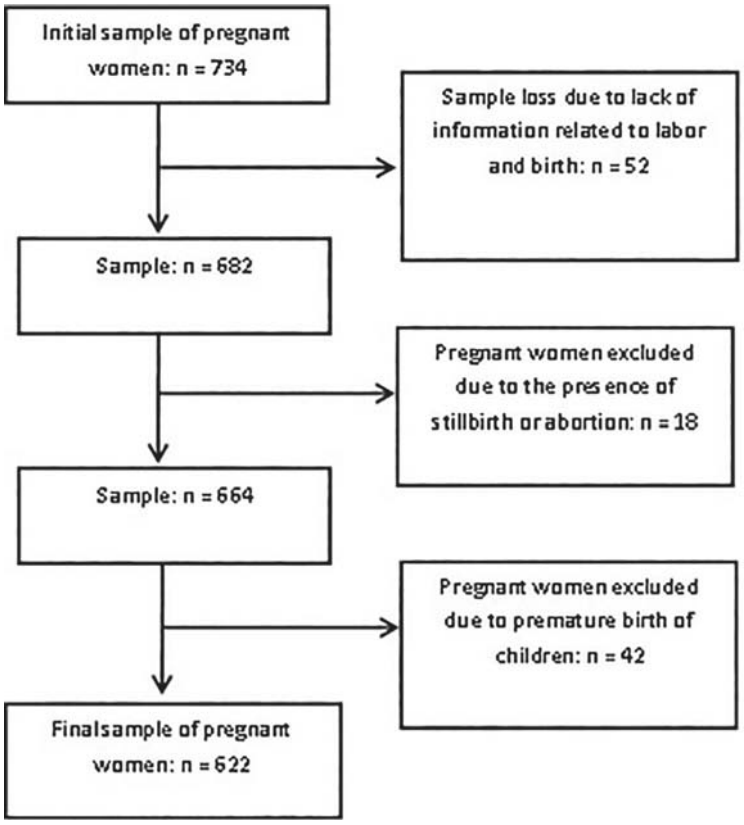

Fig 1. Flowchart of the sample participant selection process.

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The socioeconomic-demographic data are described in Table 1, and the data related to the maternal condition are shown in Table 2. Among the characteristics, only urinary infection, parity and the late onset of prenatal care showed statistically significant differences between the women with anemia and those without anemia, indicating that for most covariables, the comparison groups were homogeneous.

Regarding birth weight, 29.4% (183) of the participants had children with birth weights less than 3000 g, with 3.4% of the live births being classified as low birth weight and 26% being classified as insufficient birth weight. The frequency of mothers who had children of satisfactory weight was 70.6% (439). The centile for birthweight were 2940 grams, 3272 grams and 3565 grams for 25%, 50% and 75%, respectively

The central tendency measures of the descriptors used for the diagnosis of maternal anemia, according to birth weight, are summarized in Table 3. Notably, statistically significant differences were evident only for the mean values of hemoglobin ($p = 0.03$) and hematocrit ($p = 0.02$).

Women diagnosed with maternal anemia showed a significantly higher incidence of children with birth weights<3000 g than the women who were not exposed to anemia during pregnancy ($RR_{crude} = 1.36$; 95% CI: 1.06 to 1.76). According to the multiple-adjusted model, pregnant women with anemia had a 38% higher risk of having children with low/insufficient weight at birth than the women without anemia ($RR_{adjusted} = 1.38$; 95% CI: 1.07 to 1.77; Table 4). The model was adjusted for the following confounders: maternal age, family income, urinary infection, parity, alcoholic beverage consumption during pregnancy and gestational

Table 1. Number (n) and percentage (%) of the socioeconomic-demographic characteristics of the sample, according to the presence of anemia. Santo Antônio de Jesus, Bahia, Brazil, 2017 (n = 622).

	Maternal Anemia		
CHARACTERISTICS	**Yes**	**No**	**p†**
	n (%)	**n (%)**	
	155 (24.9)	**467 (75.1)**	
AGE (years)			
18–35	120 (24.0)	380 (76.0)	
<18	21 (33.9)	41 (66.1)	0.09
>35	14 (23.3)	46 (76.7)	0.91
EDUCATION LEVEL (years)			
≥8	108 (24.2)	338 (75.8)	
< 8	47 (26.7)	129 (73.3)	0.52
CONJUGAL STATUS			
With partner	140 (25.0)	419 (75.0)	
Without partner	15 (23.8)	48 (76.2)	0.83
RACE/SKIN COLOR			
Not black	91 (24.0)	288 (76.0)	
Black	64 (26.3)	179 (73.7)	0.51
CURRENT OCCUPATION			
Paid	65 (23.0)	218 (77.0)	
Unpaid	90 (26.6)	249 (73.4)	0.30
FAMILY INCOME*			
> 2 minimum wages	51 (27.4)	135 (72.6)	
≤ 2 minimum wages	104 (23.9)	332 (76.1)	0.35
HOUSEHOLD DENSITY (number of people per household)			
≤ 4	132 (25.8)	379 (74.2)	
>4	23 (20.7)	88 (79.3)	0.26

*Minimum wage values (per month) at the time of collection: 2013, R $ 678.00; 2014, R $ 724.00; 2015, R $ 788.00; 2016, R $ 880.00; 2017, R $ 937.00.

†p value: level of significance ≤ 0.05.

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body mass index. The quality of this model was considered good because the null hypothesis was rejected (p = 0.74).

The linear regression analysis showed that on average, there was a 21-g decrease (p = 0.03) in the weight of the newborn per 1 g/dl of reduced maternal hemoglobin during the gestational period. In the saturated model, which was adjusted for the above-mentioned confounders, there was a 0.20-g decrease (p = 0.05) in birth weight per 1 g/dl of maternal hemoglobin lost during pregnancy.

Discussion

Despite a rigorous search of a large number of electronic databases, only two cohort studies were found that discussed the relationship between maternal anemia and insufficient birth weight [5, 6]. Studies addressing anemic exposure and low birth weight were more frequent. Regardless of the lack of previous investigations on the topic, the main results of the present investigation highlighted maternal anemia as a risk factor for low/insufficient birth weight, which was consistent with data from a previous study by Raisanen et al. (2014) [5]. Thus, these findings contribute to current knowledge concerning this important public health problem.

Table 2. Number (n) and percentage (%) of the characteristics related to the health and lifestyle of the sample, according to the presence of maternal anemia. Santo Antônio de Jesus, Bahia, Brazil, 2017 (n = 622).

	Maternal Anemia		
CHARACTERISTICS	**Yes**	**No**	**p†**
	n (%)	**n (%)**	
	155 (24.9)	**467 (75.1)**	
SEX OF THE NEWBORN			
Male	70 (22.9)	236 (77.1)	0.25
Female	85 (26.9)	231 (73.1)	
URINARY INFECTION			
No	141 (24.1)	445 (75.9)	
Yes	14 (38.9)	22 (61.1)	0.05
PERIODONTITIS**			
No	111 (23.5)	361 (76.5)	0.68
Yes	23 (25.6)	67 (74.4)	
MATERNAL ARTERIAL HYPERTENSION			
No	151 (25.0)	454 (75.0)	
Yes	4 (23.5)	13 (76.5)	0.89
ABORTION			
No	128 (25.2)	380 (74.8)	
Yes	27 (23.7)	87 (76.3)	0.74
GESTATIONAL BMI*			
Proper weight	72 (25.3)	213 (74.7)	
Low weight	32 (27.6)	84 (72.4)	0.63
Overweight	40 (26.9)	109 (73.1)	0.72
Obese	11 (15.3)	61 (84.7)	0.08
PARITY			
$>$ 2 children	118 (33.5)	234 (66.5)	0.01
$\leq$ 2 children	65 (24.1)	205 (75.9)	
BEGINNING OF THE PRENATAL ACCOMPANIMENT			
$\leq$ 3 months	128 (23.4)	419 (76.6)	0.02
$>$ 3 months	27 (36.0)	48 (64.0)	
MATERNAL SMOKING HABIT‡			
No	140 (24.6)	429 (75.4)	0.89
Yes	38 (25.5)	38 (74.5)	
ALCOHOLIC BEVERAGE CONSUMPTION DURING PREGNANCY			
No	124 (25.1)	371 (74.9)	0.54
Yes	24 (22.2)	84 (77.8)	
FERROUS SALT SUPPLEMENTATION DURING PREGNANCY			
No	30 (20.0)	120 (80.0)	
Yes	125 (26.5)	347 (73.5)	0.11

* The Atalah curve was employed to calculate this covariable

** Gomes-Filho criteria for the definition of periodontitis[28]

† p value: level of significance $\leq$ 0.05

‡ There were deficits in this information.

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Other findings from the present study using linear regression analysis confirmed the above association since women with hemoglobin depletion had children with significantly reduced birth weights. Only one investigation had contrasting findings [6], showing no association

Table 3. Central tendency and dispersion measurements of the descriptors used to evaluate maternal anemia, according to the newborn weight, in users of the public health system in Santo Antônio de Jesus, Bahia, Brazil, 2017 (n = 622).

	Weight < 3000 g			Weight ≥ 3000 g			
Descriptors	**Mean**	**±SD***	**Median**	**Mean**	**±SD***	**Median**	**p†**
Hemoglobin level (g/dl) ‡	11.6	±1.1	11.6	11.8	±1.1	11.9	0.03
Red blood cell count (millions) ‡	4.1	±0.4	4.1	4.6	±8.7	4.2	0.14
Hematocrit (%)‡	35.1	±3.2	35.2	36.0	±4.2	36.3	0.02
Ferritin level (femtoliters) ‡	44.8	±38.9	31.8	45.2	±40.2	32.2	0.89
Mean Corpuscular Volume—MCV (femtoliters) ‡	85.9	±7.1	85.0	87.0	±5.5	86.4	0.06

* SD: Standard deviation

† p value: level of significance ≤ 0.05

‡ Reference value: Hemoglobin: ≥ 11 g / dl; Blood cell count: > 4 million; Hematocrit: ≥ 33%; Ferritin: ≥ 15 femtoliters; MCV = 80–96 femtoliters.

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between maternal anemia and low/insufficient birth weight. In addition, the incidence of maternal anemia in the current sample was approximately 25%, corroborating the frequency found in other studies [17, 42–44]. Among these women, the incidence of children with low/insufficient birth weight was approximately 37%, whereas in children without anemia, the incidence was 27%.

The biological plausibility of the association between maternal anemia and low/insufficient birth weight is not fully understood [45, 46]. However, previous studies have argued that maternal anemia predisposes the fetus to intrauterine growth restriction and may consequently influence the birth weight [9, 47]. Physiologically, beginning during the middle of the second trimester of pregnancy, women produce an average of 30 to 40 ml of plasma per kilogram, corresponding to hypervolemia. However, when the number of hematological cells does not increase in parallel with this process, hemodilution occurs, and maternal anemia may develop [48].

Thus, low hemoglobin levels may stimulate changes in placental angiogenesis and favor fetal hypoxia. According to this theory, a reduction in nutrients and oxygen to the fetus due to deficits in placental transport may result from hemoglobin depletion. The potential framework of uterine growth restriction begins with a reduction in blood perfusion in the uterus, an elevation in vascular resistance and growth restriction of the trophoblastic surface, which is responsible for ejecting maternal arterial blood into the placenta. These events may result in the restriction of gas exchange within the maternal-fetal complex and, consequently, in low/insufficient birth weight [49].

Table 4. Crude and adjusted Relative Risk (RR) of the association between maternal anemia and low/insufficient birth weight with the corresponding 95% confidence intervals (95% CI).

Maternal anemia	Birth weight				RR_{crude}	95% CI p*	$RR_{adjusted}$†	95% CI p*
	<3000 g		≥3000 g					
	N	%	N	%				
Yes	57	36.8	98	63.2	1.36	1.06 to 1.76 0.02	1.38	1.07 to 1.77 0.01
No	126	27.0	341	73.0				

* p value: level of significance ≤ 0.05

†Adjusted by maternal age, family income, urinary infection, parity, alcoholic beverage consumption during pregnancy and gestational BMI. Model fit test (Hosmer-Lemeshow): p = 0.74.

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Within the scope of the present investigation, the findings of only one study clearly point to the association between maternal anemia and a birth weight of less than 3000 g [5] since this exposure is often studied only in terms of its relationship with low birth weight [50–52]), without the inclusion of insufficient weight.

Multiple investigations have shown that maternal anemia is associated with low birth weight [53–55]. Conversely, several other studies that included only low birth weight as the outcome refuted the hypothesis under investigation [23, 56, 57], making the association controversial. Although discussions about the damage from insufficient birth weight have been carried out for more than 30 years, few studies have evaluated the relationship between insufficient weight and various undesirable gestational events [8–10, 58], emphasizing only the extreme ranges of birth weight, such as low weight and macrosomia [50–52].

A similarity does exist between low birth weight and insufficient weight, but the former is considered more serious than the latter for the newborn. However, the unfavorable effect produced by insufficient birth weight cannot be ignored since this condition may contribute to inadequate cognitive development and infant growth and increase the morbidity and mortality of this age group [3].

The findings of the present investigation are relevant in that they contribute to a better understanding of the importance of insufficient birth weight to pediatric health, and several method-related parameters, such as the sample size, diagnostic criteria for maternal anemia and treatment of confounders, should be carefully evaluated when comparing these results to those of previous studies on the topic.

The sample size of the present study exceeded the minimum calculated sample size to estimate the effect measurement. The total number of pregnant women involved in the study by Mesa et al. (2012) [6] was approximately half of that employed in the present investigation and may explain the non-association, which was probably due to the lack of power in the study, found between maternal anemia and low/insufficient birth weight. However, Raisanen et al. (2014) [5] evaluated a large sample comprising 290,622 pregnant women and found a positive association, corroborating the findings of the present study.

Regarding the diagnosis of anemia in the present investigation, to improve internal validity, a laboratory test was used to define maternal anemia, establishing a hemoglobin reference value <11 g/dl and confirming the result with a hematocrit $<33\%$. These criteria are recommended by the World Health Organization [32]. Mesa et al. (2012) [6] used the same criteria, although the authors did not confirm the diagnosis of maternal anemia by hematocrit. However, Raisanen et al. (2014) [5] defined anemia using only the information contained in the hospital chart.

The subclassification of maternal anemia is highly valuable to ensure the adequate monitoring of pregnant women. For example, the diagnosis of iron deficiency anemia may facilitate therapy for the disease with iron supplementation. Increasingly, iron deficiency anemia has been classified as maternal anemia since multiple reports in the literature support the hypothesis that the primary cause of anemia in pregnant women is ferritin deficiency [17, 59–62]. This notion conflicts with the findings presented in this study because most women with the anemia were diagnosed with anemia of chronic disease (18.9%), with a low frequency of iron deficiency anemia (6.0%), thus corroborating other studies [63–65].

Regarding severity levels, the participants in this study had a higher frequency of mild anemia. This severity was expected because much of the research converges in this direction [60, 66–69].

In the present investigation, the effect measurement was adjusted by confounders, due to knowledge of the possible effects of these covariables on both the exposure factor and the outcome. This criterion was also used in the study by Raisanen et al. (2014) [5], which

corroborated the findings of this study. In contrast, Mesa et al. (2012) [6] did not adjust for the confounding covariables, and this lack of adjustment may explain why their findings contrasted the association verified in the present research.

According to the conceptual framework adopted here and the multicausality involved in the association between maternal anemia and low/insufficient birth weight, the following covariables were considered in the adjustment of the final model: maternal age, family income, urinary infection, parity, alcoholic beverage consumption during pregnancy and gestational BMI.

Unfavorable socioeconomic-demographic factors can influence both the exposure and the gestational outcome of interest. Maternal age, in its extreme age ranges, is a classical confounding variable because younger women do not have complete biological maturity for gestation and because older women are more likely to have comorbidities, such as maternal anemia [25, 64]). Regarding family income, pregnant women who have lower purchasing power are more vulnerable in terms of poor living conditions and, consequently, health [43, 55]).

Infectious processes, such as urinary infection, influence the metabolism of new hemoglobin, leading to the development of maternal anemia [16], and intrauterine growth restriction, contributing to low/insufficient birth weight. Another relevant factor is parity since multiparity is a condition that can favor both low/insufficient birth weight and maternal anemia [25, 43].

Alcoholic beverage consumption during pregnancy can cause inflammatory disorders that restrict intrauterine growth, a contributing factor to low/insufficient birth weight [69, 70]. Alcohol consumption can also compromise caloric intake, making it insufficient and, consequently, favoring the development of maternal anemia [69, 70]. Women with inadequate nutrition are susceptible to both maternal anemia and having low/insufficient-birth-weight children, probably due to the poor dietary intake of essential micronutrients during pregnancy [43, 70].

Regarding the limitations of this investigation, the self-reported information may have produced calibration bias. Although the sample is representative of the urban population of the municipality investigated, caution should be exercised when interpreting the results by extrapolating them to other locations that do not have a population group that is similar to the one in this study. Other limitation is the exclusion of preterm births, since the source of information in Brazil about gestational age may be distorted, due to the absence of standardization of criteria used to define preterm birth. On the other hand, the low birth weight as outcome gave higher quality to the measurement due to its standardized form of collection [29, 71]. Regarding the definition of anemia, the criterion used was that standard, known worldwide and suggested by the WHO [32], which does not take into account the gestational trimester. As in any other investigation, the possibility of residual confounding remains since some factors may not have been measured in the present study.

Finally, this research can contribute information that has not previously been elucidated toward confirming the hypothesis. The temporality of the events, namely, the order of the exposure relative to the outcome, is established since the laboratory tests for the diagnosis of maternal anemia preceded delivery and birth. Possible sample losses were measured prior to the study, which assures the representativeness and power of the sample size and the reliability of the presented findings. The adoption of these criteria also minimizes the possibility of a spurious association. Furthermore, the use of validated instruments by the researchers, who were previously trained, strengthens the internal validity of this study.

Based on the method employed and the limitations described, the exposure investigated was confirmed as a risk factor for low/insufficient birth weight. Given the findings, a far-

reaching measure in public health would be the implementation of healthcare actions for the prevention and control of maternal anemia, aiming to reduce unfavorable gestational outcomes.

Author Contributions

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Research Article

Prevalence of Anemia and Iron Deficiency among Palestinian Pregnant Women and Its Association with Pregnancy Outcome

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Background. Anemia is a public health problem especially among pregnant women. This study aimed to investigate the prevalence of anemia and iron deficiency among pregnant women and its association with pregnancy outcome in Hebron Governorate in southern Palestine. *Methods*. This is a cross-sectional study that included 300 pregnant women in their first trimester and 163 babies. Maternal anthropometric and socioeconomic and newborns' data were collected. Complete blood count for study subjects and maternal serum ferritin were measured. *Results*. The prevalence of iron deficiency anemia among pregnant women was 25.7% and 52% of them had depleted iron stores. When pregnant women were grouped into three hemoglobin (Hb) tertile groups, a significant difference was observed between maternal Hb and newborns' birth weight (P= 0.009), height (P= 0.022), head circumference (P= 0.017), and gestational age (P= 0.012). There was a significant association between maternal serum ferritin and frequency of low birth weight (P= 0.001) and frequency of preterm delivery (P= 0.003). No significant association was observed between maternal anthropometric measures or the socioeconomic status and pregnancy outcomes. *Conclusion*. Iron deficiency is a moderate public health problem among the study subjects. Maternal Hb and serum ferritin significantly affect pregnancy outcomes.

1. Introduction

Anemia is a widespread public health problem associated with an increased risk of morbidity and mortality, especially in pregnant women and young children. Anemia also negatively influences the social and economic development in countries with high prevalence of anemia [1, 2]. In general, it is assumed that 50% of the cases of anemia are due to iron deficiency [3, 4]. Iron deficiency anemia (IDA) is considered to be one of the top ten contributors to the global burden of disease [1, 2].

Iron deficiency is the most common nutritional deficiency worldwide, particularly among pregnant women. Because of the increased iron requirements during pregnancy, pregnant women are recognized as the group most vulnerable to iron deficiency anemia [2, 5]. In Eastern Mediterranean region, the WHO estimates the prevalence of anemia to be 32.4% in nonpregnant and 44.2% in pregnant women [2]. Anemia during pregnancy is a significant concern. During pregnancy, the fetal demand for iron increases maternal daily iron requirements around 10-fold, increasing from 6 mg/day to 22 mg/day in first and third trimesters of pregnancy, respectively. This increased demand for iron is covered mostly from maternal iron stores, which makes pregnant women at higher risk of developing iron deficiency and IDA [6].

The consequences of IDA during pregnancy are often serious and long lasting for both the mother and fetus. Mothers with anemia often experience increased fatigue levels, reduced exercise performance, and reduced mental performance [7]. Furthermore, severe anemia (Hb < 90 g/L) is related to an increased risk of premature delivery with

subsequent low birth weight, small for gestational-age babies, and spontaneous abortion [6–10]. Additionally, maternal IDA may contribute to low iron status and poor health of infants. Also, pregnant women with anemia are at a greater risk of perinatal mortality and morbidity [10, 11]. Fetal iron metabolism is completely dependent upon maternal iron delivery via the placenta and so the effects of anemia on the fetus are directly related to the extent of maternal iron deficiency with increased mortality linked to severe IDA [6].

The prevalence of IDA varies among countries but is a major public health problem in the developing world, reflecting differences in race, socioeconomic factors, nutritional habits, medical care, and the frequency of parasitic illnesses [7].

In Palestine, the Ministry of Health (MoH) has protocols for IDA management and prevention that involves free iron supplements for pregnant women. In 2016, the overall prevalence of anemia among pregnant women (Hb <110 g/L) who visited maternal and child healthcare (MCH) centers of MoH was 29.5% (18.7% in West Bank region and 40.3% in Gaza Strip) [12]. Earlier in 2009 Khader et al. [13] reported an overall prevalence of anemia of 38.6% among pregnant women attending/accessing the UNRWA (United Nations Relief and Works Agency) clinics in Palestine with a substantial difference between those living in West Bank (31.1%) and Gaza Strip (44.9%). In the latter report [13], anemia prevalence revealed a significant increase in Gaza strip in 2009 (44.9%) compared to an earlier survey (35.7%) conducted in 2004 by UNRWA. The former report [12] surveyed the general population in Palestine excluding refugees who were surveyed by UNRWA [13]. Although these data revealed a high prevalence of anemia among pregnant women in Palestine, the association of anemia among Palestinian pregnant women with pregnancy outcome was not investigated. Therefore, this study aimed to assess the prevalence of anemia and IDA among pregnant women in Hebron Governorate (south of Palestine) and to investigate the association between maternal anemia and pregnancy outcome.

2. Materials and Methods

2.1. Study Subjects and Design. The study included 11 maternal and child healthcare (MCHC) centers distributed all over Hebron Governorate, Palestine. All pregnant women in their first trimester and presenting for the first time during current pregnancy at one of the MCHC centers covered in this study were asked to participate in this study. All participants were presenting at the MCHC centers for general medical examination related to the current pregnancy in the period March to October 2015. Pregnant women included in this study were contacted immediately after delivery (6-9 months after time of enrollment of pregnant women) and asked to include their newborns in the study. Inclusion criteria included apparently healthy according to the physical examination and laboratory data obtained at their first (current) visit, being not on iron supplementation, no previous pregnancy complications, and free of pregravid chronic diseases. A total of 300 pregnant women and 163 newborns born to them were included in the study.

All study subjects were briefed about the study and gave a written informed consent for themselves and on behalf of their babies. The principles of Helsinki Declaration were applied.

The Hebron Governorate (study region) is located in the southern part of West Bank and has a population of 0.729 million from around 3 million in West Bank, Palestine [14].

2.2. Data Collection and Analysis of Blood Samples. Anthropometric and socioeconomic data from the subjects were collected using a structured questionnaire. All pregnant women at their first trimester who met the inclusion criteria were asked to donate a blood sample and provide all information required to fill up the first part of the questionnaire concerned with the mothers. Collection of blood samples from pregnant women took place during their first visit to collaborating centers for the purpose of medical examination concerning current pregnancy. Participants were contacted immediately after delivery and asked for a permission to collect a blood sample from their newborns and provide all information needed to fill the second part concerned with the newborns. Blood samples were collected from newborn babies on the 5^{th} to 7^{th} day following delivery when babies were presenting at the MCHC center for their first vaccination date.

Blood samples were used for testing of Complete Blood Count (CBC) using Medonic (version CA 620; Boule Medical, Sweden) or Drew (version 6.3 model 2902-0531; Drew Scientific group, USA) hematology analyzers immediately after sample collection. Hematology analyzers were calibrated using the appropriate calibrators. Reliability of tests was assessed by running appropriate controls every day. Anemia was determined by hemoglobin concentration level less than 110 g/L for pregnant women based on the recommendations of WHO [15]. The severity of anemia was assessed based on WHO recommendations as follows: severe for Hb < 70 g/L, moderate for Hb 70-99 g/L, and mild for Hb 100-109 g/L [15].

Serum from mothers was collected, stored at -18°C, and used later for analysis of serum ferritin. Serum ferritin was determined using ferritin reagent kits and the automated chemistry analyzer machine (Abbott, USA) per the instructions of the manufacturer. For calibration, six ferritin standards (corresponding to ferritin levels of 0, 10, 50, 250, 500, and 1000 ng/ml) were used per the instructions of manufacturer. The ferritin standard calibrators were traceable to the WHO standards. Additionally, the ferritin controls (low, medium, and high) were assayed in each run for verification of the accuracy and precision of the test.

2.3. Statistical Analysis. Descriptive statistics including (mean and standard deviation) were calculated for all variables using SPSS software (Version 23). Inferential statistics were used to reach conclusions and make generalizations about the characteristics of populations based on data collected from the study subjects. These statistical tests include independent sample t-test, one-way ANOVA, and Chi-Square tests. A P-value < 0.05 was considered statistically significant.

Table 1: General characteristics of the study subjects/pregnant women at first trimester.

General characteristics	n	Mean ± SD	95% CI	Minimum value	Maximum value
Age (years)	300	26.3 ± 5.9	25.6 – 26.9	15	45
BMI (kg/m^2)	300	24.8 ± 4.1	24.3 – 25.2	15.2	41.2
No. of children	300	2.1 ± 2.0	1.9 – 2.4	0	10
No. of abortions	300	0.66 ± 1.18	0.53 – 0.79	0	8
Educational level (years)	300	11.6 ± 3.2	11.3 – 12.0	0	16
Monthly income (NIS)∗	264	1832 +-1154	1700 - 1963	700	7000
Biochemical status					
Hb (g/L)	300	118 ± 14	117 – 120	73	153
Hct (%)	300	34.1 ± 3.7	33.7 – 34.5	24.5	49.3
Serum ferritin (ng/mL)	300	20.2 ± 23.2	17.5 – 22.8	1.1	192.0

∗NIS: New Israeli Sheqel, the currency used mostly in Palestine.

Table 2: General characteristics of the newborns (pregnancy outcome).

General characteristics	n	Mean ± SD	95% CI	Minimum value	Maximum value
Birth weight (gm)	163	3022 ± 585	2932 - 3113	1900	4350
Birth height (cm)	96	48.3 ± 2.7	47.8 – 48.9	43	55
Head circumference (cm)	96	34.6 ± 1.4	34.3 – 34.9	31	37
Gestational age (weeks)	122	38.5 ± 1.5	38.5 – 38.7	33	40
Biochemical status					
Hb (g/L)	79	162 ± 22	157 – 167	111	214

3. Results

The general characteristics of pregnant women are described in Table 1. The average serum ferritin and Hb levels were within the normal range. However, out of 300 pregnant women, 77 women (25.7%) had Hb levels below 110 g/L and thus were considered anemic based on the recommendation of WHO [15]. Of the anemic pregnant women, 51 (17%) had mild anemia, 26 (8.7%) had moderate anemia, and none of the women had severe anemia, based on recommendation of WHO for assessment of anemia severity [15]. Analysis of serum ferritin levels showed that 156 pregnant women (52%) had serum ferritin levels below 15 ng/mL which indicates depleted iron stores (iron deficiency) based on the recommendations of the WHO [16]. Seventy-seven of the pregnant women (25.7%) were found to meet the clinical criteria (Hb < 110 g/L and serum ferritin < 15 ng/mL). These results indicate that all cases of anemia observed among our study subjects were due to iron deficiency. For the newborns, their average weight, gestational age, and Hb level were within the normal reference range (Table 2).

In order to examine the association between maternal characteristics and pregnancy outcome on one side with the maternal Hb levels on the other side, the mothers were divided into three Hb tertile groups (Table 3). A statistically significant difference was observed among the Hb tertile groups when compared with maternal serum ferritin, where serum ferritin levels increased with increasing Hb levels (Table 3). For the pregnancy outcome (newborns) a statistically significant difference was observed among maternal Hb tertile groups when compared with birth weight, birth height, and head circumference of newborns as well as with gestational age (Table 3). The results showed that birth weight, height, and head circumference of newborns as well as gestational age was increasing with increased maternal Hb levels.

As shown in Table 4, a statistically significant difference was observed between maternal serum ferritin levels when compared with maternal BMI kg/m^2. For the pregnancy outcome, a significant difference between maternal serum ferritin levels was observed when compared with birth height and head circumference of newborns as well as with gestational age, where birth height, head circumference, and gestational age were lower in mothers with iron deficiency (serum ferritin <15 ng/mL) compared to mothers with normal serum ferritin (serum ferritin ≥ 15 ng/mL) (Table 4). The latter findings confirm the significant differences among Hb tertile groups when compared with these parameters (Table 3). Additionally, a statistically significant difference was observed between maternal serum ferritin levels when compared with frequency of low birth weight and frequency of preterm delivery (Table 4).

The correlation between maternal iron status and anthropometric indices versus pregnancy outcome was assessed by Pearson's correlation (Table 5). A significant positive correlation was observed between maternal Hb levels and newborns' birth weight, birth height, head circumference and gestational age. Similarly, a significant positive correlation was observed between maternal Hematocrit (Hct) levels and newborns' birth weight, birth height, gestational

Table 3: **Maternal characteristics and pregnancy outcome by Hb tertile groups.** Statistical analysis was performed by one-way ANOVA, except for frequency of low birth weight and frequency of preterm delivery that were analyzed by Kruskal-Wallis test.

	All	HbTertile groups			
	(Mean ± SD)	HbT1 Hb< 110 g/L	HbT2 Hb 110- 120 g/L	HbT3 Hb> 120 g/L	*P*-value
Maternal characteristics (n= 300)∗					
Serum ferritin (ng/mL)	20.2 ± 23.2	14.8 ± 30.2	15.9 ± 10.6	25.0 ± 22.6	0.001
Age (years)	26.3 ± 5.9	27.1 ± 6.2	25.8 ± 6.3	26.1 ± 5.4	0.324
BMI (kg/m^2)	24.8 ± 4.1	24.3 ± 3.2	24.4 ± 4.5	25.1 ± 4.2	0.250
No. of children	2.1 ± 2.0	2.4 ± 2.1	2.2 ± 2.2	2.0 ± 1.9	0.268
No. of abortions	0.66 ± 1.2	0.73 ± 1.03	0.52 ± 0.94	0.69 ± 1.35	0.503
Educational level (years)	11.6 ± 3.2	11.9 ± 3.5	11.4 ± 3.0	11.6 ± 3.1	0.657
Monthly income (NIS)	1832 ± 1154	1888 ± 1262	1667 ± 913	1883 ± 1201	0.375
Pregnancy outcome					
Birth weight (gm)	3022 ± 585 (n= 163)[1]	2817 ± 568	3030 ± 577	3144 ± 571	0.009
Birth height (cm)	48.3 ± 2.7 (n= 96)[1]	47.3 ± 2.5	48.3 ± 2.5	49.1 ±2.8	0.022
Head circumference (cm)	34.6 ± 1.4 (n= 96)[1]	34.1 ± 1.5	34.5 ± 1.2	35.0 ± 1.3	0.017
Gestational age (weeks)	38.5 ± 1.5 (n= 122)[1]	37.8 ± 1.5	38.6 ± 1.4	38.8 ± 1.6	0.012
	Frequency (%)	**HbT1**	**HbT2**	**HbT3**	***P*-value**
Frequency of low birth weight (< 2500 gm)	39 (23.9%)	16 (9.8%)	9 (5.5%)	14 (8.6%)	0.053
Frequency of preterm delivery (< 37 weeks)	16 (13.1%)	8 (6.6%)	4 (3.3%)	4 (3.3%)	0.53

∗n= 300 for all maternal characteristics except for monthly income it was 264. [1]The indicated numbers of samples were assessed for each parameter.

age, and Hb levels. Also, a significant positive correlation was observed between maternal serum ferritin levels and newborns' birth height, gestational age, and Hb levels. No significant correlation was found between maternal age, BMI, number of children, number of abortions, educational level, and monthly income on one side and pregnancy outcome on the other side (Table 5).

4. Discussion

The prevalence of IDA among pregnant women from Hebron Governorate was 25.7% and 52% of them had depleted iron stores (iron deficiency). These data indicate that anemia among pregnant in Hebron region is a public health problem that can be classified as moderate [15]. The prevalence of anemia among pregnant women reported in this study was within the average rates reported for several Arab countries [17–21] concerning pregnant women in their first trimester. In Jordan, Al-Mehaisen et al. [19] reported an overall prevalence of anemia of 34.7% among pregnant women in rural areas, and the prevalence rate ranged from 18.9% among women in first trimester to 32.7% in second trimester to 42.5% in third trimester. In Kuwait, the prevalence of anemia among pregnant women was reported at 24.1% [20]. In the latter report [20] the prevalence of anemia varied with the stage of pregnancy, being lowest in first trimester (14.8%), highest in second trimester (49.2%), and intermediate in third trimester (36%). In Saudi Arabia, the prevalence of anemia among pregnant women in their first trimester was reported at 29.6% [18] and 27.7% [21] in two different regions of Saudi Arabia. In our study, the percentage of pregnant women with depleted iron stores (52%) is higher than those with anemia (25.7%) in first trimester and this may indicate that the prevalence of anemia would become more common and more severe in second and third trimester.

Anemia or iron deficiency during pregnancy is associated with intrauterine growth retardation, premature birth, low birth weight, increased labor time, higher risk of infection, elevated maternal and prenatal mortality, muscle dysfunction, and low physical capacity [8, 9, 22–24]. In accordance with previous reports [9–11], our study revealed a significant difference among maternal Hb tertile groups when compared to newborns' birth weight, height, and head circumference as well as gestational age. The birth weight, height, and gestational age were lowest with maternal HbT1 (< 110 g/L) and highest with maternal HbT3 group (> 120 g/L). Although HbT1 (in our study included Hb values from 73 to 109 g/L) was not as low as Hb < 70 g/L, which is considered as severe anemia [15] the adverse effect of moderate/mild anemia on pregnancy outcome was clearly demonstrated. Additionally, there was a significant association between maternal low serum ferritin and frequency of low birth weight and frequency of preterm delivery.

Table 4: **Maternal characteristics and pregnancy outcomes by maternal serum ferritin levels.** Statistical analysis was performed by independent sample *t*-test, except for frequency of low birth weight and frequency of preterm delivery that were analyzed by Chi-square test.

	All (Mean ± SD)	Serum ferritin		*P*-value
		Normal (≥ 15 ng/mL)	Iron deficiency (< 15 ng/mL)	
Maternal characteristics (n= 300)∗				
Age (years)	26.3 ± 5.9	26.0 ± 5.4	226.3 ± 6.3	0.436
BMI (kg/m^2)	24.8 ± 4.1	25.3 ± 4.4	24.2 ± 3.7	0.017
No. of children	2.1 ± 2.0	2.0 ± 1.9	2.3 ± 3.1	0.158
No. of abortions	0.66 ± 1.2	0.59 ± 1.1	0.72 ± 1.2	0.328
Educational level (years)	11.6 ± 3.2	11.8 ± 2.8	11.5 ± 3.5	0.439
Monthly income (NIS)	1832 ± 1154	1835 ± 1096	1829 ± 1209	0.961
Pregnancy outcome				
Birth weight (gm)	3022 ± 585 (n= 163)[1]	3123 ± 538	2945 ± 610	0.053
Birth height (cm)	48.3 ± 2.7 (n= 96)[1]	49.1 ± 2.3	47.9 ± 2.8	0.026
Head circumference (cm)	34.6 ± 1.4 (n= 96)[1]	35.0 ± 1.1	34.4 ± 1.4	0.025
Gestational age (weeks)	38.5 ± 1.5 (n= 122)[1]	38.9 ± 1.5	38.1 ± 1.5	0.008
	Frequency	**Normal (≥ 15 ng/mL)**	**Iron deficiency (< 15 ng/mL)**	***P*-value**
Frequency of low birth weight (< 2500 gm)	39 (23.9%)	9 (5.5%)	30 (18.4%)	0.001
Frequency of preterm delivery (< 37 weeks)	16 (13.1%)	2 (1.6%)	14 (11.5%)	0.003

∗n= 300 for all maternal characteristics except for monthly income it was 264.
[1]The indicated numbers of samples were assessed for each parameter.

Table 5: Pearson's correlation coefficients between pregnancy outcome (newborns) and maternal iron status and anthropometric/socio-economic factors.

Maternal data↓	**Newborn data**				
	Birth weight	Birth height	Head circumference	Gestational age	Hb
Hb	**0.191∗**	**0.307∗∗**	**0.257∗**	**0.275∗∗**	0.197
Hct	**0.171∗**	**0.224∗**	0.178	**0.228∗**	**0.235∗**
Serum ferritin	0.008	**0.216∗**	0.174	**0.254∗∗**	**0.287∗∗**
Age	0.025	0.103	0.124	0.038	0.052
BMI	0.061	0.074	0.022	-0.016	0.008
No. of Children	0.126	0.107	0.130	0.147	-0.052
No. of abortions	0.046	0.054	0.088	-0.037	0.001
Educational level	-0.023	-0.138	-0.080	-0.062	0.170
Monthly income	0.095	-0.033	-0.020	0.167	0.106

∗ Correlation is significant at the 0.05 level (2-tailed). ∗∗ Correlation is significant at the 0.01 level (2-tailed).

The birth weight is affected by a complex and independent factors in addition to maternal Hb and serum ferritin. The anthropometry of the mother and her nutritional intake are thought to be among the most important [25, 26]. Among the anthropometry measures, prepregnancy BMI has received especial interest and was addressed by many studies. Despite this, the direct relationship between prepregnancy BMI and fetal growth is still not known [27]. Several reports have shown that underweight women or those with low BMI are at high risk of having low birth babies and other adverse pregnancy outcome [27–30]. Also, high BMI (but still in the normal category) has a favorable effect on pregnancy outcome, a BMI in the overweight/obese/severely obese categories has been reported to increase the risk of adverse obstetric and neonatal outcomes such as maternal diabetes, preterm delivery, macrosomia, increasing risk of admission

of baby to intensive care unit, and perinatal death [30–32]. In the present study no significant correlation was observed between maternal anthropometric measures (age and BMI) and pregnancy outcome. Also, no statistically significant difference was observed among maternal Hb tertile groups when compared with maternal age and BMI; the maternal Hb showed a slight increase with increasing BMI (Table 3). Our findings concerning BMI and pregnancy outcome are contradictory to previous reports [30–32] and may be due to the limited number of overweight/obese women among the study subjects.

Furthermore, several studies have investigated the effect of socioeconomic status of the mother on pregnancy outcome. Anemia has been linked to poverty [1, 24, 33], which in turn is considered as a consequence of many factors including low monthly income and low levels of education. Therefore, in this study we have examined the association of the mother's socioeconomic status (monthly income, level of education, and parity) with maternal Hb, maternal serum ferritin, and low birth weight and did not find a significant correlation. In consistence with our findings, a previous study that investigated a cohort of pregnant women from Nablus-Palestine did not find a significant association between monthly income, level of education, and size of family and prevalence of anemia among this group [34]. While Khader et al. [13] reported a significant association between parity and prevalence of anemia among Palestinian pregnant women living in Refugee camps in West Bank and Gaza but no significant association was found with regard to level of education. A recent report from rural areas of Jordan has found no significant association between socioeconomic status of mothers and prevalence of anemia among pregnant women [19]. In contrast to our findings, a study from Malaysia found that older age of the mother, parity of four or above, Indian origin, and per capita monthly income are significant risk factors for low birth weight [27]. Another study from Nigeria found that less educated pregnant women had significantly higher prevalence of anemia compared to educated women, and no significant association between parity and prevalence of anemia [35]. Thus, further studies are needed to study the effect of the socioeconomic status of mothers' on the pregnancy outcome using a larger sample size and preferably from different regions in Palestine. Additionally, the role of some factors in the contradictory results concerning anthropometric parameters among different studies from different geographic regions such as prevalence rate of anemia, ethnicity, and local environmental factors may be better tackled by meta-analysis studies.

A limitation in our study is that only one blood sample was collected from pregnant women and that was in their first trimester. However, anemia usually becomes more common and more severe as pregnancy progress. Thus, a second blood sample collected at the end of second trimester or beginning of third trimester could provide more information on the association between maternal anemia in second or third trimester and pregnancy outcome compared to first trimester.

5. Conclusion

Our study indicated that IDA is a moderate public health problem among pregnant women in Hebron Governorate and more than half of study subjects have depleted iron stores. Maternal Hb and serum ferritin were found to affect pregnancy outcome (birth weight, height, and gestational age). Newborns born to women with low Hb levels tended to have lower birth weight and height, head circumference, and lower gestational age. No significant association was observed between maternal anthropometric measures (age and BMI) or the socioeconomic status (level of education, monthly income, and parity) and pregnancy outcome. The high prevalence of anemia in our subjects was probably due to low iron intake and poor dietary habits rather than food insecurity or disease. Therefore, the etiological factors associated with maternal anemia during pregnancy in Palestine should deserve more attention.

Data Availability

The raw data (CBC and anthropometric data) used to support the findings of this study are available from the corresponding author upon request.

Disclosure

The current address of Khaled M. Srour is University of Toledo Medical Center, Internal Medicine Department, Toledo, OH, USA. The current address of Samah S. Aqel is Al-Ramah clinic, Directorate of Primary Health Care of Hebron, Ministry of Health, Hebron, State of Palestine.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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U-Shaped Association between Maternal Hemoglobin and Low Birth Weight in Rural Bangladesh

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Abstract. Low birth weight (LBW) is associated with a higher risk of neonatal mortality and the development of adult-onset chronic disease. Understanding the ongoing contribution of maternal hemoglobin (Hgb) levels to the incidence of LBW in South Asia is crucial to achieve the World Health Assembly global nutrition target of a 30% reduction in LBW by 2025. We enrolled pregnant women from the rural Tangail District of Bangladesh in a Maternal Newborn Health Registry established under The Global Network for Women's and Children's Health Research. We measured the Hgb of pregnant women at enrollment and birth weights of all infants born after 20 weeks gestation. Using logistic regression to adjust for multiple potential confounders, we estimated the association between maternal Hgb and the risk of LBW. We obtained Hgb measurements and birth weights from 1,665 mother–child dyads between July 2019 and April 2020. Using trimester-specific cutoffs for anemia, 48.3% of the women were anemic and the mean (±SD) Hgb level was 10.6 (±1.24) g/dL. We identified a U-shaped relationship where the highest risk of LBW was seen at very low (< 7.0 g/dL, OR = 2.00, 95% CI = 0.43–7.01, $P = 0.31$) and high (> 13.0 g/dL, OR = 2.17, 95% CI = 1.01–4.38, $P = 0.036$) Hgb levels. The mechanisms underlying this U-shaped association may include decreased plasma expansion during pregnancy and/or iron dysregulation resulting in placental disease. Further research is needed to explain the observed U-shaped relationship, to guide iron supplementation in pregnancy and to minimize the risk of LBW outcomes.

INTRODUCTION

Low birth weight (LBW) continues to be a pressing global health concern as approximately 20 million babies are born each year with a weight of < 2,500 grams.[1] This threshold for LBW was established by epidemiologic studies that demonstrated that babies with a birth weight of less than 2,500 grams were 20 times more likely to die in infancy.[2,3] LBW is associated with 80% of all neonatal deaths and has been linked to the development of stunting and adult-onset-noncommunicable disease through malnutrition and fetal programming in utero.[1,4,5]

In 2012, the WHO set global nutrition targets under the Millennium Development Goals (MDGs) that include a 30% reduction in LBW by the year 2025.[1,6] These goals have brought attention to South Asia as about half of all LBW infants are born in India and Bangladesh. National LBW surveys conducted in Bangladesh in 2003–2004 and again in 2015 document significant progress in reducing the incidence of LBW in the region from 36% in 2003–2004 to 22.6% in 2015.[3] This progress has been attributed to improvement in socioeconomic conditions and widespread implementation of routine iron-folate supplementation.[3] Despite this progress, further work is needed to reduce LBW in South Asia to a rate comparable with the 6% of all births seen in many developed nations.[3,6]

Adequate iron stores are required during pregnancy for expansion of the maternal red cell mass that supports the growing placenta and fetus. Inadequate iron stores at the start of pregnancy place women at risk for the development of iron-deficiency anemia.[7,8] For this reason, universal preventative iron supplementation is routinely included in prenatal care.[9,10] This practice is supported by a positive correlation between iron supplementation and birth weight.[11,12] Anemia, however, which is often used as a proxy for iron deficiency, is inconsistently associated with LBW.[13] The national LBW survey in Bangladesh in 2015 found no association between hemoglobin (Hgb) and birth weight whereas a large systematic review and meta-analysis conducted in 2016 found the anemia-attributable proportion of LBW in low-income countries was 25%.[3,14,15] Some studies have found an association between only severe anemia (< 7.0 g/dL) and LBW, whereas others document an increased risk of LBW at any Hgb level less than 11.0 g/dL, particularly when combined with a low maternal body mass index (BMI).[16,17]

Here, we report findings on the association of maternal Hgb with risk of LBW from an ongoing Maternal and Newborn Health Registry. It is important to further clarify the relationship between anemia and LBW in Bangladesh to bolster progress toward meeting the global nutrition target of a 30% reduction in LBW by the year 2025.

MATERIALS AND METHODS

Data sources and sampling procedure. This was a population-based study that is part of the National Institute of Child Health Global Network Maternal Newborn Health Registry (MNHR) (ClinicalTrials.gov Identifier: NCT01073475.) MNHR is a multisite, prospective, ongoing, and active surveillance system that is tracking pregnancies and births in defined geographic communities (clusters), each with approximately 300–400 deliveries per year. The Bangladesh site is located in the Tangail District of Bangladesh and is composed of 12 study clusters each with 17,500–19,500 people. Through a bimonthly house-to-house surveillance, pregnant women were identified and 99.7% of all eligible pregnant women were enrolled upon providing consent to participate. Mother–child dyads were followed up at birth (within 72 hours) and at 42 days postpartum for collection of maternal and newborn outcomes. Details of the registry are

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described elsewhere.[18,19] Pregnant women who were screened between July 2019 and April 2020 were included in this analysis as presented in Figure 1.

Outcome variable. LBW, the main outcome variable, was dichotomized as yes = 1 (baby born with birth weight < 2,500 g) or no = 0 (otherwise). Birth weights were obtained in the field by trained personnel using an AWS H-110 (American Weigh Scales, Inc., Cumming, GA) digital hanging scale, calibrated daily. A large number of newborns in this region of Bangladesh are born at home or in small healthcare facilities, which presents a major challenge to collecting accurate birth weight information.[20] In this analysis, 226 newborns were excluded because of no reliable birth weight (Figure 1). Of the analyzed birth weights, over 50% were taken on the day of birth, 88% within the first 3 days of life, and 100% before 2 weeks postdelivery. Birth weights taken on day of life 1–13 were adjusted according to expected neonatal weight loss to reduce the risk of overreporting LBW because of the delay in birth weight measurements.[21]

Explanatory variables. Blood Hgb, the main explanatory variable, was collected in the field by trained personnel using a point of care hemoglobinometer (HemoCue 301, HemoCue AB, Ängelholm Sweden). The HemoCue 301 analyzer has shown moderate agreement of Hgb level estimation when compared with the gold standard hematology autoanalyzer.[22] Of the 1,981 eligible mother–child dyads, 90 were excluded because the mother refused a Hgb measurement (Figure 1). Measurements were used as both a continuous and discrete variable categorized into severe anemia, moderate anemia, mild anemia, normal Hgb, and high Hgb. Anemia was defined according to the WHO and the U.S. CDC using trimester-specific cutoffs, which control for normal plasma expansion during pregnancy.[23] These cutoffs use Hgb < 11.0 g/dL in the first and third trimester and Hgb < 10.5 g/dL in the second trimester as the threshold for anemia.[23] Trimester of pregnancy at the time of Hgb measurement was determined using the last menstrual period (LMP), which is the most accurate method of determination given low early ultrasound coverage in the rural setting.

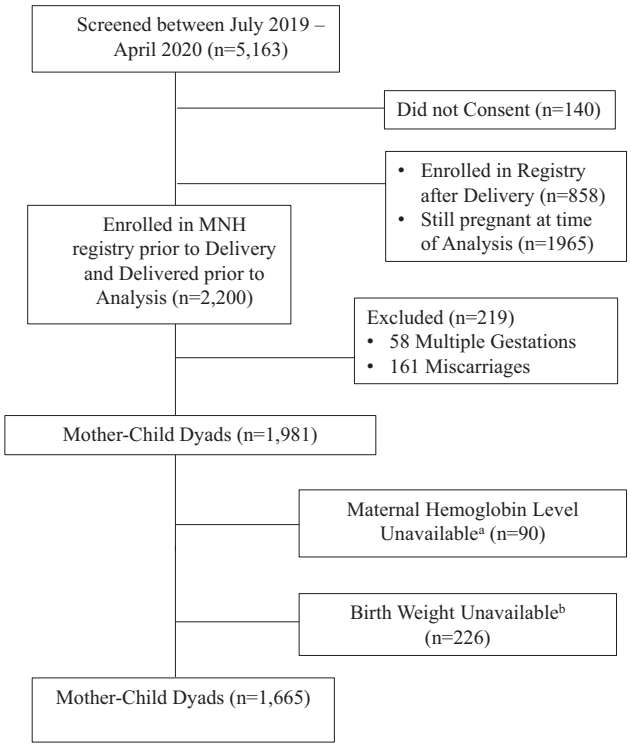

FIGURE 1. Diagram of maternal newborn health registry enrollment in Bangladesh, 2019–2020. [a]Of the eligible population for this analysis, 90 women refused to allow a hemoglobin level; [b]Accurate birth weight information was not recorded for 226 neonates (107 of these had birth weight estimates recorded, 63 had birth weights taken after 14 days of life, and 56 neonates had no birth weight recorded).

The sociodemographic and obstetric characteristics were considered as explanatory variables of occurrence and nonoccurrence of LBW in newborns. The selection process to identify these explanatory variables drew on a range of studies carried out to assess the magnitude of LBW and to identify its determinants.[1,2,20,46] Clinically significant cut points were used to create categorical variables for maternal age, BMI, and parity. Locally weighted scatterplot smoothing (LOESS), a nonparametric method for fitting a smooth curve to data points, was used to determine appropriate cut points to convert inter-delivery interval to a categorical variable. A composite score using principal component analyses of household assets was used to determine socioeconomic status. A complete list of explanatory variables is presented in Table 1. Given the number of missing prenatal Hgb and birth weight measurements in this dataset, we explored the possibility of systematic differences in explanatory variables between the group analyzed ($N = 1{,}665$) and the group with missing key variables ($N = 316$). All variables found to have an association with the LBW outcome of interest on univariate analysis were included in this exploration and presented in Table 2.

Statistical analysis. Data were entered and calculated fields were determined at the study site before secure transmission to the central data center (RTI International) where further data quality checks were performed before statistical analyses. Maternal characteristics were examined using descriptive statistics. Crude associations between maternal characteristics and LBW were assessed using χ^2, Fisher's exact tests, and *t*-tests as appropriate. In bivariate analysis, we used χ^2 and Fisher's exact for categorical variables to examine whether the outcome was associated with each of the explanatory variables. Independent variables identified in univariate models to be associated with LBW ($P < 0.1$) were included in a multivariable binomial logistic regression. A *P* value of < 0.05 was considered significant when interpreting associations identified by the multivariate analysis. Finally, we used a LOESS to visualize the relationship between maternal Hgb concentration and probability of LBW.

All statistical analyses were conducted in R (version 4.0.3, https://cran.r-project.org/). The MNHR study was reviewed and approved by the ICDDR,B's (International Centre for Diarrhoeal Disease Research, Bangladesh) Research Review and Ethical Review Committees and the Institutional Review Boards of the corresponding U.S. partners (University of Virginia and RTI International). All women provided informed consent before participation.

RESULTS

Between July 2019 and April 2020, 5,163 women–child dyads were screened for eligibility. Of those screened, 140

TABLE 1
Sociodemographic and obstetric characteristics of women–child dyads

Variable	Characteristics	Frequency (%) (N = 1665)
Maternal age (years)*	Less than 16	78 (4.7)
	16–35	1,522 (91.4)
	Greater than 35	60 (3.6)
Maternal education	No formal schooling	100 (6.0)
	Primary	566 (34.0)
	Secondary	895 (53.8)
	University+	104 (6.2)
Maternal body mass index (kg/m^2)*	Underweight	125 (7.5)
	Normal	968 (58.1)
	Overweight	571 (34.3)
Socioeconomic status	Low	149 (8.9)
	Medium	1,301 (78.1)
	High	215 (12.9)
Type of household fuel	Dung/Wood/Charcoal/Straw/Shrubs/Grass	1,476 (88.6)
	LPG/Electricity	189 (11.4)
Antenatal visits	$\geq$ 4 visits	189 (11.4)
	$<$ 4 visits	1,476 (88.6)
Evidence of hypertensive disease*	Yes	81 (4.9)
	No	1,580 (94.9)
Parity	Nulliparous	648 (38.9)
	One–Two	908 (54.5)
	Greater than two	109 (6.5)
Inter-delivery interval	$<$ 40 months	228 (13.7)
	40–70 months	287 (17.2)
	$>$ 70 months	469 (28.2)
	Nulliparous	681 (40.9)
Iron Supplementation*†	Yes	1,371 (82.3)
	No	293 (17.6)
Delivery mode	Vaginal delivery	747 (44.9)
	C-section	918 (55.1)
Season of delivery	Summer (March–October)	556 (33.4)
	Winter (November–February)	1,109 (66.6)
Sex of the baby	Female	821 (49.3)
	Male	844 (50.7)
Trimester of hemoglobin measurement‡	First trimester	195 (11.7)
	Second trimester	749 (45.0)
	Third trimester	721 (43.3)

*Less than 1% of data missing.
†Iron supplementation reported at any time during pregnancy for any duration, note that iron supplementation in this population is common but rarely achieves an adequate dose of 180 tablets during pregnancy.[45]
‡Trimester of hemoglobin measurement determined using last menstrual period (LMP), which is the most accurate method of gestational age dating in this population where ultrasound is not readily available.

did not provide consent to participate in the MNHR. At the time of the analysis, 1,965 women had not yet delivered and 161 suffered miscarriages. The 58 women with multiple gestations were excluded. Of those remaining, 1,665 mother–child dyads were ultimately included in this study as they had both a Hgb measurement taken during pregnancy and a birth weight measured within the first 2 weeks of life (Figure 1). Over half of these women were enrolled in the MNHR within the first or second trimester ($\leq$ 27 weeks gestation) of pregnancy.

The mean maternal Hgb level in this cohort was 10.6 g/dL with a standard deviation of 1.24 g/dL. The prevalence of anemia was 48.3% and 46% of all anemia cases fell into the category of mild anemia. Only 0.7% of these women exhibited a severe anemia ($<$ 7.0 g/dL). Maternal sociodemographic and obstetric characteristics are displayed in Table 1.

Infant birth weight outcomes by maternal Hgb category are displayed in Table 3. The prevalence of LBW was 15.3%. We noted that a high maternal Hgb ($>$ 13 g/dL) was associated with a 2-fold higher risk of LBW when compared with a normal Hgb (OR = 2.17, 95% CI = 1.01–4.38, P = 0.0362). A LOESS plot of Hgb versus LBW revealed a U-shaped relationship with the lowest risk of LBW associated with Hgb concentrations between 9.0 and 11.0 g/dL (Figure 2). Although no statistically significant association was found between severe anemia (Hgb $<$ 7.0) and risk of LBW, this finding is limited by the small sample size of only 11 severely anemic women (OR = 2.00, 95% CI = 0.43–7.01, P = 0.311).

In bivariate analysis, maternal BMI, age, education, socioeconomic status, sex of the infant, mode of delivery, inter-delivery interval, and type of household fuel were also associated with LBW status (Table 3). Recognizing that significant confounding may exist with these covariates, we used multivariable modeling to control for the impact of these variables (Table 3). Covariates associated with the risk of LBW in this multivariate model include sex of the infant,

TABLE 2
Analysis of systematic differences between included and excluded women–infant dyads

Variable	Characteristics	Excluded ($N = 316$)	Included ($N = 1665$)	P value
Maternal age (years)*	Less than 16	5 (1.6)	78 (4.7)	0.0292
	16–35	292 (92.4)	1,522 (91.4)	
	Greater than 35	15 (4.7)	60 (3.6)	
Maternal education	No formal schooling	33 (10.4)	100 (6.0)	0.00654
	Primary	120 (38.0)	566 (34.0)	
	Secondary	147 (46.5)	895 (53.8)	
	University+	16 (5.1)	104 (6.2)	
Maternal body mass index (kg/m^2)*	Underweight	29 (9.2)	968 (58.1)	0.115
	Normal	193 (61.1)	125 (7.5)	
	Overweight	89 (28.2)	571 (34.3)	
Socioeconomic status	Low	40 (12.7)	149 (8.9)	0.0516
	Medium	244 (77.2)	1,301 (78.1)	
	High	31 (9.8)	215 (12.9)	
Type of household fuel	Dung/Wood/Charcoal/Straw/Shrubs/Grass	285 (90.2)	1,476 (88.6)	0.483
	LPG/Electricity	31 (9.8)	189 (11.4)	
Inter-delivery interval	$<$ 40 months	44 (13.9)	228 (13.7)	0.723
	40–70 months	54 (17.1)	287 (17.2)	
	$>$ 70 months	98 (31.0)	469 (28.2)	
	Nulliparous	120 (38.0)	681 (40.9)	
Delivery mode*	Vaginal delivery	239 (75.6)	747 (44.9)	$<$ 0.0001
	C-section	75 (23.7)	918 (55.1)	
Sex of the baby*	Female	156 (49.4)	821 (49.3)	0.751
	Male	153 (48.4)	844 (50.7)	

* Less than 1% of data missing.

mode of delivery, maternal BMI, age, and education. Using the bottom category on the U-shaped Hgb curve, mild anemia (Hgb 10.0–11.0 g/dL) as the reference, the risk of LBW was associated with a high Hgb of >13.0 g/dL (AOR = 2.28, 95% CI = 1.01–4.86, $P = 0.0385$). Although the sample size was too small to reach statistical significance, a Hgb level <7.0 g/dL was associated with a 2.7-fold risk of LBW (AOR = 2.73, 95% CI = 0.57–10.20, $P = 0.159$). Moderate anemia was not significantly associated with LBW outcomes.

DISCUSSION

The results from this study suggest that high maternal Hgb concentration (>13 g/dL) is associated with a 2-fold increase in risk of LBW. On the other end of the spectrum, severe anemia (Hgb <7 g/dL) may be associated with a similar risk of LBW but the relationship in this cohort was not significant likely due to small numbers ($N = 11$) in this category. The prevalence of maternal anemia in Bangladesh is higher in this cohort than the global average previously described by the WHO, 48.3% versus 42% globally.[24] Despite this high rate of maternal anemia, the majority of anemic women (mild-moderate anemia) face no increased risk of LBW outcomes in this cohort of 1,665 mother–child dyads.

The literature regarding the impact of maternal anemia on LBW outcomes has not achieved a clear consensus. Early studies found a direct correlation between low Hgb levels and LBW babies.[9,14,15,23,25] Other studies have found no association between mild-moderate anemia and LBW.[15,26] For example, a large study of over 70,000 mother–child dyads in India found an association between LBW and maternal anemia at all levels.[16] Another cohort study in India and Pakistan found an association between only severe maternal anemia and LBW.[17] The most recent national LBW survey in Bangladesh found no association at all between maternal anemia and LBW outcomes.[3] Other studies have noted an association between LBW and maternal anemia detected during the first or second trimester of pregnancy but not during the third trimester.[27,28] These disparities in study findings likely have to do with the multidimensional causation of maternal anemia where not all types of anemia contribute to LBW in the exact same manner.[24]

The most common cause of anemia in pregnant women is iron-deficiency anemia and it is often assumed that over 50% of all cases of maternal anemia in high-prevalence regions like Bangladesh can be attributed to iron deficiency alone.[29] Iron deficiency has been independently associated with LBW outcomes because the mother's body does not have sufficient iron stores to adequately expand the red blood cell mass and support the growth of the placenta and developing fetus.[7,9,30] This is especially true for iron deficiency before conception and early in the first trimester.[11,14,27,28] Routine iron supplementation and nutrition education has been shown to effectively reduce the incidence of LBW in iron-deficient populations.[12,31] However, the impact of anemia on LBW may not be as robust in places where the prevalence of iron deficiency is not common as has been suggested in Bangladesh.[24,32] The high rate of mild to moderate anemia in this cohort could be secondary to a condition such as thalassemia rather than iron deficiency. Of note, thalassemia-related anemia may not have as large an impact on LBW rates as iron-deficiency anemia.[30,33]

An important finding of this study is the documentation of a U-shaped relationship between maternal Hgb levels and LBW infant outcomes. This relationship has only recently been described in low- and middle-income countries where many variables impact infant birth weight.[34–38] Most recently, a study involving 130,888 pregnant women across

TABLE 3
Low birth weight risk factors

Variable	Characteristics	LBW*	NBW*	Univariate model P value†	Multivariate model AOR‡	(95% CI)‡	P value‡
Hemoglobin (g/dL)	Severe anemia	3 (1.2)	8 (0.6)	0.0942	2.73	0.57–10.20	0.159
	Moderate anemia	59 (23.1)	364 (25.8)		0.96	0.63–1.45	0.833
	Mild anemia	52 (20.4)	318 (22.6)		Ref	Ref	Ref
	Normal hemoglobin	130 (51.0)	693 (49.1)		1.11	0.78–1.60	0.573
	High Hemoglobin	11 (4.3)	27 (1.9)		2.28	1.01–4.86	0.0385*
Sex of the baby	Male	106 (41.6)	738 (52.3)	0.00195	Ref	Ref	Ref
	Female	149 (58.4)	672 (47.7)		1.49	1.13–1.97	0.00525*
Mode of delivery	Vaginal Delivery	138 (54.1)	609 (43.2)	0.00158	Ref	Ref	Ref
	Cesarean Delivery	117 (45.9)	801 (56.8)		0.74	0.56–0.99	0.0420*
Season of delivery	Summer (Mar.–Oct.)	76 (29.8)	480 (34.0)	0.212	–	–	–
	Winter (Nov.–Feb.)	179 (70.2)	930 (66.0)		–	–	–
Iron supplementation	Yes	207 (81.2)	1,164 (82.6)	0.642	–	–	–
	No	48 (18.8)	245 (17.4)		–	–	–
Maternal body mass index (kg/m^2)	Underweight ($<$ 18.5)	27 (10.6)	98 (7.0)	0.000604	1.29	0.79–2.04	0.289
	Normal (18.5–24.9)	165 (64.7)	803 (57.0)		Ref	Ref	Ref
	Overweight ($\geq$ 25)	62 (24.3)	509 (36.1)		0.67	0.48–0.93	0.0170*
Maternal age	$<$ 16	22 (8.6)	56 (4.0)	0.00915	1.91	1.08–3.28	0.0219*
	16–35	224 (87.8)	1,298 (92.1)		Ref	Ref	Ref
	$\geq$ 35	8 (3.1)	52 (3.7)		0.71	0.30–1.50	0.407
Maternal education	No Formal Schooling	25 (9.8)	75 (5.3)	0.0261	Ref	Ref	Ref
	Primary	87 (34.1)	479 (34.0)		0.53	0.32–0.91	0.00182*
	Secondary	132 (51.8)	763 (54.1)		0.51	0.30–0.88	0.0125*
	University+	11 (4.3)	93 (6.6)		0.47	0.20–1.07	0.0794
Socioeconomic status	Low	24 (9.4)	125 (8.9)	0.0534	Ref	Ref	Ref
	Medium	210 (82.4)	1,091 (77.4)		1.14	0.71–1.89	0.595
	High	21 (8.2)	194 (13.8)		0.83	0.42–1.63	0.592
Household fuel	LPG/Electricity	16 (6.3)	173 (12.3)	0.00502	Ref	Ref	Ref
	Dung/Wood/Charcoal/ Straw/Shrubs/Grass	239 (93.7)	1,237 (87.7)		1.72	1.00–3.14	0.0620
Evidence of hypertensive disease	No	239 (93.7)	1,341 (95.1)	0.268	–	–	–
	Yes	16 (6.3)	65 (4.6)		–	–	–
Inter-delivery interval	$<$ 40 months	24 (9.4)	204 (14.5)	0.0926	Ref	Ref	Ref
	40–70 months	39 (15.3)	248 (17.6)		1.37	0.79–2.42	0.262
	$>$ 70 months	77 (30.2)	392 (27.8)		1.63	1.00–2.74	0.0570
	Nulliparous	115 (45.1)	566 (40.1)		1.60	1.00–2.67	0.0583
Number of antenatal visits	$\geq$ 4 visits	31 (12.2)	158 (11.2)	0.739	–	–	–
	$<$ 4 visits	224 (87.8)	1,252 (88.8)		–	–	–
Parity	Nulliparous	109 (42.7)	539 (38.2)	0.397	–	–	–
	One–Two	130 (51.0)	778 (55.2)		–	–	–
	Greater than Two	16 (6.3)	93 (6.6)		–	–	–

* Low birth weight (LBW), normal birth weight (NBW).
† Significant *P* values represent a crude association between explanatory variable and birth weight outcomes based on χ^2 and Fisher exact tests for each variable separately.
‡ Independent variables identified in univariate models to be associated with LBW (using cutoff of $<$ 0.1) were included in a multivariable logistic regression model with a binomial distribution assumption and log-link accounting for potential confounders. Adjusted odds ratio (AOR), 95% CI, and *P* values reported here.

Pakistan and India found that high and low maternal Hgb concentrations are related to both LBW and neonatal mortality.[34]

High maternal Hgb levels have been associated with preeclampsia, preterm delivery, and fetal growth restriction, but it is still uncertain if these outcomes are caused by high maternal iron levels or by failure of the plasma volume to expand appropriately.[39–41] During pregnancy, a woman's blood plasma will increase by up to 50%, whereas the red blood cell mass only increases by about 25%.[42] This hemodilution leads to a relative anemia in most pregnancies. High Hgb levels can be a sign that the plasma volume has not expanded appropriately in women with pregnancy-induced hypertension, preeclampsia, and fetal growth restriction.[36,41] However, a study of more than 57,000 pregnancies in Norway found that increasing Hgb levels were associated with lower placental weight and impaired fetal growth in women with and without preeclampsia suggesting another mechanism may be involved apart from failed plasma expansion.[43] There is also evidence that a primary elevation in iron levels could cause adverse outcomes in pregnant women via damage to the placenta. High Hgb levels have been associated with placental infarction, which could be caused by an increase in oxidative stress.[44] Elevated iron levels also have been shown to inhibit the uptake of trace elements such as Zn, which are necessary for a healthy pregnancy and fetal growth.[44]

Further research is needed to understand the causal link between high Hgb levels and adverse pregnancy outcomes, including LBW. Although many women did not routinely take their iron supplements, 34 out of 38 of the women with a Hgb $>$13.0 g/dL in this cohort were receiving iron

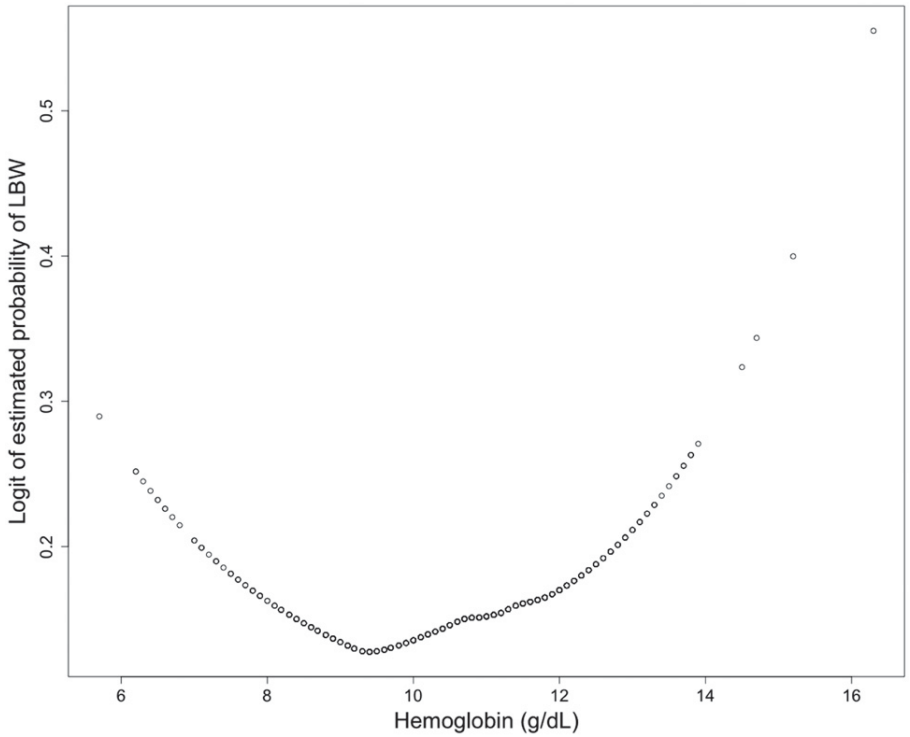

FIGURE 2. U-shaped association of hemoglobin with low birth weight (LBW) outcome. Note: Locally weighted scatterplot smoothing (LOESS) plot of LBW outcome depicting the logit of the estimated probabilities of LBW at given hemoglobin levels, binomial variables are plotted at 0 for normal birth weight (NBW) and 1 for LBW. The current figure is truncated for better viewing of the LOESS curve.

supplementation. It is therefore important to delineate the role, if any, of maternal iron levels in the pathophysiology of hemoconcentration-associated adverse birth outcomes to ensure that iron supplementation does not inadvertently cause harm. Iron supplementation is routinely recommended for pregnant women with normal Hgb levels as it is possible to be pre-anemic and iron deficient. However, it is also possible to be anemic and iron sufficient, as has been documented in Bangladesh.[24,32] It is imperative to understand the impact of these routine iron supplementation programs so as to not cause any harm with these interventions.

STRENGTHS AND LIMITATIONS

The bimonthly house-to-house surveillance, and enrollment of eligible pregnant women into the MNHR highlights both a strength and a limitation of this study. Although the registry achieves an almost 100% catchment and enrollment of pregnant women in this rural area, a considerable number ($N = 316$) of eligible maternal–child dyads were excluded from this analysis due to missing key variables. Given the major challenges to obtaining these variables in a rural setting with limited antenatal care and a large number of home deliveries, the current study performed well when contrasted to comparable studies where as many as 71% of newborns show no birth information.[20] However, as this limitation could not be avoided, we have explored the possibility of systemic differences between the included and excluded groups (Table 2). Compared with those who were excluded, the included group had a slightly higher percentage of educated women and a slightly larger percentage of women in the less than 16 years of age category. These two variables might be expected to have an opposite impact on LBW outcomes and would not be expected to impact the U-shaped relationship of maternal Hgb to the risk of LBW. Other limitations of the study include that Hgb measurements were taken at different times during pregnancy and that some of the Hgb categories had a very small number of subjects.

CONCLUSION

This study demonstrated an overall low rate of severe anemia in this cohort and revealed no significant increase in the risk of LBW in pregnant women with mild-moderate anemia. In contrast, high maternal Hgb values (> 13 g/dL) were associated with an increased risk of neonatal LBW. These findings suggest that iron-deficiency anemia may not be a significant contributor to the high rate of LBW seen in this population. Further research is needed to understand the U-shaped association of maternal Hgb with LBW outcomes, particularly the biological mechanism underlying the association between adverse outcomes and high maternal Hgb values. Understanding this association will give further guidance to the benefits and possible dangers of routine universal iron supplementation during pregnancy.

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OPEN AIMJ ORIGINAL ARTICLE

Obstetrics and Gynecology

Severity of Maternal Iron Deficiency Anemia and Risk for for Low Birth Weight Babies

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ABSTRACT

Background: Anemia is one of the most prevalent diseases in the world affecting all ages and races of patients. Root causes and prevalence vary by age group and socio-economic state.

Aim of the work: is to evaluate maternal Iron deficiency anemia before birth and to know its effect on fetal weight at birth.

Patients and Methods: This is a cross-sectional study which included 500 pregnant females who had presented and admitted to Obstetrics and Gynecology Department of Bab Alseheiria University Hospital at the time of delivery.

Results: Birth weight ranged from 1850 to 3500 gm with mean 2593.192 gm. Thirty six percent (36%) had fetuses with . Hemoglobin level ranged from 6.5 to 10.9 g/dL with mean 9.258 g/dL. Forty-five (45%) had moderate anemia, while 22.6 % had severe anemia. There are statistically non- s between mild, moderate and severe anemic groups regarding age, gravidity, parity, history of abortion and mode of delivery.

Conclusion: Maternal anemia is associated with low birth weight . Also, anaemia in pregnancy is still a major health problem. The improvements achieved in the developed world may largely be due to more effective diagnosis and treatment.

Keywords: *Iron Deficiency;Low Birth;Weight.*

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INTRODUCTION

Anemia is one of the most common disorders in the world and affects patients of all ages and races. The underlying causes and prevalence vary according to age group and socio-economic background, but pregnant women everywhere are highly vulnerable to developing anemia, and the vast majority of cases are attributable to iron deficiency.[1] Iron deficiency is the most common nutritional disorder and the main cause of anemia during pregnancy. Published research shows that maternal iron deficiency affects the health of the mother and the baby, and is also likely responsible for decreased uterine growth, premature births, and cognition. Weakness and lack of nutrition.[2] Babies whose birth weight is less than 2,500 grams are known to be infants, regardless of gestational age. The extent to which maternal hemoglobin affects fetal weight remains uncertain. Some studies showed a strong association between low prenatal hemoglobin, while others did not find a significant association. [3] Therefore, the aim of this study is to evaluate maternal Iron deficiency anemia before birth and to know its effect on the weight of the fetus at birth.

PATIENTS AND METHODS

This is a cross-sectional study which included 500 pregnant females who had presented and admitted to Obstetrics and Gynecology Department of Bab Alseheiria University Hospital at the time of delivery.

The study group was anemic pregnant females according to WHO definition of anemia with pregnancy which is hemoglobin level below 11 gm%.

Inclusion criteria: Singleton, viable pregnancy. Accurate dates Last Menstrual Period (LMP). deficiency anemia: Hb level less than 11g%. Serum iron < 7.1µg/l. Serum ferritin < 30ng/l. Total iron binding capacity > 13.1 µmol. BMI > 19.

Exclusion criteria: Women with multiple pregnancies. Pregnancy duration was less than 37 weeks of gestation. Associated medical maternal complications, which may affect fetal birth weight e.g. diabetes, hypertension and cardiac diseases. History of antiphospholipid syndrome. BMI < 19.

Methods:

Verbal and written informed consent was taken before the start of study. The group of study was evaluated for data collection through: Full history obstetric and gynecological history. Examination finding and exclusion of medical disorders. Hb level measurement before delivery. Assessment of fetal outcome birth weight. Serum ferritin. Serum iron. Total iron binding capacity.

Data collection:

Mother's age and risk(primigravida)They are the females who have never become pregnant, the midwives who have given birth two or three times before are chosen, and the Grand Multara who have given birth five or more times before are chosen. Gestational age (calculated using Nigel's formula).

RESULTS

About 26% were primigravida, 26.4% were nullipara and 87% had no history of abortion. Gravidity ranged from 1 to 6 with median 3. Parity ranged from 0 to 5 with median 2. Abortion ranged from 0 to 3 with median 0. Forty percent (40%) delivered via CS.

Parameter	N=500 (%)
Gravidity:	
Median	**3**
Range	**1 – 6**
Primigravida	**129 (25.8%)**
2 – 3	**284 (56.8%)**
4 – 6	**87 (17.4%)**
Parity:	
Median	**2**
Range	**0 – 5**
Nullipara	**132 (26.4%)**
2 – 3	**307 (61.4%)**
4 – 5	**61 (12.2%)**
Abortion:	
Median	**0**
Range	**0 – 3**
0	**435 (87%)**
1 – 2	**63 (12.6%)**
3	**2 (0.4%)**
Mode of delivery:	
VD	**300 (60%)**
CS	**200 (40%)**

Table 1: Distribution regarding obstetric history:

Birth weight ranged from 1850 to 3500 gm with mean 2593.192 gm. Hemoglobin level ranged from 6.5 to 10.9 g/dL with mean 9.258 g/dL.

Parameter	N=500 (%)
Birth weight (gram):	
Mean ± SD	**2593.192 ± 420.063**
Range	**1850 - 3500**
Hemoglobin:	
Mean ± SD	**9.268 ± 1.189**
Range	**6.5 – 10.9**

Table 2: Birth weight and hemoglobin level among the studied patients:

Thirty six percent (36%) had fetuses with Forty-five (45%) had moderate anemia, while 22.6 % had severe anemia.

Parameter	N=500 (%)
Birth weight:	
	180 (36)
Normal birth weight	**320 (64)**

Table 3: Distribution regarding occurrence of :

There is statistically non- between the studied groups (with various degrees of anemia severity) regarding gravidity, parity, history of abortion or mode of delivery.

Severity	N=250	%
Mild (10 - <11 g/dL)	**162**	**32.4**
Moderate (8 - <10 g/dL)	**225**	**45**
Severe (<8 g/dL)	**113**	**22.6**

Table 4: Distribution of the studied anemic patients according to severity of anemia:

Studied groups (with various degrees of anemia severity) regarding occurrence of . On LSD comparison, the difference is significant between each two groups (LBW prevailed in 73.5% within severe group while it occurred in 11.1% within mild group)

Mode of delivery	Severity			Test	
	Mild	Moderate	Severe	KW/χ^2	p
	N=162	N=225	N=113		
Gravidity: Median Range	**2 1 – 6**	**2 1 – 6**	**3 1 – 6**	**4.589**	**0.101**
Parity: Median Range	**2 0 – 5**	**1 0 – 5**	**2 0 – 5**	**5.814**	**0.055**
Abortion: Median Range	**0 0 – 2**	**0 0 – 3**	**0 0 – 2**	**0.098**	**0.952**
Mode of delivery Vaginal delivery CS	**107 (66) 55 (44)**	**130 (57.8) 95 (42.2)**	**63 (55.8) 50 (44.2)**	**3.783**	**0.151**

Table 5: Relation between obstetric history, mode of delivery and anemia severity:

Birth weight	Severity			Test	
	Mild	Moderate	Severe	χ^2	p
	N=162	N=225	N=113		
LBW	18 (11.1)	79 (35.1)	83 (73.5)	109.5	<0.001**
Normal	144 (88.9)	146 (64.9)	30 (26.5)		
P (χ^2)	P1<0.001**	P2<0.001**	P3<0.001**		

Table 6: Relation between birth weight and anemia severity:

DISCUSSION

Around 7-15% of all live births per year worldwide are of , a pregnancy result that is a significant public health concern that is more common in countries with less financial resources. [4] There is a greater chance of child mortality and morbidity for babies born with a weight of less than 2,500 grams. can be favoured by hormonal, social, environmental variables and insufficient lifestyle, either before or during pregnancy. Some dietary factors, such as a diet that is deficient in nutrients and inadequate weight gain during pregnancy, lead to a reduction in nutrient intake that is necessary for fetal development.such as B vitamins and iron. .[5]

Ionic iron is the mineral that encourages fresh hemoglobin production and is the primary source of transfer of energy and oxygen to the organs of the body. (6) At any point of pregnancy and <100 G / l after birth, the World Health Organisation describes anemia as hemoglobin(Hb)Less than 110g / L. (1) In the second trimester of pregnancy, biochemical changes arise, resulting in increased plasma volume along with less rise in red cell mass, resulting in blood thinning known as "physiological anemia." Thus, in the second trimester, a threshold Hb < 105 G / l is commonly used in all international standards for assessing and directing treatment [7]

It is anemia caused by iron deficiency (IDA). Roughly 50 percent of cases are worldwide. In terms of iron status, it is necessary to remember that with reduced iron reserves, a significant number of women start pregnancy. In the United States, iron stores are robbed of more than a third of women of childbearing age. At the onset of birth, CRI is 3.8 times more common in pregnant women, which confirms the hypothesis of reduced iron reserves before conception. [8]

Brannon and Taylor estimated [6] 18 percent of IDA distributed among women who are pregnant with hemoglobin levels lower than 115 g/L and ferritin levels lower than <12 Ng/ml increased by 19.6 percent, identified as <12 Ng/ml.

in infancy and adolescence is a significant determinant of death, morbidity and injury and has a long-term health effect in adult life. In babies with a (LBW), newborns are 20 times more likely to die than larger babies (about 2.5 Kg) worldwide. It has also been found to be a significant neonatal morbidity risk factor. There are two results, namely short gestational age (premature birth) and limited gestational age, presumably representing a group LBW (childbirth of eight babies less than 2.5 kg) (SGA). [10]

Regarding the obstetric history of the group studied in this study, approximately 26% were virologists, 26.4% were drug-dependent and 87% had no history of miscarriage.. Gravity ranged from 1 to 6 with an average 3. It ranged from parity from 0 to 5 with an average 2. Ranging abortion Z from 0 to 3 average 0 .

In our study, forty percent (40%) were delivered via computer science. Terefe et al.compare [13] Hematological features and iron status in newborns from mothers with various anemia and found that most babies were born via vaginal delivery (78.7%).

In our study ranged from birth weight for patients undergoing a study from 1850 to 3500 grams with an average 2593.192 grams. Thirty-six percent (36%) had fetuses with . Terefe et al.is found [13] The children had an average weight 3,100 grams and was the number of a few of them low weight when childbirth Dah .

In our study, ranged hemoglobin level from 6.5 to 10.9 g / dl an average of 9.258 g / dl. Terefe et al.is found [13] The average level of hemoglobin mothers was 12.2 g / dl .

In our study, the 45 patients study subjects (45%) suffer from anemia average , while it was 22.6 % suffer from anemia blood acute . There are statistically s is statistically significant between the groups of blood anemia mild, medium and severe with regard to age and gravity , and Altec Equal and history of abortion and the method of birth .

Color et al. [14] In the anemic population, the probability of reduced birth weight was 1.9 times greater. [14] Jones et al. [15] In anemic mothers, a rise in the occurrence of was also found, but the difference from the non-anemic population was marginal.

Terefe et al. [13] Cohort mothers with low levels of hemoglobin (<11 g/dL) under IDA. Mothers with average levels of hemoglobin (11 g / dL) were graded as: NA. 21 mothers (23.6 percent) were then classified as IDA Bloody, while the remaining 68 mothers (76.4 percent) are in the NA. They concluded that IDA Maternal may have an effect on the baby's iron reserves

CONCLUSION

This research revealed that iron deficiency anemia in pregnant women is a reasonably common disease. High risk factors are low socioeconomic status, various groups, and old maternal age, and should be taken into account. These reports showed that as a prevention measure, intensive monitoring and supplementation in high-risk pregnancies should be assessed. The latest studies show that is linked with maternal anemia. Anemia still remains a significant health concern during breastfeeding. Improvements made in the developing world can be partly due to more successful care and diagnosis..

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Determinants of Low Birth Weight Among Women Who Gave Birth at Public Health Facilities in North Shewa Zone: Unmatched Case-Control Study

Berhanu Senbeta Deriba[1] and Kemal Jemal[2]

Abstract

Globally, more than 20 million newborns are born with low birth weight (LBW) every year. Most of the LBW occurs in low- and middle-income countries. It is the most critical risk of neonate mortality. Therefore, this study aims to identify determinants of low birth weight among women who gave birth in public health facilities in the North Shewa zone. Institutional-based unmatched case–control study was conducted from February to June 2020 to select 180 cases and 380 controls. Interviewer-administered questionnaire was used to collect data. Data were entered through EPI Info and exported to Statistical Package for Social Science (SPSS) for analysis. Text, percentage and tables were used to present data. Bivariate and multivariate logistic regression analyses were performed to see the association, and adjusted odds ratios with 95% confidence interval (CI) and *P*-value < .05 were considered to declare statistical significance. Lack of nutritional counseling (adjusted odds ratio [AOR] = 2.14; 95% CI = [1.13, 4.04]), unable to take iron-folate supplement (AOR = 2.3.78; 95% CI = [2.1, 6.85]), insufficient additional meal in take (AOR = 6.93; 95% CI = [3.92, 12.26]), restriction of foods (AOR=2.29; 95% CI =[1.81, 4.09]), maternal mid upper arm circumference (MUAC) < 23 cm (AOR=2.85; 95% CI = [1.68, 4.85]), maternal height ≤155 cm (AOR=3.58; 95% CI = [1.92, 6.7]), anemia (AOR = 2.34; 95% CI = [1.21, 4.53]), pregnancy-related complications (AOR=3.39; 95% CI = [2.02, 5.68]), and alcohol drinking during pregnancy (AOR = 2.25; 95% CI = [1.24, 4.08]) were significantly associated with LBW. Nutritional counseling, iron-folate supplementation, additional meal intake, restriction of some foods in pregnancy, MUAC of the mother, maternal stature, maternal anemia status, pregnancy-related complications, and history of alcohol drinking during pregnancy were identified as determinants of low birth weight. The intervention-targeted nutritional counseling, early detection and treatment of anemia, and behavioral change communication to pregnant women are mandatory.

Keywords

Determinants, low birth weight, North Shewa, public health facilities, Ethiopia

What do we already know about this topic?

The prevalence of low birth weight was already assessed, and factors like socio-demographic, disease-related and pregnancy-related were identified.

How does your research contribute to the field?

This research finding was contributed to the current research field because our study findings are unique in obtaining

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determinants of low birth weight like food taboo and substance use (alcohol drinking) which are new findings in Ethiopia.

What are your research's implications toward theory, practice, or policy?

We anticipated that our findings provide basis for low birth weight determinants that are significant for intervention of pregnant mothers.

Background

The World Health Organization (WHO) defined LBW as weight at birth less than 2500 g.[1] Birth weight is the main indicator of the child's susceptibility to childhood diseases. Most of the time, the cause of LBW is premature birth, intrauterine growth restriction, or the combination of both.[2] In developing countries, the cause of LBW is premature birth, whereas intrauterine growth restriction in developed nations.[3]

Low birth weight is the most critical risk for neonate mortality,[4] which contributes 60-80% of neonatal morbidity and mortality.[5] LBW newborns are almost 20 times at high risk to die than newborns with normal birth weight.[6]

Long-term complications of LBW include hypertension, diabetes mellitus, later-age renal diseases, eye problems, deafness, neurologic complications like cerebral palsy, developmental delay, seizure, and psychological disturbances.[7-9] Another impact of LBW is being at higher risk of infection, poor mental development, stunting, and developing noncommunicable diseases.[5]

More than 20 million newborns are born with LBW globally every year.[10] Most of the LBW occurs in low- and middle-income countries.[11] The prevalence of LBW is ranging from 9 to 35.1% in developing countries.[12] The prevalence of LBW in Africa was 22%[13] and 13% in Ethiopia.[14] Some of the factors that are positively associated with LBW in developing countries include advanced maternal age (35-49 years), mothers who have informal education, female newborns, delayed conception, inadequate antenatal care, primiparity, living in rural areas, and low socioeconomic status.[12] Other different studies from Ethiopia reported that pregnancy-induced hypertension, low maternal educational status, low maternal height, incomplete antenatal care, household food insecurity, lack of iron supplementation, anemia, unable to take additional food, preterm birth, medical problems during pregnancy, MUAC of mother <23 cm, lack of nutritional counseling, and previous history of abortion are factors that are associated with LBW.[15-19]

The WHO planned to achieve a reduction of LBW by 30% in 2025, but the prevalence of LBW is not decreasing to achieve the WHO target.[10] Even though the Ethiopian Federal Ministry of Health also developed a national nutrition strategy to improve the micronutrient deficiency among pregnant women through increasing the system to give comprehensive and routine nutritional assessment intervention, the magnitude of LBW was not decreased yet. Additionally, the Ministry of Health of Ethiopia provided routine iron–folate supplementation and deworming during pregnancy to mitigate adverse birth outcomes like LBW, but the prevalence of LBW was not reduced.[20] Even if this strategy strives to improve LBW, it is still a public health problem among newborns in Ethiopia. Despite food taboo is very common in Ethiopia, its relationship with the occurrence of adverse birth outcome like low birth weight was not studied. Therefore, this study aimed to identify low birth weight determinants among women who gave birth in public hospitals in the North Shewa zone, central, Ethiopia.

Methods

Study Design, Period, and Setting

Unmatched case-control was conducted from February to June 2020 in five public hospitals and 14 health centers in the North Shewa zone. Fiche is the capital city of the zone and 114 km away from Addis Ababa. The North Shewa zone has a total population of 1.6 million according to 2007 census. From the total population, 49,667 were pregnant women and expected to give birth according to the North Shewa Zone health office report. The Zone has five hospitals and 50 health centers that provide antenatal care, delivery, and postnatal services to the North Shewa Zone communities.

Source and Study Population

All women who gave birth in public hospitals in the North Shewa zone during data collection were source population for both cases and controls, whereas those included in the study were the study population for both cases and controls. Women who were deaf, unable to speak or communicate, severely ill (comatose women and women who had postpartum hemorrhage), and those who delivered deformed newborns were excluded from the study. Cases were mothers who gave live birth weighed less than 2500 g, whereas mothers who gave live birth weighed greater than 2500 g were controls.[1]

Sample Size Calculation and Sampling Procedure

The sample size was calculated by using double population proportion formula through EPI INFO version 7 statistical software package with the assumption of confidence level 95% ($Z\alpha/2 = 1.96$), power 80% ($Z\beta = .84$), case to control ratio 1:2, where P1 is the proportion of cases exposed, and P2 is the proportion of controls exposed. By taking unable to take iron and folic acid supplementation during pregnancy as identified, the study was conducted in Dessie town, Ethiopia in 2017 (proportion of cases that did not take iron-folate supplementation is31.2%, and the proportion of controls that did not take iron-folate supplementation is 10.8%, and AOR = 2.84).[18]

This gave 95 cases and 190 controls with a total of 285. After multiplying this by design effect 2, the final sample was 190 cases and 380 controls with a total of 570 study participants. The study was conducted at five hospitals and randomly selected 14 health centers. The number of study participants was allocated proportional to each health facility based on estimations obtained from the average of previous quarter delivery services by referring to delivery registration books at each hospital. Therefore, the sample of each hospital was calculated by multiplying the average number of pregnant women who delivered in each hospital per 5 months with the total sample size, dividing by a total number of pregnant women attending antenatal care units for 5 months of all hospitals, which was obtained from delivery registration of the previous months. Multi-stage sampling was used to select health facilities. Cases were selected by taking all cases until the required sample size obtained, and controls were selected using systematic random sampling.

Data Collection Tools, Procedure, and Management

The data were collected by an interviewer-administered questionnaire, which was developed from different similar works of the literature.[12,9,16] The questionnaire was prepared in English and translated to a local language Afan Oromo for a better understanding of both data collectors and respondents. It was translated back to the English language by language experts to check for consistency. The questionnaire contained socio-demographic characteristics (age, marital status, educational status, place of residence, religion, ethnicity, occupation, and monthly income), maternal nutritional factors (nutritional counseling, iron–folic acid (IFA) supplementation), restriction of food or food taboo (restriction of food made from butter, fruits, and vegetables during whole pregnancy due to fear of fetus overdevelopment and attachment to the fetus during pregnancy), food frequency (meal), additional food (adding frequency of food and amount of food intake during pregnancy), fasting (unable to take any food and fluid for 9 h on Wednesday and Friday), and substance use-related factors (cigarette smoking, alcohol drinking, and chat chewing during pregnancy) were obtained by face-to-face interview. MUAC of the mother, height of mother, obstetrics and gynecologic factors (previous history of abortion, number of abortion, previous history of adverse birth outcomes [LBW, premature birth, and stillbirth]), gravidity, parity, birth interval, pregnancy status, antenatal care (ANC) visit, number of ANC visits, medical illness for recent pregnancy (hypertension, diabetes, urinary tract infection, and sexually transmitted diseases) and pregnancy-related complications (gestational hypertension, premature rupture of membrane, antepartum hemorrhage, gestational age, and anemia status) were obtained from patients' 'records.

Ten BSc mid-wives were recruited for data collection, and five BSc public health officers were superviced data collection. Three days of training was given for data collectors and supervisors on the objective of the study and how to maintain the confidentiality of the respondents. Additionally, data collectors and supervisors were trained about COVID-19 prevention technique and offered the prevention materials (mask, alcohol or sanitizer, and soap) to implement during data collection. Pretest was conducted on 5% of the sample at Chencho Hospital which is outside the study area. Investigators, data collectors, and supervisors discussed the questionnaire and made necessary correction where necessary after pretest before actual data collection. Close supervision was done during data collection.

The interview was conducted 1 h after delivery and after the newborn's weight was measured. The weight of newborn was measured 1 h after delivery using a balanced digital Seca scale (Germany). The scales were always calibrated using the materials with the standard weight and the reading on each scale by taking to zero levels before weighing each newborn. Mother's height was also measured using a height board while the mother was in the standing position which was taken from height measured before delivery. The height of each mother was taken to the nearest .1 cm. Mother was asked to stand without shoes in front of the height board with head erect and arms hanging naturally at the sides. The MUAC of the mother was measured using a flexible, non-stretchable standard tape meter to the nearest .1 cm to determine the nutrition of the mother. The outcome (low birth weight) is identified according to the WHO definition, weight at birth less than 2500 g.[1] The reliability of the questionnaire was checked with Cronbach's alpha with the value of .876.

Data Processing and Analysis

After data collection, data were checked for completeness and coded, cleaned, and entered using EPI INFO version 7 and were exported to SPSS version 23 for data cleaning and analysis. After cleaning data for inconsistencies and missing values, texts, tables, and proportions were used to present data. Logistic regression was carried out to identify independent predictors of low birth weight. Bivariate analysis was carried out to determine a significant association between each predictor variable and low birth weight at a P-value < .25. Bivariate and multivariate logistic regression analyses were carried out to determine an association between low birth weight and independent variables.

Multivariate logistic regressions were carried out to identify determinants of low birth weight among women who gave birth in public hospitals. The goodness-of-fit model (Hosmer and Lemeshow) was used to select the best multivariate model. Multicollinearity was checked by using standard error. Finally, AOR with 95% CI and P-value < .05 were considered to declare statistical significance.

Ethical Consideration

The Salale University Ethical Review Committee approved the ethical clearance with Reference number SLUERC/019/2020. A formal letter of cooperation was written to each

hospital. Written consent was obtained from study participants who were above 18 years old, and written assent was obtained from their parents or guardians where participants were women under 18 years of age. The privacy and confidentiality of study participants were also protected strictly. Data collectors were informed about coding the questionnaire and not to write the name of the study participants. Only data collectors saw the records of the study participants.

Result

Socio-Demographic Characteristics of the Study Participants

A total of 555 study participants (185 cases and 370 controls) were participated in this study, making a response rate of 97.37%. The mean ages of study participants were 27.71 ± 5.72 for cases and 26.98 ± 5.20 for controls; ranging from 17-42 for cases and 17-43 for controls. Nearly one-third, 62 (32.4%) of cases and 91 (24.6%) of controls, had no formal education (Table 1).

Table 1. Socio-Demographic Characteristics of Women Who Gave Birth at Public Health Facilities in the North Shewa Zone from February to June 2020 (n = 185 Cases and n = 370 Controls).

Variable	Cases: n (%)	Controls: n (%)
Residence		
Urban	68 (36.8)	176 (47.6)
Rural	117 (63.7)	194 (52.4)
Age groups in years		
<20	16 (8.6)	30 (81.1)
21-34	151 (81.6)	312 (84.3)
≥35	18 (9.8)	28 (7.6)
House hold monthly income in Ethiopian Birr		
<1650	81 (43.8)	74 (20)
1651-3199	30 (16.2)	64 (17.3%)
3200-5249	15 (8.1)	52 (14.1)
≥5250	59 (31.9)	180 (48.6)
Ethnicity		
Oromo	134 (34.2)	259 (70)
Amahara	48 (25.9)	85 (23)
Others[a]	3 (1.6)	26 (7)
Religion		
Orthodox	83 (44.9)	195 (52.7)
Protestant	73 (39.5)	129 (34.9)
Muslim	22 (11.9)	26 (7)
Others[b]	7 (3.8)	20 (5.4)
Family size		
≤5	106 (57.3)	237 (64.1)
>5	79 (42.7)	133 (35.9)
Educational level of the mother		
Have no formal education	62 (32.4)	91 (24.6)
Have formal education	123 (67.6)	279 (75.4)
Marital status		
Married	183 (99.9)	355 (95.9)
Single	2 (1.1)	15 (4.1)
Educational level of husband		
Have no formal education	60 (32.4)	54 (14.6%)
Have formal education	125 (67.6%)	316 (85.4%)
Occupation of mother		
Employed	38 (20.5)	102 (27.6)
Unemployed	147 (79.5)	268 (72.4)
Occupation of husband		
Employed	41 (22.2)	122 (33)
Unemployed	144 (77.8)	248 (67)

[a]Tigre and Gurage.
[b]Catholic and WaKefata.

Nutritional-Related Characteristics of Study Participants

Seventy-six (41.1%) of cases and 50 (13.5%) of controls had no nutritional counseling for their recent pregnancy. One hundred nine (58.9%) of cases and 54 (14.6%) of controls did not take iron-folate supplementation for their recent pregnancy. More than three-fourths (142; 76.8%) of cases and around half (184; 49.7%) of controls did not take additional meals for their recent pregnancy. Seventy-one (38.4%) of cases and 63 (17%) of controls were restricted to eat foods made from meat, butter, fruits, and vegetables during pregnancy due to fear of fetal overdevelopment and attachment to the fetus. Eighty-six (46.5%) of cases and controls had MUAC less than 23 cm. Fifty (13.2%) of cases and 49 (13.2%) of controls did not eat dark green leafy vegetables totally (Table 2).

Food Frequency of the Respondents

The study participants who did not eat red meat were 55.2% for cases and 29.7% for controls. Greater than one-fourth of cases and 13.2% of controls did not eat dark green leafy vegetables at all. More than one-third of cases and 14.6% of controls did not eat fruits at all times. Greater than one-fourth of cases and 34.3% of the controls take milk and milk products daily (Table 3).

Obstetrics and Gynecologic Characteristics of the Study Participants

Sixty-three (34.1%) of cases and one-third, 123 (33.2%), of controls were nulliparous. More than one-fourth, 33 (27%) of cases and 50 (20.2%) of controls, had birth interval <2 years. Twenty (10.8%) of cases and 33 (8.9%) of controls faced abortion. Half, 62 (50.4%), of cases and 42 (17%) of the controls had a history of adverse birth outcomes. Twenty-nine (23.77%) of cases and 10 (4.5%) of the controls had LBW history. Near to three-fourths, 135 (73%) of cases and 344 (93%) of controls, had ANC visits in their recent pregnancy. One hundred fifteen (62.2%) of cases and 137 (37%) of controls faced pregnancy-related complications like PROM, PIH, and

Table 2. Nutritional-Related Characteristics of Women Who Gave Birth at Public Health Facilities in North Shewa Zone, from February to June 2020 (n = 185 Cases, and n = 370 Controls).

Variables	Cases: n (%)	Controls: n (%)
Nutritional counseling		
Yes	109 (58.9)	320 (86.5)
No	76 (41.1)	50 (13.5)
Meal frequency		
≤2 times	61 (33)	34 (9.2)
3 times	72 (38.9)	192 (51.9)
≥4 times	52 (28.1)	144 (38.9)
Iron-folate supplementation during the recent pregnancy		
Yes	76 (41.1)	316 (85.4)
No	109 (58.9)	54 (14.6)
Took additional food during the recent pregnancy		
Yes	43 (23.2)	186 (50.3)
No	142 (76.8)	184 (49.7)
Had history of food restriction for recent pregnancy		
Yes	71 (38.4)	63 (17)
No	114 (61.6)	307 (83)
Types of restricted foods for recent pregnancy		
Butter and fatty meat	2 (2.8)	11 (17.46)
Fruits and vegetables	69 (97.2)	52 (82.54)
Reason for food restriction		
Fear of fetal overdevelopment	53 (74.65)	46 (73)
Fear of attachment to the fetus	18 (25.35)	17 (27)
Fasting during recent pregnancy		
Yes	78 (42.2)	141 (38.1)
No	107 (57.8)	229 (61.9)
MUAC of mother in centimeters		
<23	86 (46.5)	78 (21.1)
≥23	99 (53.5)	292 (78.9)
Height of mother in centimeters		
≤155	60 (32.4)	46 (12.4)
>155	125 (67.6)	324 (87.6)

Table 3. Food Frequency of Women Who Gave Birth at North Shewa Public Health Facilities From February to June 2020 (n = 185 Cases, and n = 370 Controls).

Variables	Cases: n (%)	Controls: n (%)
Frequency of eating red meat		
At least once/weak	11 (5.9)	37 (10)
Once per 2 weeks	72 (38.9)	223 (60.3)
Do not take	102 (55.2)	110 (29.7)
Frequency of eating organ meat		
At least once/weak	9 (4.9)	26 (7)
Once per 2 weeks	18 (16.8)	84 (22.7)
Do not take	31 (76.4)	260 (70.3)
Frequency of eating dark green leafy vegetables		
Daily	13 (7)	36 (9.7)
Every other day	46 (24.9)	108 (29.2)
1-2 times/weak	28 (15.1)	93 (25.1)
Once per 2 weeks	48 (25.9)	84 (22.8)
Do not take	50 (27)	49 (13.2)
Frequency of eating fruits		
At least every other day	25 (13.5)	76 (20.5)
1-2 times/weak	47 (25.4)	140 (37.8)
Once/2 weeks	48 (25.9)	100 (27)
Do not take	65 (35.1)	54 (14.6)
Frequency of eating eggs		
Daily	5 (2.7)	17 (4.6)
Every other day	41 (22.2)	113 (30.5)
1-2 times/weak	57 (30.8)	116 (31.4)
Once/2 weeks	45 (24.3)	86 (23.2)
Do not take	37 (20)	38 (10.3)
Frequency of taking milk and milk products		
Daily	49 (26.5)	127 (34.3)
Every other day	49 (26.5)	116 (31.4)
1-2 times/weak	48 (25.9)	81 (21.9)
Once/2 weeks	22 (11.9)	40 (10.8)
Do not take	17 (9.2)	6 (1.6)
Frequency of eating foods made from teff		
Daily	116 (62.7)	284 (76.8)
Every other day	46 (24.9)	62 (16.8)
Once/weak	21 (11.6)	8 (2.2)
1-2 times/weak	1 (.5)	12 (3.2)
Do not take	1 (.5)	4 (1.1)

APH during their recent pregnancy. Near to one-third, 64 (34.6%) of cases and 40 (10.8%) controls, had anemia (Table 4).

Substance Use-Related Characteristics of the Study Participants

Five (2.7%) of cases and 7 (1.9%) of the controls had a history of cigarette smoking in recent pregnancy. Seventy-six (41.1%) of cases and 76 (20.5%) of controls also had a history of alcohol drinking in recent pregnancy. Nearly one-tenth, 17 (9.2%) of cases and 8 (2.2%) of the controls, had a history of chat chewing during the recent pregnancy (Table 5).

Determinants of Low Birth Weight

Bivariate logistic analysis was performed for each independent variable. All variables that showed association in binary logistic regression and had no collinearity were entered into multivariate logistic regression. The results of multivariate logistic regression showed that mothers who had no nutritional counseling had 2.14-folds higher odds of delivering LBW newborn compared to those who had nutritional counseling (AOR, 2.14; 95% CI, 1.13, 4.04). Mothers who did not take iron-folate supplementation had 3.78 higher odds of giving LBW newborn compared to their counterparts (AOR, 3.78; 95% CI, 2.1, 6.85). Mothers who did not take additional food had 7-folds higher odds of giving LBW newborn compared to their counterparts (AOR, 6.93; 95% CI, 3.92, 12.26). Mothers who were restricted to eat some foods

Table 4. Obstetric and Gynecologic Characteristics of Women Who Gave Birth at Public Health Facilities in North Shewa Zone, from February to June 2020.

Variables	Cases: n = 166 (%)	Controls: n = 332 (%)
Gravidity		
Nulliparous	63 (34.1)	123 (33.2)
Multiparous	122 (65.9)	247 (66.8)
Parity		
1-4	153 (82.7)	327 (89.2)
≥5	32 (17.3)	40 (10.8)
Birth interval		
<24 months	33 (27)	50 (20.2)
≥24 months	89 (73)	197 (79.8)
Previous mode of delivery		
Spontaneous vaginal delivery	116 (95)	207 (83.8)
Cesarean section	4 (3.28)	14 (5.67)
Instrumental	2 (1.72)	26 (10.53)
History of abortion		
Yes	20 (10.8)	33 (8.9)
No	165 (89.2)	337 (91.1)
Previous history of adverse birth outcomes		
Yes	62 (50.4)	42 (17)
No	60 (49.6)	205 (83)
Previous history of low birth weight		
Yes	29 (23.77)	10 (4.5)
No	93 (76.33)	237 (95.5)
Status of recent pregnancy		
Wanted and planned	82 (44.3)	254 (68.6)
Wanted but not planned	50 (27)	86 (23.2
Neither wanted nor planned	53 (28.6)	30 (8.2)
Had visited ANC for her recent pregnancy		
Yes	135 (73)	344 (93)
No	50 (27)	26 (7)
HIV/AIDS status of the mother		
Positive	13 (7)	9 (2.4)
Negative	172 (93)	361 (97.6)
Had diagnosed medical illness		
Yes	37 (20)	44 (11.9)
No	148 (80)	326 (88.1)
Obstetrics complication for recent pregnancy		
Yes	115 (62.2)	137 (37)
No	70 (37.8)	233 (63)
Hemoglobin level		
<11 g/dl	64 (34.6)	40 (10.8)
≥11 g/dl	121 (65.4)	330 (89.2)
Gestational hypertension		
Yes	37 (20)	44 (11.9)
No	148 (80)	326 (88.1)
Premature rupture of membrane		
Yes	70 (37.8)	67 (18.1)
No	115 (62.2)	303 (81.9)
Ante partum hemorrhage		
Yes	12 (6.5)	23 (6.2)
No	173 (93.5)	347 (93.8)

Table 5. Substance Use-Related Characteristics of Women Who Gave Birth at Public Health Facilities in North Shewa Zone, from February to June 2020 (n = 185 Cases, and n = 370 Controls).

Variables	Cases	Controls
Mother history of cigarette smoking		
Yes	5 (2.7%)	7 (1.9%)
No	180 (97.3%)	363 (98.1%)
Mother history of alcohol drinking		
Yes	76 (41.1%)	76 (20.5%)
No	109 (58.9%)	294 (79.5%)
Frequency of alcohol drinking		
Daily	5 (6.6%)	14 (18.4%)
Once per week	19 (25%)	18 (23.7%)
Occasionally	49 (68.4%)	44 (57.9%)
Mother history of chat chewing		
Yes	17 (9.2%)	8 (2.2%)
No	168 (90.8%)	362 (97.8%)
Husband history of cigarette smoking		
Yes	31 (16.8%)	24 (6.5%)
No	154 (83.2%)	346 (93.5%)

had 2.29-folds higher odds delivering LBW newborn compared to their counterparts (AOR, 2.29; 95% CI, 1.81, 4.09). Mothers who had MUAC <23 cm had 2.85-folds higher odds of delivering LBW newborn compared to those who had MUAC ≥23 cm (AOR, 2.85; 95% CI, 1.68, 4.85). Women whose height was ≤155 cm had 3.58-folds higher odds of delivering LBW newborn compared to their counterparts (AOR, 3.58; 95% CI, 1.92, 6.7). Anemic women had 2.34-folds higher odds of giving LBW newborn than non-anemic women (AOR, 2.34; 95% CI, 1.21, 4.53). The odds of giving LBW newborn were 3.39 folds higher among women who had pregnancy-related complication compared to their counterparts (AOR, 3.39; 95% CI, 2.02, 5.68). Women who drank alcohol had 2.25-folds higher odds of delivering LBW babies compared to their counterparts (AOR, 2.25; 95% CI, 1.24, 4.08) (Table 6).

Discussion

Unable to get nutritional counseling during pregnancy was a significant determinant of low birth weight in this study. This finding is similar to a case-control study conducted in Dassie town,[18] where nutritional counseling was an independent predictor of LBW. This might be because nutritional counseling enables and improves women's food intake, improves their nutritional status, and finally decreases the risk of giving LBW babies. The present study revealed that mothers who did not take iron-folate supplementation during their recent pregnancy had higher odds of giving LBW babies than mothers who received iron-folate supplementation. It is in line with a study conducted in Dassie town,[18] Kambata,[16] Amhara, Ethiopia,[17] Rural Ethiopia,[21] Gahana,[22] Auckland, New Zealand,[23] and Bangladesh[24] that showed unable to take iron-folate during pregnancy associated positively with LBW. This might be due to intake of iron helps women not to develop anemia and risk of delivering LBW babies since the required amount of iron cannot be obtained from nutrients alone during pregnancy.[25]

Intake of additional meals at recent pregnancy had a significant association with LBW in our study. It is consistent with the study conducted in Kambata,[16] Dassie town,[18] and Ghana[26] where the chance of giving LBW newborns is higher among mothers who did not eat additional food compared to their counterparts. Taking additional meals is important for women themselves and their fetuses in pregnancy.[27] The only way the fetus obtains nutrients from the mother is through the placenta. When the mother did not get additional meals during pregnancy, the nutrients transferred to the fetus through the placenta are reduced, which causes restriction of fetal growth that leads to LBW.[28] Unable to take additional meals also attributes to anemia, premature birth, and pregnancy-related complications that, in turn, lead to LBW.[29]

Women who had MUAC <23 cm have higher odds of delivering LBW neonates than those who had MUAC ≥23 cm. It is similar to studies conducted in Dassie town, Ethiopia,[18] Amhara, Ethiopia,[17] Guinea-Bissau,[30] and Bangladesh[12] where maternal under-nutrition is positively associated with LBW. The reason behind this fact is that low nutritional status of the mother leads to different diseases that may cause LBW. Moreover, maternal under-nutrition may also cause fetal retardation because of the very low transfer of nutrients from the mother to her fetus, which leads to LBW.[31]

Food taboo was positively associated with occurrence of LBW. This is because these restricted foods are vital food groups whose deficiencies cause malnutrition like anemia, which leads to LBW. Furthermore, when mothers do not take enough foods, nutrients transferred to the fetus through the placenta can be decreased, leading to fetus growth restriction and LBW. In contrast, a study conducted in Addis Ababa, Ethiopia, found the opposite.[9] The reason for the disparity between the two findings is due to the socio-cultural characteristics of the two populations; the current study was conducted in rural and town settings, whereas the previous study was conducted in the country's capital city, where the community may have extensive knowledge. The pregnancy-related complication was another predictor of LBW. It is in agreement with a case-control study conducted in Addis Ababa,[9] a case-control study conducted at public hospitals in the Amhara region,[17] at referral hospitals in North Ethiopia,[32] where pregnancy-related complication was positively associated with LBW. The reason behind this fact is that pregnancy-related complications can cause a reduction in nutrients and oxygen to the fetus, which in turn leads to LBW.[17]

Low maternal stature was an independent predictor of LBW. This finding is in line with studies conducted in Addis Ababa,[9] Morocco,[33] Cameroon,[34] Nigeria,[35] Eastern Nepal,[36] and India,[37,38] where maternal stature is significantly

Table 6. Factors Associated With Low Birth Weight Among Women Who Gave Birth at Public Health Facilities in the North Shewa Zone from February to June 2020 (n = 185 Cases, and 370 Controls).

Variables	Cases	Controls	COR, 95% CI	AOR, 95% CI
Educational status of the mother				
Has no formal education	62 (32.4%)	91 (24.6%)	1.55 (1.05, 2.27)	.59 (.33, 1.04)
Has formal education	123 (67.6%)	279 (75.4)	1	1
Nutritional counseling				
Yes	109 (58.9%)	320 (86.5%)	1	1
No	76 (41.1%)	50 (13.5%)	4.46 (2.94, 6.78)	2.14 (1.13, 4.04)[a]
IFA supplementation				
Yes	76 (41.1%)	316 (85.4%)	1	1
No	109 (58.9%)	54 (14.6%)	8.39 (5.56,12.66)	3.78 (2.1, 6.85)[a]
Additional meal				
Yes	43 (23.2%)	186 (50.3%)	1	1
No	142 (76.8%)	184 (49.7%)	3.34 (2.24, 4.97)	6.93 (3.92,12.26)[a]
Restriction of foods during pregnancy				
Yes	71 (38.4%)	63 (17%)	3.04 (2.03, 4.54)	2.29 (1.81, 4.09)[a]
No	114 (61.6%)	307 (83%)	1	1
MUAC of the mother				
<23 cm	86 (46.5%)	78 (21.1%)	3.25 (2.22, 4.77)	2.85 (1.68, 4.85)[a]
≥23 cm	99 (53.5%)	292 (78.9%)	1	1
Height of the mother				
≤155 cm	60 (32.4%)	46 (12.4%)	3.38 (2.19, 5.23)	3.58 (1.92,6.7)[a]
>155 cm	125 (67.6%)	324 (87.6%)	1	1
Frequency of eating DGLV				
Daily	13 (7%)	36 (9.7%)	1	1
Every other day	46 (24.9%)	108 (29.2%)	1.18 (.57, 1.43)	.5 (.19, 1.32)
1-2 times per week	28 (15.1%)	93 (25.1%)	.83 (.4, 1.79)	.31 (.11, 1.01)
Once per 2 weeks	48 (25.9%)	84 (22.8%)	1.58 (.77, 3.27)	.39 (.15, 1.04)
Do not take	50 (27%)	49 (13.2%)	2.83 (1.34, 5.96)	.68 (.26, 1.8)
ANC for recent pregnancy				
Yes	135 (73%)	344 (93%)	1	1
No	50 (27%)	26 (7%)	4.9 (2.93,8.19)	1.03 (.47, 2.26)
Anemia status of the mother				
<11 g/dl	64 (34.6%)	40 (10.8%)	4.36 (2.79, 6.82)	2.34 (1.21, 4.53)[a]
≥11 g/dl	121 (65.4%)	330 (89.2%)	1	1
Medical illness on recent pregnancy				
Yes	37 (20%)	44 (11.9%)	1	1
No	148 (80%)	326 (88.1%)	4.9 (2.93, 8.19)	1.53 (.78, 3)
Pregnancy-related complication				
Yes	115 (62.2%)	137 (37%)	2.79 (1.94, 4.02)	3.39 (2.02, 5.68)[a]
No	70 (37.8%)	233 (63%)	1	1
Drinking alcohol				
Yes	76 (41.1%)	76 (20.5%)	2.7 (1.83, 3.97)	2.25 (1.24, 4.08)[a]
No	109 (58.9%)	294 (79.5%)	1	1
Gestational age in weeks				
<37	64 (30.8%)	57 (17.3%)	2.13 (1.41, 3.22)	.91 (.5, 1.66)
≥37	306 (69.2%)	128 (82.7%)	1	1

Note. 1= reference; COR = crude odds ratio; AOR = adjusted odds ratio.
[a]Statistically significant at *P*-value < .05.

associated with the occurrence of LBW. This might be because mothers with short stature may also have narrow pelvis with limited intrauterine space that restricts the fetus's intrauterine growth, leading to LBW.[39]

Anemia of mother was statistically significantly associated with LWB. This finding is in agreement with a case-control study conducted at Kambata,[16] Dassie town,[18] Gahana,[22] Nigeria,[35] and Nepal[40] that found a statistically significant

association between anemia and LBW. This is because anemia is caused due to the reduction of red blood cells (hemoglobin), and it can cause the amount of maternal blood production, which leads to the reduction of nutrients received by the fetus. This reduced amount of fetal nutrient causes restriction of fetal growth and leads to LBW.

Drinking alcohol was positively associated with occurrence of LBW. It is similar to another study where consuming one drink at least once per day was associated with LBW.[41] This is because due to unknown factor that leads to an increased risk of fetal retardation. Finally, the limitation of this study is that it may be susceptible to recall and social desirability bias.

Conclusion

Nutritional counseling, iron-folate supplementation, additional meal intake, restriction of some foods in pregnancy, mid-upper arm circumference of the mother, maternal stature, maternal anemia status, pregnancy-related complications, and history of alcohol drinking in pregnancy were identified determinants of low birth weight. Intervention on LBW prevention should consider nutritional counseling, additional meal intake, iron-folate supplementation, early detection, and treatment of anemia, avoiding alcohol drinking in pregnancy. Behavioral change communication targeting pregnant women to reverse food taboos by health professionals.

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Authors Contributions

BSD and KJ were involved in idea creation, proposal development, supervising, data collection, data analysis, interpreting results, editing, supervision, guiding during the whole research proposal development, research result writing, and manuscript preparation. BSD and KJ made important contributions to the work's idea and design, as well as the gathering, analysis, and interpretation of data. They also contributed to the work's writing or critical revision for key intellectual substance. BSD and KJ both gave their approval for the final version to be published. They committed to take responsibility for all elements of the work, including ensuring that any issues about the truth or integrity of any portion of it are thoroughly examined and addressed.

Declaration of Conflicting Interests

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Ethical Approval

The Salale University Ethical Review Committee approved the ethical clearance with Reference number SLUERC/019/2020. A formal letter of cooperation was written to each hospital.

Informed Consent

Written consent was obtained from every study participants who were above 18 years old, and written assent was obtained from their parents or guardians where participants were women under 18 years of age. The privacy and confidentiality of study participants were also protected strictly. Data collectors were informed about coding the questionnaire and not to write the name of the study participants. Only Data collectors saw the records of the study participants.

Data Availability

The data for this study cannot be made publically available at present. It will be made available from the corresponding author on a reasonable request.

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PEDIATRIC ONCALL
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ORIGINAL ARTICLE

RELATIONSHIP OF ANEMIA IN PREGNANCY AND LOW BIRTH WEIGHT INFANTS

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ABSTRACT

Aim: The study was done to understand the relationship between pregnant women with anemia and low birth weight (LBW) in neonates born to them.

Methods and Materials: This cross sectional study was done from medical records of infants born in a tertiary referral hospital between January-March 2019. Total 379 medical records taken by total sampling. Bivariate analysis using chi-square was done to find the relationship between anemia of pregnant women and the incidence of LBW infants. Multivariate binary logistic regression analysis was conducted to find the relationship between maternal age, total parity, gestational age, infant gender, and anemia simultaneously with LBW infants.

Results: From 379 pregnant women, 138 (36.4%) had anemia and 60 (15.8%) pregnant women among them gave birth to LBW infants. Pregnant women who were not anemic amounted to 241 pregnant women (63.6%), which 114 (30.1%) of them gave birth to LBW infants (p=0.47). From the multivariate analysis, the variables anemia in pregnancy, maternal age, and gender of the infant were not associated with LBW, while the amount of parity and gestational age were significantly associated with LBW incidence. Nuliparous women [p=0.039, AOR 1.91 (95% CI 1.03-3.54)] were more likely to deliver LBW infants than multiparous women. Infants born to mothers at preterm gestation [p=<0.001, AOR 32.9 (95% CI 18.28-59.24)] were more likely to experience low birth weight compared to mothers at term gestation.

Conclusion: There was no relationship between anemia in pregnancy and LBW infants.

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Introduction

According to the World Health Organization (WHO) in 2011, the maternal anemia global prevalence was 38.2%, with the largest proportion in Southeast Asia at 48.7%.[1] Based on statistical data from Indonesia Basic Health Research (Riset Kesehatan Dasar/RISKESDAS) there has been an increase in the prevalence of maternal anemia formerly 37.1% in 2013 to 48.9% in 2018.[2] From the same statistical data, it is known that proportion of low birth weight (LBW) infants in Indonesia reached 6.2% in 2018. The province with the highest proportion of LBW infants was in Central Sulawesi with 8.9% prevalence, while West Java had a proportion of LBW infants of around 6.3%.[2] According to the Health Profile of West Java Province in 2017, Bandung is the city with the highest presentation of LBW incidents (7.52%), while the lowest is Sukabumi (0.36%).[3]

The increase in maternal blood plasma volume in pregnancy serves to meet the needs of blood supply from the uterus to the fetus. The increase in blood plasma volume is also accompanied by an increase of red blood cells. However, because the increase in red blood cells is not proportional to the increase of plasma volume, it will cause an unbalanced condition called hypervolemia.[4] Hypervolemia is a condition where there is too much plasma volume in the blood, decreasing the ratio of red blood cells to blood plasma.[5] This can makes the normal concentration of hemoglobin (Hb) of pregnant women to decrease when compared to non-pregnant women.[6] If the Hb concentration continues to drop to less than 11 g/dl during the first, second, or third trimester, this condition can be called anemia in pregnancy or maternal anemia.[1]

About 60% of severe anemia in pregnancy are caused by iron deficiency.[1] The prevalence of maternal anemia was higher in pregnant women who did not take iron supplements (38.8%) compared to those who took iron supplements (29.2%).[7] Iron deficiency anemia in pregnancy occurs due to the need for iron to increase significantly because of the rapid growth and development of the fetus.[8] Various studies have reported that pregnant women with iron deficiency anemia will have a poor outcome for both mother

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and infant. In a systematic review research and international meta analysis using electronic databases, it is stated that anemia in pregnancy is considered to be a factor for the incidence of LBW.[9]

Birth weight is divided into three conditions, LBW, normal birth weight, and large birth weight. Normal birth weight is a infant weighing ≥2500-3999 grams, a infant with large birth weight is weighing ≥4000 grams, while LBW is a infant weighing <2500 grams.[10] LBW infants have a higher risk for developing various health problems as they grow. For example LBW infants in South Asia, especially those weighing less than 2000 grams, have substantial cognitive and motor impairment compared with normal birth weight infants.[11] Children with more disabilities and developmental delay have history of premature and LBW, so there is a need for developmental screening tests and interventions to reduce malnutrition in infants.[12] Regarding the school performance, LBW infants were 2-6 times more likely to have a worse performance than the infants with normal weight.[13]

Based on the explanation above, this study was conducted to find the relationship between anemia in pregnancy and the incidence of LBW infants in a tertiary referral center in Indonesia.

Methods & Materials

This cross sectional study was done from the medical records of infants born in Dr. Hasan Sadikin Central General Hospital, Bandung, Indonesia from January to March 2019. Infants born to mothers who had checked their hemoglobin levels just before delivery were included in the study. Infants with major congenital abnormalities, infants of mothers with maternal hypertension, and multiple pregnancy were excluded from the study. Data was collected from the Neonatology Division of the Department of Child Health, Dr. Hasan Sadikin Central General Hospital with the ethical exemption permit number 907/UN6. KEP/EC/2020 by the Research Ethics Commission of Padjadjaran University and online data collection permit by the Director of Human Resources, Education and Research Dr. Hasan Sadikin Central General Hospital.

By total sampling method, data was taken from 379 infant medical records and included maternal age, total parity, history of anemia in pregnancy, gestational age, gender of infant, and birth weight. Maternal gestational age was considered as the duration of gestation measured from the first day of the mother's last menstrual period until the date of examination. Term pregnancy was defined if the pregnancy has reached 37 weeks, below that range was called preterm pregnancy.[10] Maternal anemia was classified into mild and moderate anemia. Mild anemia had a Hb level from 9 to 10.9 g/dL and moderate anemia had a Hb level of 7 to 8.9 g/dL.[14] LBW infant was an infant weighing <2500 grams.[10]

Statistical analysis: The data were analyzed using univariate, bivariate, and multivariate analysis. Univariate analysis used to identify the characteristics of the research subjects. Chi-square test was used to find the relationship between anemia of pregnant women and the incidence of LBW infants, with results of p value, X^2 value, and Prevalence Ratio (PR). Bivariate analysis was also used to see differences in the distribution of LBW in other groups of variables. Multivariate binary logistic regression analysis was conducted to find the relationship between maternal age, total parity, gestational age, infant gender, and anemia simultaneously with LBW infants. Adjusted Odds Ratio (AOR) with 95% Confidence Interval (CI) was used to measure the strength of this relationship. The level of significance in this study was considered to be $p<0.05$.

Results

The characteristics of subjects are shown in Table 1. Based on Table 2 it can be seen that the proportion of LBW in this study was 45.9%. From 379 pregnant women, 138 (36.4%) had anemia and 60 pregnant women (15.8%) among them gave birth to LBW infants. Pregnant women who were not anemic amounted to 241 pregnant women (63.6%), which 114 (30.1%) of them gave birth to LBW infants (p=0.47). Other variables that also showed no difference in distribution of LBW infants were maternal age (p=0.41) and gender of the child (p=0.29). From the multivariate analysis (Table 2), the variable anemia in pregnancy, maternal age, and gender of the infant were not associated with LBW, while the amount of parity and gestational age were significantly associated with LBW incidence. Nuliparous women [p=0.039, AOR 1.91 (95% CI 1.03-3.54)] were more likely to deliver LBW infants than multiparous women. Infants born to mothers at preterm gestation [p=<0.001, AOR 32.9 (95% CI 18.28-59.24)] were more likely to experience low birth weight compared to mothers at term gestation.

Table 1. Characteristics of Research Subjects

Characteristics	N (%)
Maternal Age	
≤20 years	60 (15.8)
21-35 years	265 (69.9)
>35 years	54 (14.2)
Total Parity	
1	167 (44.1)
2-3	188 (49.6)
≤4	24 (6.3)
Gestational Age	
Premature	166 (43.8)
Term	213 (56.2)
Gender	
Female	174 (45.9)
Male	205 (54.1)
Anemia Classification	
Mild	110 (79.7)
Moderate	28 (20.3)

Table 2. Distribution and Relationship of Anemia in Pregnancy and other variables and Low Birth Weight (LBW) Infants

	LBW		p value	X2	PR (95% CI)	p value	AOR
	Yes N (%)	No N (%)					
Anemia							
Yes	60 (15.8)	78 (20.6)	0.47	0.52	0.86 (0.56-1.3)	0.43	0.79 (0.43-1.43)
No	114 (30.1)	127 (33.5)				1	1
Maternal Age							
<35 years	152 (40.1)	173 (45.7)	0.41	0.67	1.28 (0.71-2.3)	0.76	1.14 (0.47-2.76)
>35 years	22 (5.8)	32 (8.4)				1	1
Total Parity							
Nulliparous	91 (24)	76 (20.1)	0.003	8.85	1.86 (1.23-2.8)	0.039	
Multiparous	83 (21.9)	129 (34)				1	
Gestational Age							
Premature	141 (37.2)	25 (6.6)	<0.001	181.19	30.76 (17.5-54.1)	<0.001	
Term	33 (8.7)	180 (47.5)				1	
Gender							
Female	85 (22.4)	89 (23.5)	0.29	1.12	1.24 (0.83-1.86)	0.05	
Male	89 (23.5)	116 (30.6)				1	

Note: AOR - Adjusted Odds Ratio, PR - Prevalence Ratio.

Discussion

Anemia is a problem that often occurs in pregnancy. This study found that anemia in pregnancy occurred quite often, namely 36.4%. However, there is a big difference in the proportion of maternal anemia in different countries such as US where only 10% of the mothers were diagnosed with anemia in pregnancy.[15] Proportion of infants born with LBW also varies in different countries from 11.4% in India while our study has 45.9% infants with LBW.[16] This means Indonesia especially Bandung still needs an extra attention to maternal and child healthcare for a better health outcome.

Anemia in pregnancy raise the risks of bad outcomes for the infant, such as premature birth and LBW infant. Anemia can cause LBW in infant due to decreased oxygen supply through the placenta to the fetus.[15] Explanation regarding the relationship between anemia and LBW infants is due to the decreased oxygen supply reducing fetal fat and glycogen stores. If the fat and glycogen stores are reduced, it will cause the fetus to be in a hypoglycemic state. This will make Insulin like Growth Factor-I (IGF-I) decrease, because the regulation is regulated and is directly proportional to the supply of glucose to the fetus. The function of IGF-I is to stimulate proliferation, differentiation, protein and glycogen synthesis from fetal cells, and growth of neurons and brain. Decreased levels of IGF-I have been shown to make the fetal growth rate decrease and when the infant is born it will make his birth weight lower below normal limits.[17,18,19]

Contrary to the above, research by Bencaiova et al. (2014) states that anemia in pregnancy did not have a negative impact on the infant, because mild anemia which was also the most prevalent degree of anemia in this study (79.7%), was not associated with poor outcome in infants due to the protective effect that can still be obtained from adequate iron supplementation.[20] In this study it was found that anemia did not lead to LBW infants.

An infant can have LBW due to fetal growth restriction, premature birth or both. Fetal growth restriction is divided into three main causative factors, that are maternal, fetal and placental factors. Maternal factors are under nutrition, hypertension and preeclampsia. Fetal factors are chromosomal or congenital abnormalities, multiple pregnancy, and infection. Placental factor is the most common cause and generally described as placental insufficiency, i.e., several types of diseases cause reduced transfer of oxygen and nutrients to the fetus.[17,21] The cause of LBW infant due to infants born prematurely occurred in this study. It showed that preterm infants had the chance to be born LBW by 32.9 (95% CI=18.28-59.24).

Based on the explanation above, the internal risk factors for LBW infant can be due to various things. The assumption for the results of this study that there is no relationship between anemia in pregnancy and LBW infants is because there are still many factors that cannot be excluded as confounding factors in this study. Moreover, Dr. Hasan Sadikin Central General Hospital Bandung is a class A hospital which is the highest referral hospital in West Java Indonesia. This hospital accepts many patients from other hospitals with various conditions of pregnant women including diseases that have been mentioned in the previous paragraph.

Another result obtained in this study was no relationship between pregnant women aged ≤35 years and >35 years with the LBW infants (p=0.76). According to Goisis et al. (2017), there was no relationship between advanced maternal age and LBW infant due to unobserved factors such as the social background of parents and genetic factors.[22]

It was found that nulliparous women had a chance of giving birth to LBW 1.91 times more than multiparous women (95% CI 1.03-3.54). Nulliparous women often have complications because the mother is probably can not adapt well to pregnancy, causing excessive anxiety which results in stress and affects the development of the fetus.[23] However according to a cohort study by Tellapragada et al. in India, amount of parity was not a risk factor for LBW, but rather periodontitis, hypertension, maternal height <150 cm, and late-pregnancy genital infection.[16]

Even though the data sample consists of more male infants than female infants, but the proportion of female was higher in LBW infants (48.8%) than those without LBW infants (43.4%). The proportion of male was higher in non LBW infants (56.6%) compared to LBW infants (51.1%). This proportion was in accordance with other studies, although statistically there was no relationship between gender and LBW (p=0.05). Andayasari et al. concluded that most of the LBW infants were female (55.2%) and the risk of giving birth to LBW was higher in female than male (ORa=1.42; P=0.017).[24] The exact mechanism of gender differences on the effect on infant birth weight is still unknown, but several studies have hypothesized that these differences in birth weight were due to differences in the effect of androgens on body composition.[25]

The weakness of this research was due to confounding factors that cannot be fully controlled. Confounding factors greatly influence the relationship between the independent and dependent variables. In this study, the confounding factors assumed to have a lot of influence were conditions that can cause impaired fetal growth, such as diabetes in pregnancy, maternal nutritional status before and during pregnancy, and maternal infections. This study also could not identify the timing of anemia during pregnancy because of the limited data.

Conclusion

The result showed that there was no relationship between anemia in pregnancy and LBW infants. Most of the anemia in this study was mild anemia, therefore iron supplementation can be promoted to pregnant women and preconception women as the preventive measure for more severe anemia.

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Compliance with Ethical Standards

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Clinical Science

The Correlation between Hemoglobin Concentration during Pregnancy with the Maternal and Neonatal Outcome

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Abstract

BACKGROUND: The prevalence of anaemia is higher among women, including pregnant women. The estimation was about 24.8% of the population in the world suffering anaemia. Anaemia during pregnancy is a big problem because it can contribute morbidity and mortality, either in mother or newborn. The impacts of anaemia during pregnancy included post-partum haemorrhage, low birth weight (LBW), preterm delivery, and low Appearance, Pulse, Grimace, Activity, Respiration (APGAR) score.

AIM: This study aimed to determine the correlation between haemoglobin concentration during pregnancy and the outcome of mothers and newborns.

METHODS: It was a cohort study that included 200 pregnant women in second or third trimester at antenatal care of Sundari General Hospital Outpatient Clinic on February until September 2018. The participants were interviewed using a questionnaire, and their blood was checked to measure haemoglobin concentration using portable Easy Touch Hemoglobinometer. In the next three until six months, the following investigation was conducted to assess the maternal and neonatal outcome.

RESULTS: The result of this study showed among the maternal outcome, only antepartum haemoglobin concentration had a statistically significant correlation with the haemoglobin concentration during pregnancy ($p < 0.05$), meanwhile, among the neonatal outcome. LBW was the only factor that statistically significantly correlated to the haemoglobin concentration during pregnancy ($p < 0.05$).

CONCLUSION: We can conclude that once anaemia occurs in pregnant women, then the women kept suffering from anaemia with its correlation was statistically significant.

Introduction

In all over the world, anaemia has been a global health burden since it can affect anyone without considering age or gender group [1]. However, the prevalence of this nutritional disorder is higher among women, including pregnant women. About 24.8% of the population in the world suffers from anaemia [2], [3].

Anaemia during pregnancy has become a widespread nutritional disorder either in developing or even developed countries. According to the World Health Organization (WHO), the proportion of the population suffering from anaemia in pregnancy was 14% in developed countries and 51% in developing countries. WHO also estimated that among the population, the cases were the most frequently found in Africa and Southeast Asia. Indonesia is a part of Southeast Asia. Thus, anaemia in pregnant women is frequently found here. It is proven by the data from Basic Health Research Ministry of Health of the Republic of Indonesia in 2013 showing that the prevalence was about 37.1% [1], [2], [4].

Anaemia during pregnancy is defined as the haemoglobin criteria is less than 11 g/dL. Once pregnant women suffer from anaemia, iron deficiency becomes the most common cause that should be considered [3]. Other risk factors related to maternal anemia are unhealthy lifestyle, poor socio-economic

status, malnutrition, hemoglobinopathies, age (under 20 years or above 35 years), early marriage or teenage pregnancy, decreasing period of pregnancy interval, smoking or alcohol use, history of menstrual disorder or infection, and gemelli or multiple pregnancies [5].

Anaemia is a big problem especially when it occurs during pregnancy because it may contribute to morbidity and mortality, either in mothers or newborns. Anaemia (regardless the severity) accounts 12.8% maternal death which is the second leading cause of the death. In Indonesia, the national Maternal Mortality Rate (MMR) is still so high with 307/100.000 live births. Anaemia during pregnancy becomes an indirect cause of postpartum haemorrhage and results in maternal mortality in the latter [4], [5]. Meanwhile, the national Neonatal Mortality Rate is much higher with 987/100.000 live births. Moreover, the fetal or neonatal complication can include prematurity, low birth weight, and low APGAR Score. All complications were significantly ended with maternal and neonatal mortality [4], [6], [7].

Although anaemia during pregnancy may lead to many adverse effects, actually anaemia can be the most preventable cause of maternal and neonatal mortality. In the upcoming years, anaemia in pregnant women should be eradicated to improve maternal and neonatal health status. Hence, this study was aimed to investigate the correlation between haemoglobin concentration during pregnancy and the outcome of mothers and newborns. In the future, hopefully, this study can be the reference to counsel pregnant women, especially in Indonesia, to be more aware of how threatening anaemia is and to decrease the prevalence of anaemia itself.

Material and Methods

This study was conducted at antenatal care of Sundari General Hospital Outpatient Clinic. It was a prospective randomised study that included 200 pregnant women in the second or third trimester who met the inclusion and exclusion criteria.

This study took a period of 7 months — February until September 2018. After obtaining the consent, we interviewed the pregnant women who consumed Fe tablets, consist of ferrous sulfate 200 mg which contains 60 mg elemental iron for 90 days after the first trimester using a questionnaire to know their characteristics including age, gestational age, education background, and occupation. Then, the haemoglobin measurement was conducted by using Easy Touch portable hemoglobinometer. The data was collected during their antenatal care in the second or third trimester.

In the next three until six months, following investigation was conducted by asking the pregnant women to come again before giving birth. Then, we assessed the second haemoglobin measurement during their antepartum by the same portable measurement.

A few weeks later, the data about the outcome of maternal and neonatal was collected from the medical record if the subjects are giving birth in Sundari General Hospital. Unless they did not give birth in the same hospital, follow up was done by the phone. The maternal outcome includes the estimation of haemoglobin antepartum, bleeding volume while giving birth, and the initial breastfeeding. The neonatal outcome includes the data whether the newborn alive or not. Among the alive and healthy newborn, other data was collected, including preterm birth, low birth weight, and APGAR score. In this study, low birth weight defined as the infant birth weight which less than 2500 gram and preterm birth was considered as gestational age under 37 weeks. Because of our limitation, APGAR score was measured by only asking whether the newborn cried spontaneously or not. The newborn crying spontaneously was considered as good APGAR Score, but if they did not, it probably showed poor APGAR Score

Statistical Analysis

All data collected and recorded using the Statistic Product and Service Solution (SPSS) program 21st version. Values were expressed with the mean ± SD or percentage as appropriate. The analysis of the correlation between haemoglobin concentration during pregnancy and the outcome of mother and newborn were computed statistically using Chi-Square Test. A difference was considered significant at the p-value < 0.05.

Results

There were 200 pregnant women involved with their newborns that evaluated in this study. There was found no maternal mortality. In this study, the mean of haemoglobin (Hb) concentration was 10.73 ± 2 g/dl, the median was 10.6 g/dl, the maximum was 15.8 g/dl, and the minimum was 7.8 g/dl. The mean birth weight was 3015 ± 584 gram.

The subject characteristics were shown in Table 1. The mean age of all participants was 29 ± 5.5 years. For all characteristics, except birth method, either anaemia or normal group, had the similar result of majority variable. The most common age was 20 – 35 years. The majority of participants were in the third trimester of gestational age. Most of the participants were housewives. The majority education background

was senior high school. Most of the participants gave birth in a hospital. Otherwise, for the birth method, the anaemia group had different result compared to the normal group. The majority birth method in anaemia group was spontaneous birth. Meanwhile, cesarean birth was most commonly conducted in the normal group. By using Chi-Square Test, there were no characteristics which had a significant correlation with the hemoglobin during pregnancy (p-value > 0.05).

Table 1: Demographic of subject characteristics

Characteristics	Haemoglobin concentration during pregnancy		Total	P value
	Anemia (52.5%)	Normal (47.5%)		
Age	Mean 29 ± 5.5 years			0.218
< 20 years	0 (0%)	2 (2.1%)	2 (1%)	
20 – 35 years	88 (83.8%)	79 (83.2%)	167 (83.5%)	
> 35 years	17 (16.2%)	14 (14.7%)	31(15.5%)	
Gestational Age				0.267
2nd Trimester	28 (26.7%)	19 (20%)	47 (23.5%)	
3rd Trimester	77 (73.3%)	76 (80%)	153 (76.5%)	
Occupation				0.974
Housewife	77 (73.3%)	72 (75.8%)	149 (74.5%)	
Civil servant	9 (8.6%)	7 (7.4%)	16 (8%)	
Private servant	9 (8.6%)	7 (7.4%)	16 (8%)	
Entrepreneur	10 (9.5%)	9 (9.5%)	19 (9.5%)	
Education background				0.453
Elementary school	4 (3.8%)	2 (2.1%)	6 (3%)	
Junior high school	13 (12.4%)	14 (14.7%)	27 (13.5%)	
Senior high school	59 (56.2%)	57 (60%)	116 (58%)	
Diploma	6 (5.7%)	9 (9.5%)	15 (7.5%)	
Undergraduate	23 (21.9%)	13 (13.7%)	36 (18%)	
Mode of Delivery				0.121
Normal vaginal	76 (72.4%)	36 (37.9%)	112 (56%)	
Cesarean	29 (27.6%)	59 (62.1%)	88(44%)	
Birth location				0.210
Hospital	56 (53.3%)	59 (62.1%)	115 (57.5%)	
Midwifery unit	49 (46.7%)	36 (37.9%)	85 (42.5%)	

Chi-Square Test. p-value < 0.05 were considered as statistically significant.

The indication of cesarean birth can be seen in Table 2. The most common indication was the previous cesarean delivery. The other indications related to pregnancy problems, such as obstructed labour, placenta previa, abnormal fetal presentation, and cephalopelvic disproportion.

Table 2: The indications of cesarean birth

Factors	Anaemia	Non-anemia
Previous cesarean birth	21 (72.4%)	20 (58.8%)
Obstructed labor	3 (10.3%)	5 (14.7%)
Placenta previa	2 (6.9%)	1 (2.9%)
Cephalopelvic disproportion	1 (3.4%)	2 (5.8%)
Abnormal fetal presentation	2 (6.9%)	5 (14.7%)
Others	0 (0%)	1 (2.9%)

Table 3 showed how maternal outcome related to haemoglobin concentration during pregnancy. Among the three variables, only antepartum haemoglobin concentration that significantly associated with haemoglobin concentration during pregnancy (p < 0.05).

Table 3: The correlation between haemoglobin concentration during pregnancy and maternal outcome

Maternal outcome		Haemoglobin concentration during pregnancy		P value
		Anaemia	Normal	
Antepartum hemoglobin concentration	Anemia	89 (84.8%)	57 (60%)	0.000*
	Non-anemia	16 (15.2%)	38 (40%)	
Postpartum hemorrhage (PPH)	< 500 cc	85 (81%)	78 (82.1%)	0.834
	≥ 500 cc	20 (19%)	17 (17.9%)	
Initial breastfeeding	Yes	27 (25.7%)	27 (28.4%)	0.791
	No	74 (74.3%)	68 (71.6%)	

Chi-Square Test *p-value < 0.05 were considered as statistically significant.

It means that the pregnant women in either second or third trimester kept suffering from anaemia until the antepartum period.

Table 4 showed that among all participants, unfortunately, stillbirth (3.8%) was found. All stillbirth cases occurred in the anaemia group. There was no significant correlation between haemoglobin concentration during pregnancy and neonatal condition (p > 0.05).

Table 4: The correlation between hemoglobin concentration during pregnancy and neonatal condition

Neonatal condition	Hemoglobin concentration during pregnancy		P value
	Anemia	Normal	
Alive newborn	101 (96.2%)	95 (100%)	0.157
Stillbirth	4 (3.8%)	0 (0%)	

Chi Square Test.

To analyse the correlation between haemoglobin concentration during pregnancy and fetal outcome, participants with stillbirth were excluded. We found four cases of stillbirth. Thus, there were only 196 participants involved in this analysis. The result showed in Table 5. Among all variables of neonatal outcome, low birth weight was the only outcome that significantly related to the haemoglobin concentration during pregnancy (p < 0.05).

Table 5: The Correlation between haemoglobin concentration during pregnancy and fetal outcome

Neonatal outcome		Haemoglobin during pregnancy		P value
		Anaemia	Non-anemia	
Spontaneous cry	Yes	92(96.8%)	86 (90.5%)	0.892
	No	9(3.2%)	9 (9.5%)	
Preterm delivery	Yes	4 (4%)	10 (10.5%)	0.074
	No	97 (96%)	85 (89.5%)	
Low birth weight	Yes (< 2500 gram)	4 (81%)	11 (82.1%)	0.045*
	No (≥ 2500 gram)	97 (19%)	84 (17.9%)	

Chi-Square Test *p-value < 0.05 were considered as statistically significant.

Discussion

Out of 200 pregnant women in this study, more than half (52.5%) of them were suffering from anaemia. It is relevant to the previous study which stated that half population of pregnant women in the world affected by anemia. Meanwhile, the proportion of anemic pregnant women varies in each countries, such as 58% in China, 50% in Southeast Asia, and 40% in Istanbul [8].

Based on Chi-Square Test, this study showed that no significant correlation between hemoglobin concentration during pregnancy with any characteristic variables, included maternal age (p-value = 0.218), gestational age (p-value = 0.267), education background (p-value = 0.974), occupation (p-value = 0.453), mode of delivery (p-value = 0.121) and place of birth (p-value = 0.210). It was relevant to

the previous study conducted by Vural *et al*., showing that there was a statistically significant correlation between anaemia prevalence and mode of delivery. Otherwise, in Vural *et al.,* study, the correlation between maternal age and anaemia prevalence was statistically significant [8].

This study found that the mean of haemoglobin concentration was about 10.73 ± 2 g/dl. Based on both the World Health Organization (WHO) and the Center for Disease Controls and Preventions (CDC), the mean is defined as anaemia since the haemoglobin concentration less than 11 g/dl. [9]. Although it was categorised as anaemia according to criteria of WHO and CDC, the concentration of 10 g/dl in the mid-trimester of gestational age seems to reflect the adequate expansion of plasma volume [10].

Although more than half of the population were anaemic, there was found no maternal mortality in this study. It was suggested that the haemoglobin concentration still able to compensate for optimal plasma volume expansion. It was relevant to the previous study stated that the cutoff of extremely low haemoglobin concentration was less than 6.5 g/dl. This condition with other factors can contribute to maternal mortality. Even, the other cutoff with 8.9 g/dl associated with twice risk of maternal mortality [11].

In this study, out of 115 anaemic pregnant women, 20 participants (19%) had bleeding after birth ≥ 500 cc without significant correlation between haemoglobin level during pregnancy and the bleeding volume. The previous study of Frass had similar result showing 29.1% of anaemic pregnant women developed postpartum haemorrhage during cesarean delivery because of the uterine atony [12]. Even, the study of Kayle *et al.* showed that there was a strongly significant correlation between moderate-to-severe anaemia and blood loss severity [13]. Despite the widespread postpartum haemorrhage in all over the world, unfortunately, there is still a lack of data in the literature about contributing factors of it, especially in developing countries where many PPH and maternal death occur. David study stated that weak uterine muscular strength and lower resistance to infectious disease possibly occur due to severe anaemia. Meanwhile, the higher risk of PPH experience related to severity anaemia still needs further studies [13], [14].

This study investigated whether there is a correlation between initial breastfeeding and the haemoglobin concentration during pregnancy. Our study showed that most of the initial breastfeeding failure found in the anaemia group (74.3%). Despite the fact, the correlation was statistically not significant (p-value = 0.791). Another complication of anaemia during pregnancy that still not familiar is breastfeeding failure. However, an article review mentioned breastfeeding failure becoming the impact of anaemia during pregnancy, after puerperal sepsis and sub-involution [15].

Investigation of neonatal outcome was done by analysing three factors, including spontaneous crying to assess APGAR Score, preterm delivery, and low birth weight. Among the factors, only low birth weight had a significant correlation with the haemoglobin level during pregnancy (p = 0.045).

Birth weight is a good indicator to evaluate whether the mother supports the fetus adequately or not. Besides, it is the only determinant factor of newborn mortality in the first year of life. Birth weight less than 2500 gram is defined as low birth weight that is most commonly caused by anaemia during pregnancy. Previous meta-analysis literature showed that there was a significant correlation between anaemia during pregnancy and low birth weight in the 3rd trimester. Otherwise, the same study showed no significant correlation between both variables in 1st and 2nd trimester [9], [16]. Haemoglobin concentration of less than 10.5 g/dl was reported to increase the sevenfold risk of low birth weight [17]. Abnormally a previous literature stated that several studies reported low birth weight in anaemic pregnant women, but high haemoglobin concentration in 1st and 3r trimester also correlated with the risk of low birth weight due to similarly poor plasma volume expansion [10], [17].

Besides low birth weight, preterm delivery and low APGAR score were the other impacts of anaemia during pregnancy in neonatal outcome. This study showed that there is no significant correlation between haemoglobin concentration during pregnancy with any factor (p > 0.05). It seems relevant with the previous study conducted in Moshi Municipality showing a similar result about no correlation between anaemia and low birth weight and preterm delivery. However, a different study showed that maternal anaemia and preterm delivery had significant correlation statistically. Even, Hb < 10.5 g/dl can increase fivefold risk of preterm delivery [17], [18]. Our study can give more information about how the impact of haemoglobin concentration on the outcome of maternal and neonatal. However, our study had a limitation that did not bring any information about the dietary pattern of the pregnant woman, especially during pregnancy. This study also did not give any intervention for the anaemia correction before the childbirth.

In conclusion, from this study, we can conclude that once anaemia occurs in pregnant women, then the women kept suffering from anaemia with its correlation was statistically significant. Several studies showed that there was a significant correlation between anaemia during pregnancy and postpartum haemorrhage. However, this study found a different result with no significant correlation between haemoglobin concentration with PPH and initial breastfeeding. Therefore, further studies are needed to investigate more about the maternal and neonatal outcome due to anaemia during pregnancy. Moreover, this kind of study is still limited developed in Indonesia.

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3	24/11/2021	Konsultasi bab 1 via whatsApp		3	23/11/2021	ACC Judul	
4	11/12/2021	Konsultasi revisi BAB 1, lanjut BAB 2		4	29/11/2021	Konsultasi BAB 1	
5	17/12/2021	Konsultasi BAB 2		5	06/12/2021	Konsultasi BAB 1	
6	26/12/2021	Konsultasi revisi BAB 2		6	30/12/2021	Konsultasi BAB 1	
7	31/12/2021	Konsultasi revisi BAB 2, lanjut BAB 3		7	19/01/2022	Konsultasi BAB 1 dan BAB 2	
8	02/02/2022	Konsultasi BAB 3		8	04/02/2022	Konsultasi BAB 1 dan BAB 2	
9	06/02/2022	Konsultasi revisi BAB 3		9	14/03/2022	Konsultasi BAB 1 dan BAB 2	
10	15/03/2022	Konsultasi revisi BAB 3		10	27/05/2022	Konsultasi revisi BAB 1, ACC dan lanjut BAB 2, BAB 3	
11	08/06/2022	Konsultasi revisi BAB 3		11	02/06/2022	Konsultasi BAB 2 dan BAB 3	

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Pembimbing I				Pembimbing II			
No	**Tanggal**	**Materi Yang Dikonsulkan & Masukan Pembimbing**	**TTD DPU**	**No**	**Tanggal**	**Materi Yang Dikonsulkan & Masukan Pembimbing**	**TTD DPA**
12	11/06/2022	Konsultasi revisi BAB 3, ACC BAB 3, dan Siapkan ujian Proposal		12	13/06/2022	Konsultasi BAB 2, 3	
13	11/08/2022	Konsultasi revisi BAB 1, 2, 3 setelah SEMPRO, ACC lanjut BAB Selanjutnya		13	23/06/2022	Konsultasi BAB 2, 3, ACC siapkan SEMPRO	
14	24/08/2022	Konsultasi BAB 4, 5, 6		14	11/08/2022	Konsultasi revisi BAB 1, 2, 3 setelah SEMPRO	
15	29/08/2022	Konsultasi revisi BAB 4, 5, 6		15	30/08/2022	Konsultasi BAB 4, 5, 6	
16	31/08/2022	Konsultasi revisi BAB 4, 5, 6. Dan ACC, siapkan SEMHAS.		16	01/09/2022	Konsultasi BAB 4, 5, 6 ACC Siapkan SEMHAS	

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LEMBAR KONSULTASI PEMBIMBINGAN PROPOSAL DAN SKRIPSI

UNIVERSITAS dr. SOEBANDI JEMBER

Nama Mahasiswa : Novie Andariyanti

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Judul Skripsi : Hubungan Antara Anemia Pada Ibu Hamil Dengan Kejadian Berat Badan Lahir Rendah

Pembimbing 1: Dr. Nikmatur Rohmah, S.Kep.Ns., M.Kes.

Pembimbing 2: Yunita Wahyu Wulansari, S.Kep., Ns., M.Kep.

Pembimbing I				Pembimbing II			
No	**Tanggal**	**Materi Yang Dikonsulkan & Masukan Pembimbing**	**TTD DPU**	**No**	**Tanggal**	**Materi Yang Dikonsulkan & Masukan Pembimbing**	**TTD DPA**
1	13/11/2021	Konsultasi judul via Zoom yaitu Hubungan Antara Anemia Pada Ibu Hamil Dengan Kejadian Berat Badan Lahir Rendah		1	16/11/2021	Konsultasi judul via whatsApp yaitu Hubungan Antara Anemia Pada Ibu Hamil Dengan Kejadian Berat Badan Lahir Rendah	
2	20/11/2021	ACC judul lanjut BAB 1		2	20/11/2021	Konsultasi urgensi untuk judul	