

Original Research Article

Prevalence of iron deficiency anemia in pregnancy and its therapeutic response to treatment: a retrospective audit in a tertiary hospital

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Received: 05 August 2022

Revised: 02 September 2022

Accepted: 16 September 2022

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ABSTRACT

Background: Iron deficiency anemia is the commonest type of nutritional anemia seen during pregnancy. Despite implementing oral iron prophylaxis in pregnancy, IDA in pregnant women constitute a major health problem. The present study aims to look at the prevalence of IDA in a pregnant population in Seremban, Malaysia and their response to treatment.

Methods: This is a retrospective study looking into the prevalence of iron deficiency anaemia among pregnant women who delivered between October 2019 to March 2020 in a state hospital in Seremban, Malaysia and their response to treatment. Main outcome measures were the prevalence of iron deficiency anaemia, associated demographic and clinical factors and response to iron therapy.

Results: About 920 patients' records were included for analysis. The prevalence of anaemia in this cohort was 42.8% (N=394). The prevalence of iron deficiency anemia (IDA) was 31.5% (N=124) among the anemic patients or 13.5% of the studied population. The mean hemoglobin level for this group was 10.0±0.74 g/dl (6.8-10.9 g/dl) and majority had mild anemia (91.9%, N=114). 68.5% IDA patients were successfully treated by 36 weeks pregnancy. Of the remaining 39 patients who were still anemic, 37 (94.9%) had mild anemia with mean hemoglobin level of 10.3g/dl (SD 0.48, range 9.0-10.9 g/dl).

Conclusion: Current treatment strategy is inadequate to achieve the set national target. There is a role for an early recourse to parenteral iron therapy to improve treatment outcome.

Keywords: Iron deficiency Anemia, Pregnancy, Prevalence, Treatment outcomes

INTRODUCTION

Pregnancy significantly increases the demand for iron requirement due to the need of feto-placental unit, the expansion of maternal red cell mass and to prepare for blood loss during delivery.^{1,2} Consequently, women with inadequate iron storage will not be able to meet these demands and will be in a state of iron deficiency which might manifest as anemia during pregnancy. This is a

significant health issue due to its established association with maternal impaired cognitive ability and reduced work capacity as well as prematurity, low birth weight and low iron storage for the newborn.³ The global prevalence of iron deficiency anaemia, which is the commonest nutritional deficiency in pregnancy is estimated to be approximately 41.8%.⁴

In Malaysia, the prevalence of anaemia in pregnant women (aged 15-49) for the year 2019 was reported to be

31% (23.2-39.2) and the number has remained almost constant for the past 10 years or so despite availability of various modalities of treatment.⁵ It is therefore a major public health issue. Presently there is a limitation of local epidemiological data regarding prevalence of iron deficiency anaemia in pregnancy and the outcomes of treatment and whether the target set by the Ministry of Health is met. Most studies focused only on the prevalence and demographic factors associated with anaemia in pregnancy, not specifically iron deficiency anaemia and there is paucity of data on response to treatment of the same. A multi-center, cross-sectional study conducted in 2005 found the prevalence of anemia among pregnant women attending government health clinics to be 35%, and majority is mild anemia with high prevalence in the Indian ethnic women.⁶ Similar findings on racial prevalence have been demonstrated in other studies.⁷ Literature survey on publications and guidelines on the frequency of iron deficiency anaemia in Malaysia discovered that 80-90% of pregnant women have low iron status and 38-42% develop anaemia with minimal data on the treatment outcomes.⁸ Treatment for iron deficiency is primarily by oral iron supplementation as dietary intake alone is insufficient to correct an iron-deficient state. A dose of 100-200mg of elemental iron daily is usually administered.⁹ Parenteral iron treatment is not the first line related to concerns about side effects.¹⁰ The role of parenteral iron is when response to oral iron has been poor or if there is compliance issue to due side effects of oral iron therapy. It has been shown that parenteral iron therapy has resulted in faster increases in hemoglobin level and better replenishment of iron stores compared to oral therapy.¹¹ The fact that anaemia remains a major health problem during pregnancy calls for a more robust action to address this problem. This study intends to establish the prevalence of iron-deficiency anaemia in a pregnant population and evaluate the effectiveness of treatment strategy employed to correct iron deficiency anaemia.

METHODS

This is a retrospective cohort study looking into the prevalence of iron deficiency anaemia among pregnant women who delivered in Hospital Tuanku Jaafar Seremban (HTJS) between October 2019 - March 2020. Inclusion criteria includes all patients who received their antenatal care in the government health clinic where hemoglobin levels were routinely checked by either a venous or capillary blood sample at booking and monthly until 36 weeks pregnancy. We define anaemia as hemoglobin concentration less than 11 g/dl and we used mid-trimester haemoglobin level to identify patient who are anaemic in our study subjects. We further classify anaemia into mild (9-10.9 g/dl), moderate (7-8.9 g/dl) and severe (<7 g/dl). Iron deficiency anemia (IDA) is diagnosed by haemoglobin <11 g/dl and a hypochromic microcytic picture on the full blood count (MVC <80 fl, MCH <27 pg) and when available by serum ferritin level of <30 ug/l. All postnatal mothers who delivered a

singleton baby were included in our study. Postnatal mothers who experienced anaemia from antepartum hemorrhage, has underlying haemoglobinopathy and who did not deliver a singleton baby were excluded. All patients in this study were routinely prescribed iron supplement in the form of ferrous fumarate 200mg which contained 65 mg elemental iron together with 5 mg folic acid. Patients who were unable to tolerate ferrous fumarate were advised to take Obimin (contains 30 mg elemental iron). When iron deficiency anaemia is detected, the dose of oral iron is increased. Common preparations used are Ferrous fumarate 400 mg daily (contains 130 mg elemental iron), Iberet 500 (105 mg elemental iron) or Zincofer (115 mg elemental iron). Patients with poor compliance or intolerable adverse effects from oral medication will be prescribed parenteral iron commonly in the form of iron dextran. Patients who had allergy to iron dextran were prescribed iron sucrose. Blood transfusion is reserved for patients with severe anaemia and symptomatic with a Hb level <7 g/dl or patients with moderate to severe anaemia close to the due date where fast correction is desirable. The sample size of our study was estimated using the prevalence of anaemia in pregnancy reported for the state of Negeri Sembilan, Malaysia in 2004 (51.10%). Using the Cochran formula, a sample size of 384 was calculated for this study. However, to cover for eventualities such as incomplete data, we over sampled to 1000 participants. Data was collected from the patients' case records and included socio-demographic information (age, ethnicity, and education level), clinical risk factors (including parity and inter-pregnancy interval), clinical data of anemic status, types of treatment, and pregnancy outcomes. Data gathered were tabulated and analyzed using the Statistical Package for Social Sciences (SPSS) Version 25. Continuous variables were described as mean and standard deviation whereas categorical variables were expressed by frequency and percentage. The results were expressed in terms of frequency, proportion, and mean. Chi-square Test was applied for comparison of categorical data. The level of significance was set at 0.05.

RESULTS

The antenatal and delivery records of 1000 consecutive patients who delivered at Hospital Tuanku Jaafar Seremban were reviewed. Of these, 41 were excluded due to unavailability of a mid-trimester hemoglobin measurement, 33 were excluded due to the presence of haemoglobinopathies and 6 due to a diagnosis of antepartum haemorrhage. 920 patient records were available for analysis.

Demography

Of the 920 patients, the majority was Malay (78.8%), between the age of 20-35 years old (79.1%), were of parity 2-4 (69.3%), had tertiary education (54.6%) and were between two to four years since the last childbirth (47.1%).

Table 1: Prevalence of anaemia based on demographics and clinical characteristics.

Demographic data	No anemia (N=526)		Anemia (N=394)		Total number of subjects	P value
	N	%	N	%		
Race						
Malay	428	59.0	297	41.0	725	0.020
Chinese	38	58.5	27	41.5	65	
Indians	40	42.1	55	57.9	95	
Others	20	61.9	15	38.1	35	
Age group (year)						
<20	4	22.2	14	77.8	18	0.009
20 - 35	460	58.3	329	41.7	789	
>35	66	56.4	51	43.6	117	
Education level						
No formal education/ Primary	14	50.0	17	50.0	31	0.156
Secondary	213	55.0	174	45.0	387	
Tertiary	299	59.6	203	40.4	502	
Parity						
1	97	59.4	66	40.6	163	0.550
2-4	350	54.8	288	45.2	638	
≥5	65	54.3	54	45.7	119	
Pregnancy interval (years) (excluding primigravida, N=749)						
<2	151	54.3	126	45.7	277	0.366
2-4	199	59.0	154	41.0	353	
≥5	74	62.2	45	37.8	119	

The mean age of patients in the study was 29.7±5.1 (14-45) years old while the mean parity was 1.8±1.4 (0-9) and mean inter-pregnancy interval was 2.04±2.34 (0-16) years. The trend of hemoglobin levels across the gestation as shown by mean Hb in the first, second and third trimester were 12.1±1.2 (7.2-18.7), 11.1±1.0 (5.9-14.6) and 11.9±1.0 (7.9-15.3) g/dl respectively, showing the expected decline in the second trimester.

Table 2: Outcome of treatment for IDA (n=124).

Severity (g/dl)	Midtrimester		36 weeks	
	N	%	N	%
Mild (9-10.9)	114	91.9	37	29.8
Moderate (7-8.9)	9	7.3	2	1.6
Severe (<7)	1	0.8	0	0
Not anaemic	0	0	85	68.5

Prevalence of anemia

Based on the second trimester hemoglobin 42.8% (N=394) of patients were found to be anaemic with a mean hemoglobin of 10.2±0.65 g/dl (5.9-10.9 g/dl). A vast majority had mild anaemia 96.2%, (N=379). The mean age of all anaemic patients was 29.5±5.4 years (14.0-43.0 years), mean parity was 1.87±1.49 (0-9), mean gestation at delivery was 37.8±1.9 weeks (27-41 weeks) and mean pregnancy interval was 2.27±1.3 years (1-9 years). Hb trend over the three trimesters were 11.5±1.15 (7.2-14.4), 10.2±0.65 (5.9-10.9) and 11.5±0.99 (7.9-14.9) g/dl respectively. Patients of Indian ethnicity and those of

less than 20 years old are significantly more likely to be anaemic when compared to other ethnic groups. No significant difference was observed between the anaemic and non-anaemic group with regards to parity, inter-pregnancy interval and level of formal education. The details are shown in (Table 1).

Prevalence of IDA

The prevalence of iron deficiency anemia among the anemic patients were 31.5% (N=124), or 13.5% of the studied population. The mean mid-trimester hemoglobin level for this group was 10.0±0.74 g/dl (6.8-10.9 g/dl). The mean age of patients with IDA was 28.6±5.5 (14-42) years old, mean parity was 1.78±1.4 (0-5) and mean inter-pregnancy interval was 2.4±2.1 (0-10) years. Mild anaemia was prevalent at 91.9% (N=114). Further analysis revealed a significant difference seen between age, ethnic groups, and education levels where young patients below age of 20 years, patients from Indian ethnic and those with only primary or no formal education were more likely to have IDA while older patients, patients of Chinese ethnic and had tertiary education were less likely to be iron-deficient. Parity and inter-pregnancy intervals showed no significant association with IDA (Table 1).

Outcomes of treatment

All patients with iron deficiency anaemia received oral iron in the form of either Ferrous fumarate 400 mg daily (contains 130 mg elemental iron), Iberet 500 (105 mg elemental iron) or Zincofer (115 mg elemental iron). 32

patients (25.8%) who responded poorly to oral iron evidenced by minimal or no improvement in hemoglobin level after three to four weeks of treatment were given parenteral iron in the form of iron dextran. Two patients who had severe anaemia received blood transfusion. Response to treatment was analysed by the hemoglobin level taken at 36 weeks. From a total of 124 patients with IDA, 85 were successfully treated by 36 weeks pregnancy, giving a response to treatment rate of 68.5%. In comparison, patients who received parenteral iron had a treatment success rate of 84.4%. Of the remaining 39 patients who were still anaemic, 37 had mild anaemia with mean hemoglobin level of 10.3 ± 0.48 g/dl (9.0-10.9 g/dl) and two had moderate anaemia with Hb levels of 8.9 g/dl. No patients had severe anaemia at 36 weeks gestation. (Table 2). Anaemia is a known risk factor for postpartum hemorrhage. An analysis was done to look at the incidence of PPH in previously diagnosed IDA who were still anaemic at the time of delivery and compared to IDA patients who were successfully treated. We found no statistical difference in the incidence of postpartum hemorrhage between both groups. The mean blood loss was 355 ± 255 ml (150-2150 ml) in the treated IDA and 311 ± 205 ml (150-1400 ml) in the group still anaemic at delivery. This difference did not reach statistical significance (Table 3). Overall, at the time of delivery, 12.4% (N=114) of patients remained anaemic despite treatment. 39 were from the IDA group and 75 were from the non-IDA group. In addition, 30 patients who were not anaemic in the second trimester were found to be anaemic at delivery. The prevalence of anaemia at the time of delivery was 15.7% (N=144), a significant reduction from 42.8% (N=394) at mid-trimester.

Table 3: Mode of delivery and incidence of postpartum hemorrhage in patients with IDA (n=124).

Parameters	Treated (N=85)		Anaemic (N=39)		P value
	N	%	N	%	
Mode of delivery					
Vaginal	44	51.8	22	56.4	0.630
Caesarian	41	48.2	17	43.6	
Postpartum hemorrhage (PPH)					
PPH	5	5.9	1	2.6	0.424
No PPH	80	94.1	38	97.4	

DISCUSSION

We report overall prevalence of anemia in our study as 42.8% (N=394) and specifically iron deficiency anemia as 31.5% (N=124). The prevalence rates are similar to recent local study reporting an overall prevalence of anaemia as 43.6% and of iron deficiency as 31.6% respectively.¹² It is a known fact that there is an increased iron requirement in pregnancy over non pregnant state. The average daily requirement in the first trimester is 0.8 mg, 4-5 mg in second trimester and 6-8 mg in the third trimester.¹³ Generally, this extra iron requirement is met through mobilization from iron stores. The deficiency

state sets in women with underlying poor iron stores. Anemia is considered to be a global disease burden; the major brunt being experienced by lower income to middle-income countries (LMIC) such as Africa and Asia. The prevalence here is estimated to be between 46.3 and 60%.¹⁴ From our study and few other studies reported so far in Malaysia highlights that there has not been a change in prevalence over the last two decades.¹⁵ As for ethnicity, our study found that the Indians had a highest prevalence followed by Chinese and Malays. Few studies reported higher prevalence among Malays and Indian and lower prevalence among Chinese. Few plausible explanations are dietary habits, lower parity, and higher social class.¹⁶ Further study by Goh et al highlighted Chinese women had higher haemoglobin and serum ferritin levels compared to the Malays and Indians.¹⁷ Anemia in pregnancy has both maternal and fetal implications. Studies report maternal effects such as fatigue, palpitations, shortness of breath, increased susceptibility to infections, psychological issues including emotional instability, depression, stress, low cognitive performance tests and overall reduced quality of life.¹⁸ Early pregnancy is most critical time and iron deficiency during this time impairs fetal brain development which is potentially not reversible by later intervention with iron supplementation.¹⁹ A study in Chilean children identifies lower memory in children aged 4 and 10 years despite sufficient treatment.²⁰ One Malaysian study highlighted negative consequences on visual motor coordination among primary school children with Iron deficiency.²¹ It is evident that anemia continues to be major health problem in Malaysia and there is certainly a need for urgent remedial measures to tackle this problem.²² The Malaysian Clinical Practice Guidelines and the National Guidelines recommend 100 mg elemental iron/day as prophylaxis in pregnant women. The therapeutic dose for mild to moderate IDA (Hb 8.0-10.5 g/dl) in the first and second trimester anemia is 200 mg elemental iron per day. The Hb concentration should increase by 0.3-1.0 g/dl per week. Treatment should be continued until Hb has optimised and serum ferritin is improved and is above 30-50 µg.²³

In our study, 96.2 % of women were diagnosed with mild anaemia and initiated on oral iron therapy. The overall response to iron treatment is 68.5% (N=85). There was a significant reduction of anemia at the time of delivery from 42.8% of mid trimester to 15.7%. The success rate was predominant in women who received parenteral iron which was 84.4%. These are the women who did not responds to oral iron and parenteral iron treatment was initiated. It is well established that serum ferritin is the most important surrogate marker of iron deficiency anemia rather than hemoglobin level. In Malaysia, the estimated prevalence of iron deficiency with serum ferritin <15 µg/l, is 50-60% and of small or absent iron reserves with ferritin <30 µg/l is 90%. The overall low iron status among Malaysian women indicates supplementation of at least 100 mg elemental ferrous iron daily.²⁴ The current recommendation in the management

of moderate and severe iron deficiency anemia in second trimester in pregnancy is oral iron treatment and parenteral iron if there is no increase in Hb after two weeks.²⁴ However, one of the major challenges in the management of iron deficiency anemia are related to its tolerability and side effects affecting its compliance. It is estimated that among pregnant women in Malaysia, the compliance to daily vitamin or supplements is only 49%.²⁵ One meta-analysis which analyzed 17 randomized trials reported significant gastrointestinal adverse effects with oral iron compared with parenteral iron administration.²⁶ It is therefore paramount to administer to appropriate form and dose to ensure iron stores are adequately replenished. There are numerous publications as randomized controlled trials, systematic reviews examining the effect of intravenous iron versus oral iron. All the studies have highlighted the faster correction of anemia at shorter duration and replenishing the iron stores more efficiently than oral iron. There was a significant difference in the ferritin level following intravenous iron with iron reserves restored only in the intravenous group of women.²⁷ It is postulated that increase in ferritin is related to iron sucrose complex releases iron rapidly to endogenous iron binding proteins with no deposition in the parenchymal tissue. The half-life of iron sucrose is approximately 5 to 6 h and is quickly cleared from serum and thus rapidly available for erythropoiesis.²⁸ This is in contrast to iron dextran compounds with long half-life, relatively slow release and possible risk of life-threatening anaphylactic reactions (sudden cardiovascular collapse, respiratory failure) occurred in 0.1 to 2% of patients.²⁹ Furthermore, one study found a significant improvement in the general health of women postpartum who received intravenous iron therapy. The duration of breast-feeding was longer in these women, and they are less likely to develop postnatal clinical depression.³⁰

Regarding maternal and fetal outcomes in anemia, there are studies documenting poor neonatal outcomes such as complications such as preterm birth and low birthweight. The maternal outcomes include risk of placental abruption and postpartum hemorrhage. However adverse maternal and fetal outcomes are associated with severe anemia.³¹ Our findings are similar with no statistical association to postpartum hemorrhage related to mild anemia in majority of our patients. Overall, at the time of delivery, 12.4% (N=114) of our patients remained anaemic despite treatment. This highlights the need for more concentrated efforts towards optimising hemoglobin levels to reach national targets levels.

Limitations

This study has several limitations. First, we were not able to measure factors such as iron supplementation and other nutritional conditions such as compliance issues during pregnancy, which may have confounded the observed associations. This is essentially due to retrospective nature of the data. Further our study only included

pregnant females seen in one tertiary hospital which precludes the generalization of the results.

CONCLUSION

The overall prevalence of iron deficiency anaemia in pregnancy is 31.5% and the majority of them were of the mild type (9-11 g/dl). There seems to be a significant association between Hb levels and age group, and ethnicity. We conclude that oral iron increase haemoglobin comparable to parenteral iron. As oral iron is cheap and easy to administer, efforts must be undertaken towards increasing the compliance of the pregnant women by using preparations and forms with least gastro-intestinal side effects. However parenteral iron was superior to oral iron in replenishing the iron stores. This is of importance in low- and middle-income group countries where women become anaemic during postpartum and lactation if their iron stores are not corrected. Intravenous (IV) iron sucrose is claimed to have better safety profile and efficacy in treatment of iron deficiency anemia than conventional oral iron supplements. Strength of our study is that it synthesizes evidence for mainstreaming parenteral treatment as feasible option for IDA. There is a need for randomised controlled trials (RCT) performed at local context to validate our results for policy makers to make recommendations.

ACKNOWLEDGMENT

Authors acknowledge the department of Obstetrics and Gynaecology, Hospital Tuanku Jaffar, Seremban, Malaysia for providing access to patient registry for data collection.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Jack MZ, Hui TJ, Ariffin NABC, Mun OS, Nagandla K, Idris N Prevalence of iron deficiency anemia in pregnancy and its therapeutic response to treatment: a retrospective audit in a tertiary hospital *Int J Adv Med* 2022;9:1090-5.