Expert recommendations for the diagnosis and treatment of iron-deficiency anemia during pregnancy and the postpartum period in the Asia-Pacific region

Breymann, C; Bian, X M; Blanco-Capito, L R; Chong, C; Mahmud, G; Rehman, R
Expert recommendations for the diagnosis and treatment of iron-deficiency anemia during pregnancy and the postpartum period in the Asia-Pacific region

Abstract

Anemia during pregnancy and the postpartum period is commonly caused by iron deficiency and is a significant worldwide issue with severe consequences for both mother and developing fetus. From a worldwide perspective, iron-deficiency anemia (IDA) during pregnancy is highest in the Asia-Pacific region; however, there has been little guidance in this region for safe and effective treatment. An expert panel was convened to develop a concise and informative set of recommendations for the treatment of IDA in pregnant and postpartum women in the Asia-Pacific region. This manuscript provides these recommendations and aims to reduce the morbidity and mortality associated with IDA in pregnant and postpartum women in the Asia-Pacific region. The consensus recommendations define anemia as a hemoglobin (Hb) level <10.5 g/dL during pregnancy and <10 g/dL during the postpartum period, and provide cut-off Hb levels to initiate therapy with oral iron, intravenous iron or red blood cell transfusion.
Title: Treatment recommendations for iron-deficiency anemia during pregnancy and the postpartum period in the Asia-Pacific region: summary of a consensus meeting

Article Type: Review article

Section/Category: Obstetrics

Keywords: Anemia; iron deficiency; iron therapy; postpartum; pregnancy

Corresponding Author: Professor Christian Breymann,

Corresponding Author's Institution: University of Zurich, Medical School

First Author: Christian Breymann

Order of Authors: Christian Breymann; Xu-ming Bian; Lourdes R Blanco-Capito; Christopher Chong; Ghazala Mahmud; Rakhshanda Rehman

Manuscript Region of Origin: SWITZERLAND

Abstract: Anemia during pregnancy and the postpartum period is commonly caused by iron deficiency and is a significant worldwide issue with severe consequences for both mother and developing fetus. From a worldwide perspective, iron-deficiency anemia (IDA) during pregnancy is highest in the Asia-Pacific region; however there has been little guidance in this region for safe and effective treatment. An expert panel was convened to develop a concise and informative set of recommendations for the treatment of IDA in pregnant and postpartum women in the Asia-Pacific region. This manuscript provides these recommendations and aims to reduce the morbidity and mortality associated with IDA in pregnant and postpartum women in the Asia-Pacific region. The consensus recommendations define anemia as a hemoglobin (Hb) level <10.5 g/dL during pregnancy and <10 g/dL during the postpartum period, and provide cut-off Hb levels to initiate therapy with oral iron, intravenous iron or red blood cell transfusion.

Suggested Reviewers: Wolfgang Holzgreve
University of Basel

Thomas Walczyk
University of Singapore

A Maniatis
University of Athens

Michael Stark

G van Asche
Treatment recommendations for iron-deficiency anemia during pregnancy and the postpartum period in the Asia-Pacific region: summary of a consensus meeting

Authors: Christian Breymann\(^a\), Xu-ming Bian\(^b\), Lourdes R. Blanco-Capito\(^c\), Christopher Chong\(^d\), Ghazala Mahmud\(^e\), Rakhshanda Rehman\(^f\)

\(^a\) Feto-maternal Hematology Unit, University Hospital, Zurich, Switzerland
\(^b\) Department of Obstetrics and Gynecology, Peking Union Medical College Hospital, CAMS & PUMC, Beijing, China
\(^c\) Department of Obstetrics and Gynecology, University of The Philippines, Philippine General Hospital, Manila, Philippines
\(^d\) Chris Chong Women and Urogynae Centre, Gleneagles Hospital, Singapore
\(^e\) Department of Obstetrics and Gynecology, Pakistan Institute of Medical Sciences, MCH Centre, Islamabad, Pakistan
\(^f\) Department of Obstetrics and Gynecology, Fatima Jinnah Medical College, Lahore, Pakistan

Corresponding author: Prof Dr Christian Breymann

Address for correspondence:
Clinic of Obstetrics, Obstetric Research
Feto-maternal Hematology Unit, University Hospital, Zurich, Switzerland
Email: christian.breymann@usz.ch
Tel: +41 44 255 51 48
Fax: +41 44 255 4430
Treatment recommendations for iron-deficiency anemia during pregnancy and the postpartum period in the Asia-Pacific region: summary of a consensus meeting

Running head: Treatment recommendations for anemia during pregnancy in the postpartum period

Keywords: Anemia, iron deficiency, iron therapy, postpartum, pregnancy

Word count: 2375
Abstract word count: 149
Abstract
Anemia during pregnancy and the postpartum period is commonly caused by iron deficiency and is a significant worldwide issue with severe consequences for both mother and developing fetus. From a worldwide perspective, iron-deficiency anemia (IDA) during pregnancy is highest in the Asia-Pacific region; however there has been little guidance in this region for safe and effective treatment. An expert panel was convened to develop a concise and informative set of recommendations for the treatment of IDA in pregnant and postpartum women in the Asia-Pacific region. This manuscript provides these recommendations and aims to reduce the morbidity and mortality associated with IDA in pregnant and postpartum women in the Asia-Pacific region. The consensus recommendations define anemia as a hemoglobin (Hb) level <10.5 g/dL during pregnancy and <10 g/dL during the postpartum period, and provide cut-off Hb levels to initiate therapy with oral iron, intravenous iron or red blood cell transfusion.
Introduction

Anemia is one of the most prevalent diseases worldwide, affecting 24.8% of the human population (1.62 billion people) (Table 1), and is a major health concern [3,29]. Iron shortage is the single most common nutritional deficit in the world [3,12] and is the major cause of anemia, accounting for approximately 50% of cases [28,29]. The prevalence of iron-deficiency anemia (IDA) varies among countries but is a particular problem in the developing world, reflecting differences in race, socio-economic factors, nutritional habits, medical care and the frequency of parasitic illnesses [12]. Numerous countries conduct interventions to reduce anemia, particularly in susceptible groups such as pregnant women and young children.

Anemia during pregnancy is a significant concern with the World Health Organization (WHO) estimating a prevalence of 41.8% amongst pregnant women (Table 1) [29]. Iron demand increases rapidly in the second and third trimester of pregnancy with the needs of the developing fetus, with a daily requirement of up to 10 mg [21]. Iron absorption from the diet also increases during pregnancy through upregulation of iron transporters in the gut [19]; however, this increase in absorption is not sufficient to meet the demand during the latter stages of pregnancy. Therefore, iron balance depends largely upon maternal iron stores [9,12]. A pre-pregnancy store of more than 500 mg of iron is required to avoid iron deficiency during pregnancy, yet such adequate levels of iron are only present in 20% of menstruating women before
pregnancy ensues [3]. These iron store deficits are exacerbated by the blood loss experienced during the delivery process and add to the considerable risk of developing postpartum anemia [9].

The consequences of IDA during pregnancy are often serious and long lasting for both the mother and fetus [12,22] (Table 2). Expectant mothers with anemia often experience increased fatigue levels, reduced exercise performance and reduced mental performance [12,22]. Furthermore, severe anemia (hemoglobin [Hb] <9 g/dL) is related to an increased risk of prematurity, small for gestational-age babies and spontaneous abortion [12]. Fetal iron metabolism is completely dependent upon maternal iron delivery via the placenta; therefore, the effects of anemia on the fetus are related to the extent of maternal iron deficiency with increased mortality linked to severe IDA [12]. Considerable efforts to decrease the prevalence of IDA during pregnancy through preventative methods have been largely unsuccessful, and access to new therapies such as intravenous (i.v.) iron and erythropoiesis-stimulating agents (ESAs), readily available in the USA or Europe, can be limited in settings where resources are scarce and guidance is negligible.

Currently, there are three main options for the treatment of IDA: oral iron, i.v. iron and red blood cell transfusion. ESAs can also be used to treat anemia in some situations [11]. Recent recommendations, published in Europe and North America, include oral iron for the treatment of mild-to-moderate IDA
during pregnancy with i.v. iron suggested for those unresponsive to oral treatment [20] (Table 3). The high costs associated with therapies such as ESAs often prevent their use in some of the world’s developing regions where anemia is most common.

Insert Table 3 near here

**Treatment of IDA arising during pregnancy and the postpartum period**

**Oral iron**

Oral iron, administered in the form of ferrous sulphate, ferrous fumerate, ferrous gluconate or iron hydroxide polymaltose complex, is considered the current standard in the treatment of IDA and is most commonly prescribed in cases of mild-to-moderate anemia [9,12]. Benefits of oral iron intervention include ease of use with no medical expertise required for administration. However, limited efficacy and low patient compliance are often an issue, particularly due to gastrointestinal side effects [18,20]. As such, oral administration of iron may take a long time to correct IDA. Moreover, among the different oral iron preparations, ferrous salts, but not a polysaccharide-ferric iron complex lead to oxidative stress as evidenced by increased levels of non-transferrin bound iron (or NTBI) [14].

**I.v. iron**

The use of i.v. iron to treat IDA in pregnant women was first examined almost 60 years ago; enhanced Hb levels following i.v. iron sucrose administration were demonstrated while iron not utilized by the hematopoietic tissues helped replenish maternal iron stores [17]. More recent studies have demonstrated i.v.
iron to be more efficient than oral iron at increasing Hb levels and replenishing iron stores [1,4,6]. The recently published recommendations for the treatment of IDA in pregnancy include i.v. iron as an effective alternative to oral iron during the second and third trimester for pregnant women who fail to respond to oral iron therapy [7] (Table 3).

I.v. iron preparations include iron sucrose, sodium ferric gluconate, low molecular weight iron dextran and newer ‘next generation’ preparations such as ferric carboxymaltose [7]; however, these preparations have substantially different safety profiles [2]. For example, dextran-containing i.v. iron preparations have been shown to be associated with an increased risk of anaphylactic reactions [2], whilst iron sucrose and sodium ferric gluconate are associated with fewer side effects [2]. Furthermore, subtle structural variations between the iron sucrose formulations produced by different manufacturers may affect the stability of the iron complex and, in turn, the safety and efficacy profile [26].

Additionally, numerous studies have demonstrated the efficacy and safety of i.v. iron sucrose in pregnant (second and third trimester) [1,10] and postpartum women [6,7]. Experience with i.v. iron sucrose in the Asia-Pacific region is growing [16,24,27] and data are comparable to results from European studies [6,10], demonstrating that i.v. iron sucrose is effective, provides rapid correction of anemia and is well tolerated in treating IDA during pregnancy [16,24,27].
**Packed cells or red blood cell transfusion**

Although blood transfusions are an effective treatment for IDA, since they deliver exactly what the body needs (red blood cells) without any further physiological effort, they do not correct the underlying cause of anemia. Furthermore, there are many inherent risks involved with this treatment, including serious infection, incorrect transfusion, negative impact on the immune system and transfusion reactions [11,13]. Additionally, certain groups of the population may refuse blood transfusions due to religious beliefs, and limited blood supply often means that stock is reserved for emergencies. Therefore, the administration of a blood transfusion should be considered as a last resort when a patient is unresponsive to i.v. iron supplementation or is in a critical condition.

**Managing IDA in pregnant and postpartum women in the Asia-Pacific region – present situation**

The prevalence of anemia during pregnancy and the postpartum period in the Asia-Pacific region is the highest worldwide and comprises a particular problem. In Southeast Asia and the Western Pacific, 48.2% and 30.7% of pregnant women have anemia, but some data indicate that prevalence could be as high as 85.6% and 90.2%, respectively [29] (Table 4). In this region, oral iron and blood transfusions are currently the most common therapies for the treatment of IDA (Table 5). However, these strategies are suboptimal since oral iron is slow to increase Hb to desired levels in moderate-to-severe anemia. Moreover, a limited availability of blood donors, high costs and risk of infection means that blood transfusions should only be used sparingly in very
serious cases [11,13]. It is, therefore, vital that effective guidelines for the
treatment of IDA in pregnancy are developed for the Asia-Pacific region to
ensure prompt intervention and optimal care of the mother and developing
fetus.

Insert Table 4 near here
Insert Table 5 near here

Physicians throughout the Asia-Pacific region face a range of unique
challenges when managing IDA in pregnant and postpartum women (Table 6).
In some areas, testing for and treatment of anemia during pregnancy are not a
priority since there is an acceptance that anemia is commonplace in the
general population accompanied by a lack of perception of the consequences
of maternal IDA. Also, the high prevalence of thalassemia and malaria in
some regions complicates diagnosis and treatment; therefore, identifying the
cause of anemia is essential before intervention is initiated. Access to the
appropriate therapy is often an issue with geographic and economic barriers,
preventing optimal care of patients in greatest need.

Evidence of the efficacy and safety of i.v. iron as a treatment for IDA is
growing through a number of international trials [1,4,6,7,10,15,16]. These
studies have shown a rapid correction of anemia and a reduced risk of blood
transfusions in the peripartum and postpartum period. As a result, the use of
i.v. iron as a treatment for IDA has increased in Europe in the
obstetric/gynecologic setting. Similar studies at the local level in the Asia-
Pacific region have been lacking and consequently the use of i.v. iron in this region has been limited. Other issues including fear of adverse events, availability of resources and economic viability (Table 6) also restrict the use of i.v. iron in these communities. However, intervention with i.v. iron is expected to grow in the Asia-Pacific region in parallel with evidence from recent trials conducted in this section of the population [16,24,27].

[Insert Table 6 near here]

**Recommendations for diagnosis and treatment of IDA in pregnancy in the Asia-Pacific region**

Accepted guidelines to assist physicians treating pregnant women with IDA are lacking in the Asia-Pacific region. An expert panel (Appendix), of physicians involved in the treatment of anemia in the obstetrics/gynecology setting and with long-term experience of iron therapy, was convened to develop a concise and informative set of recommendations for the treatment of IDA in pregnant and postpartum women in the Asia-Pacific region. This manuscript provides these recommendations and aims to raise awareness of the safety and efficacy of treatments available for IDA to meet the requirements of pregnant and postpartum women in the Asia-Pacific region.

**1. Diagnosis of IDA during pregnancy in the Asia-Pacific region**

Anemia in pregnancy is defined by the Center for Disease Control and Prevention as an Hb level of below 11 g/dL in the first and third trimester and an Hb below 10.5 g/dL in the second trimester [23]; likewise, WHO define
anemia in pregnancy as an Hb level of below or equal to 11 g/dL [29]. The Hb cut-off levels currently used in practice are often lower than these levels (Table 5); hence it is important to raise awareness of the criteria used for the diagnosis of anemia in pregnant women. A hematologic profile, including Hb levels and hematocrit, enables the diagnosis of anemia [12] and biochemical markers of iron levels are important for determining the cause of anemia before treatment is initiated. To identify IDA, both Hb (an indicator of anemia) and serum ferritin (an indicator of iron storage) should be assessed: low ferritin levels indicate iron deficiency, while normal-to-high ferritin levels can indicate thalassemia, lead poisoning and inflammation [25]. Therefore, the appropriate use of markers for iron levels should be established to aid the diagnosis of IDA during pregnancy and the postpartum period.

<table>
<thead>
<tr>
<th>Consensus recommendations for diagnosis of IDA during pregnancy in the Asia-Pacific region</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Hb &lt;10.5 g/dL</td>
</tr>
<tr>
<td>• Ferritin &lt;20 µg/L</td>
</tr>
<tr>
<td>• If ferritin &gt;20 µg/L, other causes of anemia such as thalassemia and vitamin B\textsubscript{12} deficiency should be excluded</td>
</tr>
<tr>
<td>o Consider C-reactive protein assessment to rule out underlying infection (causes elevated ferritin levels)</td>
</tr>
</tbody>
</table>
Consensus recommendations for diagnosis of IDA during the postpartum period in the Asia-Pacific region

- Hb <10 g/dL
- Ferritin measurement is not recommended in the early postpartum period since it can be normal or elevated due to inflammation
- Treatment can commence once:
  - The cardiovascular system is stable
  - There is no ongoing bleeding

2. Treatment of IDA in pregnancy and the postpartum period in the Asia-Pacific region

Due to the serious consequences of IDA in pregnancy, prompt and effective intervention is required (Tables 2 and 3). It is important to note that i.v. iron and oral iron are only licensed for the treatment of iron deficiency. Furthermore, the use of i.v. iron is contraindicated during the first trimester of pregnancy. However, the use of i.v. iron is considered safe in the second and third trimester [20]. It is, therefore, advisable to check the labels for both oral and i.v. iron compounds prior to their administration. The consensus recommendations (Figures 1 and 2) target the application of oral iron, i.v. iron and blood transfusion to specific severities of IDA (stratified by Hb level) to ensure the safest and most efficient treatment possible. The Hb cut-off values were agreed by the expert panel to indicate the need for treatment of IDA during pregnancy (Figure 1) and the postpartum period (Figure 2).

[Insert Figure 1 near here]

[Insert Figure 2 near here]
**Areas requiring further consideration**

Recent studies have demonstrated the efficacy and safety of i.v. iron in pregnant (second and third trimester) [1,4,10] and postpartum women [6,10]. Experience with i.v. iron in the Asia-Pacific region is growing [16,24,27]. However, further studies in this region are warranted to enhance confidence in the use of i.v. iron among prescribing physicians. Measures to raise awareness of the consequences of IDA are also required to ensure the appropriate testing and prompt treatment of anemia during pregnancy and the postpartum period.

**Conclusions**

IDA is the most frequent form of anemia in pregnancy and can have serious consequences for both the mother and fetus. The majority of women do not have adequate iron stores to meet the dramatic increase in requirements during the second and third trimester of pregnancy. From a worldwide perspective, IDA in pregnancy is highest in the Asia-Pacific region; however, there has been little guidance in this region for the safe and effective treatment of IDA during pregnancy and the postpartum period. Currently, the main interventions in this region are oral iron and blood transfusions. However, i.v. iron is more effective, provides more rapid Hb correction, corrects iron stores and is better tolerated than oral iron in treating IDA during pregnancy [1,4,7]. Furthermore, recent studies have demonstrated the efficacy and safety of i.v. iron in the second and third trimester of pregnancy [1,4,7] and in postpartum women [6,7]. The goal of the recommendations presented here is
to reduce the morbidity and mortality associated with IDA in pregnant and postpartum women in the Asia-Pacific region. Consensus recommendations include a definition of anemia as an Hb level below 10.5 g/dL in pregnancy and below 10 g/dL in the postpartum period. The panel also advocates the use of i.v. iron in the second and third trimester of pregnancy to correct anemia and reduce the risk of transfusion in the postpartum period. Further randomized phase III trials with i.v. iron in the Asia-Pacific region are warranted to optimize clinical outcomes for the mother and developing fetus.
Acknowledgements

This work was supported by Vifor Pharma and editorial assistance was provided by ScopeMedical Ltd.

Conflict of interest

CB is a medical external consultant for Vifor Pharma. The remaining authors have no conflicts of interest to declare.
References


Appendix

Participating physicians

Dr Kamrun Nahar (Bangladesh)
Associate Professor & Head of Department Obstetrics & Gynaecology
Mymensingh Medical College and Hospital

Dr Ferdousi Begum (Bangladesh)
Associate Professor Obstetrics and Gynaecology Department
Begum Khaleda Zia Medical College and Hospital – Dhaka

Professor Bian Xuming (China)
Vice Chairman & Professor, Department Obstetrics & Gynaecology
Peking Union Medical College Hospital

Professor Yang Zu Jing (China)
Chief Doctor Professor
Shanghai Xin Hua Hospital Jiao Tong University School of Medicine

Dr Noroyono Wibowo (Indonesia)
Head of Indonesia Obgyne Association Maternal Fetal Division – Obstetrics & Gynaecology Department
Medical Faculty – University of Indonesia Jakarta

Professor Ahm Kim (Korea)
Professor & Chairman, Department of Medicine Obstetrics and Gynaecology
Association of Perinatology and Korean Society of Ultrasound in Obstetrics & Gynecology
University of Ulsan
Professor Jong-Chul Shin (Korea)
Professor & Chairman, Department of Medicine and Obstetrics & Gynaecology
Korean Society of Fetal Medicine
Catholic University of Korea

Dr Lourdes Blanco Capito (Philippines)
Chairman of Department of Obstetrics & Gynaecology
University of the Philippines – Philippine General Hospital

Dr Rudie Frederick Bailon Mendiola (Philippines)
Assistant Chairman, Research Committee of Department of Obstetrics & Gynaecology
Dr Jose Fabella Memorial Hospital

Professor Rakhshanda Rehman (Pakistan)
Professor Gynaecology, Head of Department of Gynaecology & Obstetrics
Fatima Jinnah Medical College/Sir Ganga Ram Hospital

Professor Ghazala Mahmud (Pakistan)
Professor, Meritorious and Head of Department of Gynaecology & Obstetrics
MCH Centre Islamabad

Dr Chris Chong (Singapore)
Obstetrician, Gynaecologist and Urogynaecologist
Chris Chong Women and Urogynaec Clinic

Professor Dr Christian Breymann (Switzerland)
Titularprofessor Universitat Zurich FMH Gynakologie & Geburtshilfe
Schwerpunkt FMH/DGGG: Feto Maternale Medizin
University Hospital, Zurich

Dr Pornpimol Ruangvutilert (Thailand)
Associate Professor, Maternal and Fetal Medicine Unit,
Department of Obstetrics & Gynaecology
Siriraj Hospital, Mahidol University

Dr Pharyhas Chanprapaph (Thailand)
Associate Professor, Maternal and Fetal Medicine Unit, Department of Obstetrics & Gynaecology
Siriraj Hospital, Mahidol University

Dr Nguyen Duy Anh (Vietnam)
Vice Director of Hanoi OB–GYN Hospital
Hanoi Ob-Gyn Hospital
Figure legends

Figure 1 – Consensus recommendations for the treatment of IDA during pregnancy in the Asia-Pacific region

Figure 2 – Consensus recommendations for the treatment of IDA during the postpartum period in the Asia-Pacific region
Table 1 – Worldwide estimated prevalence of anemia [29]

<table>
<thead>
<tr>
<th>Population group</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-school-age children</td>
<td>47.4</td>
</tr>
<tr>
<td>School-age children</td>
<td>25.4</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>41.8</td>
</tr>
<tr>
<td>Non-pregnant women</td>
<td>30.2</td>
</tr>
<tr>
<td>Men</td>
<td>12.7</td>
</tr>
<tr>
<td>Elderly</td>
<td>23.9</td>
</tr>
<tr>
<td>Total population</td>
<td>24.8</td>
</tr>
</tbody>
</table>

Reproduced with permission from the World Health Organization
Table 2 – Consequences of IDA during pregnancy and postpartum
[9,12,20,22]

<table>
<thead>
<tr>
<th>Mother</th>
<th>Fetus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>Increased mortality</td>
</tr>
<tr>
<td>Increased risk for blood transfusion</td>
<td>Reduced birth weight</td>
</tr>
<tr>
<td>Reduced physical performance</td>
<td>Increased preterm birth</td>
</tr>
<tr>
<td>Reduced mental performance</td>
<td>Growth retardation</td>
</tr>
<tr>
<td>Infection</td>
<td>Neurologic impairment</td>
</tr>
<tr>
<td>Risk of hospitalization</td>
<td>Impaired placental growth</td>
</tr>
<tr>
<td>Inhibited lactation</td>
<td></td>
</tr>
<tr>
<td>Postpartum depression: ‘baby blues’</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Table 3 – Guidelines for the treatment of IDA during pregnancy [5,8,20]

<table>
<thead>
<tr>
<th>Pregnancy</th>
<th>Postpartum</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Oral iron in patients with mild-to-moderate IDA (9–10.5 g/dL)</td>
<td>- Without ongoing bleeding</td>
</tr>
<tr>
<td>- I.v. iron in second and third trimester in patients:</td>
<td>- I.v. iron if Hb 6–9.5 g/dL</td>
</tr>
<tr>
<td>o Unresponsive to oral iron</td>
<td>o ESA can be used in non-responders</td>
</tr>
<tr>
<td>o With severe IDA (&lt;9 g/dL)</td>
<td>• Consider transfusion if Hb &lt;6 g/dL</td>
</tr>
<tr>
<td>o With other factors such as requirement for rapid repletion (Jehovah’s Witnesses etc)</td>
<td></td>
</tr>
<tr>
<td>- Oral iron in first and second trimester</td>
<td></td>
</tr>
<tr>
<td>- Consider i.v. iron after 14 weeks’ gestation in patients unresponsive to oral iron (Hb increase &lt;0.5 g/dL in 2 weeks)</td>
<td></td>
</tr>
<tr>
<td>- I.v. iron in third trimester in case of IDA</td>
<td></td>
</tr>
</tbody>
</table>

IDA, iron-deficiency anemia; i.v., intravenous; ESA, erythropoiesis-stimulating agent; Hb, hemoglobin
<table>
<thead>
<tr>
<th>WHO region</th>
<th>Prevalence of anemia in pregnant women (%)</th>
<th>Number of pregnant women affected (millions) [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>57.1 [52.8–61.3]</td>
<td>17.2 [15.9–18.5]</td>
</tr>
<tr>
<td>Americas</td>
<td>24.1 [17.3–30.8]</td>
<td>3.9 [2.8–5.0]</td>
</tr>
<tr>
<td>Southeast Asia</td>
<td>48.2 [43.9–52.5]</td>
<td>18.1 [16.4–19.7]</td>
</tr>
<tr>
<td>Europe</td>
<td>25.1 [18.6–31.6]</td>
<td>2.6 [2.0–3.3]</td>
</tr>
<tr>
<td>Eastern Mediterranean</td>
<td>44.2 [38.2–50.3]</td>
<td>7.1 [6.1–8.0]</td>
</tr>
<tr>
<td>Western Pacific</td>
<td>30.7 [28.8–32.7]</td>
<td>7.6 [7.1–8.1]</td>
</tr>
<tr>
<td>Global</td>
<td>41.8 [39.9–43.8]</td>
<td>56.4 [53.8–59.1]</td>
</tr>
</tbody>
</table>

Reproduced with permission from the World Health Organization
CI, confidence interval; WHO, World Health Organization
Table 5 – Overview of treatment practice according to the panel members

<table>
<thead>
<tr>
<th>Country</th>
<th>Average patient age (year)</th>
<th>Prevalence of IDA</th>
<th>Country-specific guidelines?</th>
<th>Hb cut-offs for treatment (based on available guidelines or own practice experience)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bangladesh</td>
<td>25</td>
<td>50% pregnancy</td>
<td>Institute of Public Health and Nutrition (IPHN) 2002 (oral iron and blood transfusion)</td>
<td>First trimester&lt;br&gt;• &gt;10 g/dL (oral iron)&lt;br&gt;• &lt;10 g/dL (i.v. iron)&lt;br&gt;Second and third trimester&lt;br&gt;• &lt;9 g/dL (i.v. iron)&lt;br&gt;• &lt;8 g/dL (blood transfusion)</td>
</tr>
<tr>
<td>China</td>
<td>28–30</td>
<td>6% pregnancy</td>
<td>Yes (oral iron, i.v. iron and blood transfusions)</td>
<td>First trimester&lt;br&gt;• &gt;10 g/dL (oral iron)&lt;br&gt;Second and third trimester&lt;br&gt;• &lt;9 g/dL (oral iron)&lt;br&gt;• &lt;7 g/dL (i.v. iron)&lt;br&gt;• &lt;8 g/dL before delivery (blood transfusion)</td>
</tr>
<tr>
<td>Indonesia</td>
<td>8–48</td>
<td>67% pregnancy</td>
<td>Yes (oral iron, i.v. iron)</td>
<td>Second and third trimester&lt;br&gt;• &lt;10 g/dL (i.v. iron)&lt;br&gt;• &lt;7 g/dL (blood transfusion)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>72% postpartum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Country</td>
<td>Age Range</td>
<td>Pregnancy Rate</td>
<td>Postpartum: data</td>
<td>Hemoglobin Levels</td>
</tr>
<tr>
<td>-----------</td>
<td>-----------</td>
<td>----------------</td>
<td>------------------</td>
<td>-------------------</td>
</tr>
<tr>
<td>Pakistan</td>
<td>22–34</td>
<td>88%</td>
<td>None</td>
<td>7–9 g/dL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>6–7 g/dL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt;6 g/dL</td>
</tr>
<tr>
<td>Philippines</td>
<td>35</td>
<td>44%</td>
<td>None</td>
<td>&gt;8 g/dL oral iron</td>
</tr>
<tr>
<td>Singapore</td>
<td>25–30</td>
<td>10–24%</td>
<td>None</td>
<td>First to third trimester</td>
</tr>
<tr>
<td>Thailand</td>
<td>25–30</td>
<td>10–24%</td>
<td>None</td>
<td>First and third trimester</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Second trimester</td>
</tr>
<tr>
<td>Vietnam</td>
<td>15–50</td>
<td>32%</td>
<td>None</td>
<td>≥8 g/dL oral iron + folate</td>
</tr>
</tbody>
</table>

IDA, iron-deficiency anemia; Hb, haemoglobin; i.v., intravenous
Table 6 – Overview of key treatment issues for the Asia-Pacific region

| Education | • In some areas, testing for anemia is not seen as a priority since severe anemia is not perceived as a major problem  
|           | • Issues surrounding the prescription of oral iron and blood transfusions based on empirical rather than evidence-based experience  
|           | • Patients avoid injections which means that physicians have less experience in giving them  
|           | • Fear of iron-dextran anaphylaxis from previous trials  
|           | • Physicians are unaware of the difference between i.v. iron dextran and i.v. iron sucrose  
|           | • Lack of information on i.v. iron use  
|           | • Lack of guidelines for the use of i.v. iron in pregnancy  
| Cause of anemia | • Factors other than iron deficiency can cause anemia  
|             | • Thalassemia is prevalent in the Asia-Pacific region  
| Diet | • Low iron diet compared with Europe and North America  
|      | • Socio-economic background can result in greater risk of iron deficiency  
| Transfusions | • Infection risk (HIV, hepatitis B and C) [11,24]  
|             | • Shortage of available blood  
|             | • Cost  
| Cost of i.v. iron | • Governments may not finance treatment  
|             | • Where governments do not fund treatments, patients cannot afford i.v. iron themselves  
| Accessibility | • Many patients do not have easy access to medical care  
|             | • Difficult to get patient to travel to see physician or get medication to patient  
|             | • Large hospitals have good facilities but many deprived areas have poor facilities  

i.v., intravenous; HIV, human immunodeficiency virus
Figure 2

Hb level (g/dL)

≥10

No IDA
- No treatment required since patient is not anemic
- Assessment of Hb levels does not give an indication of iron stores, so presence of iron deficiency cannot be determined
  - Iron stores can be assessed by measurement of ferritin levels 6 weeks after birth

9.5–9.9

Mild IDA
- Hb <10 g/dL
- Treat with oral iron (target Hb ≥10 g/dL)
- Dose:
  - Two tablets (80–100 mg iron/tablet) per day for approximately 12 weeks
- Start treatment 24–48 hours postpartum if possible
- Switch to i.v. iron if oral treatment is not tolerated, ineffective or if there is a lack of compliance

<9.5

Moderate IDA
- Treat with i.v. iron sucrose (target Hb ≥10 g/dL)
- Dose:
  - Infusion (200 mg iron/day, 100 mL saline, 20–30 mins, over 2–4 days if possible)
  - Push (200 mg iron/day, 5–10 mins, over 2–4 days)
- Start treatment 24–48 hours postpartum if possible
- Target treatment duration for optimal Hb increase:
  - Total dose of 800 mg iron over 4 days
  - If patient leaves hospital earlier, a minimum dose of 400 mg iron should be given over 2 days

<6.5

Severe IDA
- Hematocrit ≤18–20%
- Unstable cardiovascular system
- Consider blood transfusion if patient is at risk or response to i.v. iron is not rapid enough
- Aim of treatment is patient recovery and survival

Hb, hemoglobin; IDA, iron-deficiency anemia; i.v., intravenous
Figure 1

- **Hb level g/dL**

  - **≥10.5**
    - **No IDA**
      - No treatment required since patient is not anemic
      - Assessment of Hb levels does not give an indication of iron stores, so presence of iron deficiency cannot be determined

  - **10–10.4**
    - **Mild IDA**
      - Hb <10.5 g/dL and ferritin <20 μg/L
      - If ferritin >20 μg/L, rule out other causes of IDA, eg thalassemia
      - Treat with oral iron (target Hb ≥10.5 g/dL)
      - Dose: 80–100 mg iron/day
      - Switch to i.v. iron if oral treatment is not tolerated, ineffective (ΔHb <1 g/dL in 2 weeks) or if there is a lack of compliance (Hb levels drop below 10.0 g/dL)

  - **9–9.9**
    - **Moderate IDA**
      - Treat with i.v. iron sucrose (target Hb ≥10.5 g/dL)
      - Dose
        - Infusion (200 mg iron/day in 100 mL saline, 20–30 mins, repeat once or twice weekly on alternate days)
        - Push (200 mg iron/day, 5–10 mins, repeat once or twice weekly on alternate days)
      - If Hb drops below 9.0 g/dL, consider blood transfusion

  - **<9**
    - **Severe IDA**
      - Treatment at discretion of physician and patient
      - Use i.v. iron if appropriate
      - Administer blood transfusion if safety concerns due to approaching delivery date or no response to i.v. iron

Hb, hemoglobin; IDA, iron-deficiency anemia; i.v., intravenous
TREATMENT RECOMMENDATIONS FOR IRON-DEFICIENCY ANEMIA DURING PREGNANCY AND THE POSTPARTUM PERIOD IN THE ASIA-PACIFIC REGION: A SUMMARY OF A CONSensus MEETING
Checklist

Conflict of interest

The International Committee of Medical Journal Editors approved the following statement on conflict of Interest in peer review and publication in medical journals.

Conflict of interest for a given manuscript exists when a participant in the peer review and publication process — author, reviewer, and editor — has ties to activities that could inappropriately influence his or her judgment, regardless of whether judgment is, in fact, affected. Financial relationships with industry (for example, employment, consultancies, stock ownership, honoraria, expert testimony), either directly or through immediate family, are usually considered the most important conflicts of interest. However, conflicts can occur for other reasons, such as personal relationships, academic competition, and intellectual passion.

Public trust in the peer review process and the credibility of published articles depend in part on how well conflict of interest is handled during writing, peer review, and editorial decision making. Biases can often be identified and eliminated by careful attention to the scientific methods and conclusions of the work. Financial relationships and their effects are less easily detected than other conflicts of interest. Participants in peer review and publication should disclose their conflicting interests, and the information should be made available, so others can judge their effects for themselves. Because readers may be less able to detect bias in review articles and editorials than in reports of original research, some journals do not accept reviews and editorials from authors with a conflict of interest.

Authors

When they submit a manuscript, whether an article or letter, authors are responsible for recognizing and disclosing financial and other conflicts of interest that might bias their work. They should acknowledge in the manuscript all financial support for the work and other financial or personal connections to the work.

Please answer to the following questions:

Have you accepted any funding or support from an organization that may in any way gain or lose financially from the results of your study or the conclusions of your review? Yes ☐ No ☑

Have you been employed by an organization that may in any way gain or lose financially from the results of your study or the conclusions of your review? Yes ☐ No ☑

Do you have any other conflicting interests? Yes ☐ No ☑

Please type a statement and send it to us for pasting into the article.

Author Statement

C Braymann is a medical external consultant for Vifor Pharma. The remaining authors have no conflicts of interest to declare.

Date/Signed/Print name

[Handwritten Signature]

Prof. Dr. Christian Braymann
Forschungsgruppe
Feto Maternale Hämatologie
Forschung Geburts hilfe C 118
Frauentklinikstrasse 10
CH-8091 Zürich
Copyright Agreement

1. The following agreement is valid under the condition that the article submitted be published by Walter de Gruyter GmbH und Co. KG (the "Publisher"), owner of the Journal of Perinatal Medicine (referred to as the "Journal") in whole or in part, including any illustrations, charts, diagrams, maps, outlines, tables, etc. belonging to and having been submitted with the article (in total referred to as the "Article")

2.1. The Author grants to the Publisher the following rights:

- The right to reproduce and distribute the Article in printed form, including print-on-demand
- The right to produce prepublications, reprints, and special editions of the Article
- The right to translate the Article into other languages
- The right to reproduce the Article using photomechanical or similar means such as photocopy and telecopy, as well as the production of microcopy, microfiche, or microform editions, and the right to distribute these reproductions
- The right to reproduce and distribute the Article on any and all data carriers
- The right to store the Article electronically or optically on any and all data carriers or storage media – especially in machine readable/digitized form on data carriers such as hard drive, disk, CD-Rom, DVD, HD-DVD, Blu-ray Disc (BD), Advanced Optical Disc (AOD), Mini-Disk, magnetic tape – and the right to reproduce and distribute the Article via these data carriers; the right to store the Article in databases, including online databases, and the right of transmission of the Article in all technical systems and modes; the Right to make the Article available to the public or to closed user groups on individual demand, for use on monitors or other readers (including e-books), and in printable form for the user, either via the internet, other online services, or via internal or external networks.
- The Author furthermore grants the Publisher the exclusive, permanent and territorially and substantively unrestricted rights for the unknown types of use on the date of the conclusion of this Agreement.

2.2. The rights pursuant to clause 2.1 shall be granted as exclusive rights for the duration of the copyright, each unlimited in geographic scope.

Should the author wish to reproduce and distribute the Article elsewhere after one year following publication, s/he must obtain the written consent of the Publisher. Taking into account the interests on both sides, the Publisher shall not unreasonably withhold its consent.

2.3. The Publisher may transfer the rights granted to it pursuant to clauses 2.1. and 2.2. in whole or in part to third parties, or may grant licenses to third parties to use rights to which it is entitled. Any claims from agreements between the Author and performing rights societies (Verwertungsgesellschaften), in particular VG Wort, to which the Author is entitled shall remain unaffected.

3. The Author warrants that a) s/he is entitled without restriction to grant the rights to the Article to the extent as stated in clause 2.1. to the Publisher; b) that the Article is not libellous and does not infringe on any copyrights, performing rights, trademark rights, personal rights or any other third party rights or is otherwise unlawful; c) that the Article or substantial parts thereof have not been published elsewhere.

4. Walter de Gruyter Publishers acknowledge that the author of an NIH-funded article retains the right to provide a copy of the final manuscript to NIH upon acceptance for publication or thereafter, for public archiving in PubMed Central 12 months after publication in the journal. Note that only the accepted author’s version of the manuscript, not the PDF file of the published article, may be used for NIH archiving.

5. The Author shall retain a complete copy of the manuscript for his/her files. The Author agrees that the manuscript submitted will be destroyed three months after publication in the Journal. The return of original material may be negotiated in a separate agreement between the Publisher and the Author. The Publisher will be liable only in cases of wilful misconduct or gross negligence.

6. Upon receiving the proofs, the Author agrees to promptly check the proofs carefully, correct any typographical errors, and authorize the publication of the corrected proofs.