The Impact of Severity of Antenatal Anaemia on Maternal and Perinatal Outcome in Hospital Serdang, Malaysia

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Introduction

Anaemia in pregnancy is one of the most common public health issues in developing countries, affecting approximately 60% of pregnant women worldwide. Severity of antenatal anaemia has been robustly linked with complications in maternal and perinatal outcome [1]. A recent study revealed that at a cut-off value of Hb, i.e., mild anaemia (between 10-10.9 g/dL), moderate (7.0-9.9 g/dL) and severe of less than 7.0 g/dL [3]. Maternal anaemia is commonly considered as a risk factor for poor pregnancy outcome [6] and has been associated with a multitude of problem on both woman and neonate [7]. Ghimire and Ghimire have found that severe anaemia significantly increases the risk of neonatal complication which includes pre-term delivery, low birth weight and small for gestational age [8]. Similarly, moderate anaemia have been linked with increased weakness, lack of energy, fatigue and poor work performance among the pregnant women and severe anaemia has been associated with poor maternal and fetal outcome [9]. Anemia in pregnancy also contributes to haemorrhage and infection especially amongst the severely anemic women causing cardiac failure and subsequently leading to maternal death [10]. In 2015, Brabin et al. disclosed that severe anaemia (OR 3.51, 95% CI: 2.05–6.00) has strong association with maternal mortality [11]. In addition, Ali et al. found that higher prevalence of preeclampsia have been demonstrated among the pregnant women with severe anaemia [12].

Women with Hb between 8.0 and 9.9 g/dl [13] had significantly higher risk for low birth weight, preterm birth and small for gestational age than women with Hb between 10.0 and 11.9 g/dl [1]. A recent study by Farrukh revealed that anaemia in pregnancy is associated with significantly large placental weight and a high fetoplacental ratio [14]. Moreover, previous meta-analysis studies have showed that maternal anaemia during early pregnancy is associated with increase in preterm birth and low birth weight [15]. In Malaysia, Haniff et al. revealed the prevalence of anaemia was 35% and mostly of the milder type and more prevalent in the Indian and Malays ethnicity [16]. This study revealed that at a cut-off point of 11 g/dL, grand multiparas (n=45%) and mothers in third trimester of pregnancy (n=43%) were mostly affected by anaemia. Additionally, gestational age and ethnicity were the main factors that were positively correlated with anaemia. Despite the immense effort made by the Malaysian government to

Keywords: Anaemia; Maternal outcomes; Perinatal outcome

Introduction

Anaemia is a widespread public health problem amongst pregnant women worldwide [1-3]. About half of all anaemic women live in the Indian subcontinent, where 88% of them developed anaemia during pregnancy [4]. Recent World Health Organization (WHO) data shows that Africa has the highest frequency (57.1%) of anaemia in the world [5]. WHO defines cut-offs value for anaemic pregnant women as haemoglobin (Hb) concentration of less than 11 g/dl and a haematocrit of less than 0.332 at sea level [3]. The severity of anaemia in pregnancy is based on the level of Hb, i.e., mild anaemia (between 10-10.9 g/dL), moderate (7.0-9.9 g/dL) and severe of less than 7.0 g/dL [3]. Maternal anaemia is commonly considered as a risk factor for poor pregnancy outcome [6] and has been associated with a multitude of problem on both woman and neonate [7]. Ghimire and Ghimire have found that severe anaemia significantly increases the risk of neonatal complication which includes pre-term delivery, low birth weight and small for gestational age [8]. Similarly, moderate anaemia have been linked with increased weakness, lack of energy, fatigue and poor work performance among the pregnant women and severe anaemia has been associated with poor maternal and fetal outcome [9]. Anemia in

Conclusion

Anaemia amongst pregnant women especially multipara imposed a spectrum of health problems to both, mother and child. Prevention is not insurmountable; hence active intervention by all level of health care provider is imperative in order to decrease poor maternal and perinatal outcome.

Materials and method: This retrospective cross-sectional study was conducted in a tertiary public hospital in Serdang, Selangor. 473 anaemic mothers were recruited from the electronic medical database by clinical notes and cross-referencing to the datasets of relevant test. All subjects received antenatal oral iron supplementation.

Results: Multiparous mother contributed to majority of the anemia cases in pregnancy (60.5%). Out of 473 anaemic mother suffering from Iron Deficiency Anemia (IDA), 61.3% (n=290) mothers had mild anaemia, 38.5% (n=182), and 0.2% (n=1) mothers had moderate and severe anaemia respectively. A significant association was demonstrated between severity of anaemia with postpartum haemorrhage and small for gestational age. On contrary, severity of maternal anaemia was non-significantly associated with placenta abnormalities, preeclampsia and sepsis.

Abstract

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Objective: This study aimed to analyze the relationship of antenatal anaemia with maternal and perinatal outcome among parturient delivering in Hospital Serdang.

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Keywords: Anaemia; Maternal outcomes; Perinatal outcome
reduce the health and economic burden of anaemia in pregnancy, it prevalence and impact on maternal health have not been explored comprehensively in our country.

Materials and Methods

Ethics
Ethics approval (reference NMRR-15-557-25505) was granted by the National Medical Research Register Ministry of Health, Malaysia (NMRR), Clinical Research Centre Serdang, Malaysia (CRC) and The University Research Ethics Committee, Universiti Putra Malaysia (JKEUPM).

Study population
This is a cross-sectional retrospective study conducted from January to June 2015 in Hospital Serdang, Selangor. Hospital Serdang is a government-funded multi-specialty hospital located in the district of Sepang, in the state of Selangor, Malaysia and serving approximately 570,000 populations. The hospital provides tertiary antenatal care, receiving referrals from other clinics and private hospitals and for women who live close to the hospital facility, as well as serving as teaching hospital for medical student from Faculty of Medicine and Health Sciences, Universiti Putra Malaysia.

Study criteria
Sample size was calculated using standard errors associated with confidence intervals (1.96) and standard errors associated with power (0.842). Universal sampling was used during sample selection. Eligible pregnant women were identified via electronic medical database by clinical notes and cross-referencing to the datasets of test results included full blood count (FBC), ferritin level, date of investigation and information about gestational age, such as estimated date of delivery, gestational age at the time of blood testing or follow-up and date of last menstrual period. Results were de-identified, but results for each individual woman remained linked and only mothers with singleton pregnancy diagnosed with Iron Deficiency Anemia (IDA) were included in the study. Exclusion criteria include patients with other chronic illnesses, e.g. chronic kidney disease, malignancy, thalassemia or other causes of anemia in pregnancy and previous blood transfusion at least three month prior to study recruitment. Hb level was used to classify severity of anaemia. The cut-off point of Hb level in pregnant women as defined by World Health Organization (WHO) are mild anaemia, Hb level between 10.0-10.9 g/dl; moderate anaemia, Hb level between 7.0-9.9 g/dl; and severe anemia, Hb level less than 7.0 g/dl [3]. All subjects received antenatal oral iron and folic acid supplementation (ferrous fumarate 200 mg daily, folic acid 5 mg od) as per hospital antenatal care protocol.

A total of 473 anaemic mothers diagnosed with IDA were recruited in this study. The prevalence of maternal anemia secondary to IDA during the study period was 14.3%. Data was analyzed using IBM SPSS Statistics version 21.0. Descriptive analysis was used to describe the distribution of socio-demographic, antenatal profile and severity of anaemia. The association between categorical variable which includes severity of anaemia and outcomes in mothers and newborns were analyzed using Chi square test and Fisher’s exact test. All statistical tests were evaluated at the 0.05 significance level.

Maternal and Perinatal Outcome: The maternal outcomes explored in this study were postpartum haemorrhage, placenta abnormality, preeclampsia and sepsis. Postpartum haemorrhage was defined as blood loss of more than 500 ml following vaginal delivery and 1000 ml following a cesarean section delivery. Abnormal placenta implantation (placenta previa), abnormal placental invasion (placenta accrete/increta/percreta) and premature placental separation (placenta abruptio) were described as placenta abnormality. NICE guideline 2015 defined Preeclampsia as new onset of hypertension and either proteinuria or end-organ dysfunction after 20 weeks of gestation in a previously normotensive women.

Preterm birth, low birth weight, small for gestational age and intrauterine growth restriction were the perinatal outcomes that were studied in this research. World Health Organization (WHO) defines preterm birth as babies born alive before 37 completed weeks’ gestation and low birth weight (LBW) is defined as baby’s birth weight of less than 2500 g. Small for gestational age (SGA) is defined as infant born with a birth weight less than the 10th centile for that appropriate gestational age. Intrauterine growth restriction (IUGR) refers to the foetus that has not achieved the expected in utero growth potential due to genetic or environmental factors.

Results
Total number of patients who have fulfilled the inclusion and exclusion criteria was 473, giving the prevalence rate of maternal anaemia secondary to IDA during the study period of 14.3%. The highest numbers of anaemic mothers by ethnicity were Malays (85.4%). Multiparous mother contributed to majority of the anaemia cases in pregnancy (67%). The mean gestational age at delivery was 37.67±2.68 (Table 1).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Frequency n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age</td>
<td>29.62±5.12</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
</tr>
<tr>
<td>Malay</td>
<td>404 (85.4)</td>
</tr>
<tr>
<td>Chinese</td>
<td>21 (4.4)</td>
</tr>
<tr>
<td>India</td>
<td>18 (3.8)</td>
</tr>
<tr>
<td>Others</td>
<td>30 (6.3)</td>
</tr>
<tr>
<td>Gravidity</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>131 (27.7)</td>
</tr>
<tr>
<td>2-4</td>
<td>289 (61.1)</td>
</tr>
<tr>
<td>&gt;5</td>
<td>53 (11.2)</td>
</tr>
<tr>
<td>Parity</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>155 (32.8)</td>
</tr>
<tr>
<td>2-3</td>
<td>228 (48.2)</td>
</tr>
<tr>
<td>&gt;4</td>
<td>90 (18.8)</td>
</tr>
<tr>
<td>Gestational age at delivery</td>
<td>37.67±2.68</td>
</tr>
</tbody>
</table>

Table 1: Demographic and clinical characteristics (n=473).
Out of 473 anaemic mothers suffering from IDA, 61.3% (n=290) mothers had mild anaemia, 38.5% (n=182), and 0.2% (n=1) mothers had moderate and severe anaemia, respectively. Further analysis showed 23.9% (n=113) of anaemic women suffered from placenta abnormality (placenta previa, placenta abruptio) and 10.8% (n=51) was complicated with postpartum haemorrhage. 7.2% (n=34) and 2.5% (n=12) of these anaemic mothers had preeclampsia and antenatal infection respectively. A significant numbers of mothers with IDA experienced preterm birth (15.6%); and 14.6% of the parturient gave birth to LBW newborn. Meanwhile, 5.9% (n=28) and 2.7% (n=13) new-borns were complicated with SGA and IUGR respectively (Table 2).

<table>
<thead>
<tr>
<th>Severity</th>
<th>Frequency (n)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>290</td>
<td>61.3</td>
</tr>
<tr>
<td>Moderate</td>
<td>182</td>
<td>38.5</td>
</tr>
<tr>
<td>Severe</td>
<td>1</td>
<td>0.2</td>
</tr>
<tr>
<td>Total</td>
<td>473</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 2: Severity of anaemia with maternal and perinatal outcome.

Interestingly, this study revealed four morbidity associated with mild maternal anemia namely placenta abnormality (23.9%, n=66), postpartum haemorrhage (7.9%, n=23), preeclampsia (7.2%, n=21) and infection (1.4%, n=4). These maternal related complications were slightly increased in moderate to severe anaemic mothers, i.e., placenta abnormality of 25.7% (n=47), postpartum haemorrhage of 15.3% (n=28), preeclampsia of 7.1% (n=13), and sepsis of 4.4% (n=8). A statistically significant association was revealed between postpartum haemorrhage and severity of maternal anaemia (p=0.012) (Table 3).

<table>
<thead>
<tr>
<th></th>
<th>Mild</th>
<th>Moderate &amp; Severe</th>
<th>X²</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postpartum haemorrhage</td>
<td>23 (7.9)</td>
<td>28 (15.3)</td>
<td>6.334</td>
<td>0.012a</td>
</tr>
<tr>
<td>Placenta abnormality</td>
<td>66 (22.8)</td>
<td>47 (25.7)</td>
<td>0.528</td>
<td>0.488a</td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>21 (7.2)</td>
<td>13 (7.1)</td>
<td>0.003</td>
<td>0.955a</td>
</tr>
<tr>
<td>Infection (sepsis)</td>
<td>4 (1.4)</td>
<td>8 (4.4)</td>
<td>N/A</td>
<td>0.068b</td>
</tr>
</tbody>
</table>

Table 3: Severity of anaemia with maternal adverse outcomes.

The study demonstrated a significant association between severity of maternal anaemia and SGA (p=0.004). 9.8% of the babies delivered by mother who suffered from moderate to severe anaemia were born as SGA as compared to 3.4% in mother who had only mild anaemia in pregnancy (Table 4).
supplementation was uncertain as the data were retrieved from the Andhra Pardesh [19] whereas 4% of severely anemic mother were

statistical data shows that 25% of maternal deaths occur due to PPH

multitude of complications such as maternal infection, prematurity, IUGR and low birth weight [17]. Nutritional Iron Deficiency Anaemia

IDA. In the present study, the prevalence of maternal anemia secondary to IDA during the study period was 14.3%. A local study in South-ease of Peninsular Malaysia reported that 35% of Malaysian mothers were inflicted by anemia in pregnancy and mostly of the mild type and more prevalent in the Indian and Malays communities [16]. This difference may possibly attributed by the difference geographical distribution whereby our study was conducted in urban area and the later was undertaken in rural district region. All patients in this study received oral iron supplementation of ferrous fumarate 200 mg daily along with folic acid 5 mg daily as per the government antenatal care protocol. These prescriptions are freely available in all our health care centers and prescribed to all pregnant women as early as 14 weeks period of gestation. Nonetheless, patient's compliance towards iron supplementation was uncertain as the data were retrieved from the electronic medical database. In the present study, maternal anemia was detected at late second trimester and early third trimester. Majority (85.4%) of the anaemic mother were of Malay ethnicity which is the predominant race in Malaysia, followed by Chinese (4.4%) and Indian (3.8%). 61.3% (290/473) of the mothers had moderate anaemia and 0.2% (1/473) had severe anaemia. These findings are comparable with other Asian country. Baig-Ansari found that 0.7% mothers were severely anaemic in an urban setting in Pakistan [18]. Likewise, Bentley and Griffiths has discovered that 2.2% pregnant women suffered from severe anaemia in Andhra Pardesh [19] whereas 4% of severely anemic mother were reported in Vietnam [5].

Table 4: Severity of anaemia with perinatal adverse outcomes.

<table>
<thead>
<tr>
<th></th>
<th>Mild</th>
<th>Moderate and Severe</th>
<th>χ²</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preterm birth</td>
<td>38 (13.1)</td>
<td>36 (19.7)</td>
<td>3.668</td>
<td>0.055a</td>
</tr>
<tr>
<td>Small for gestational age</td>
<td>10 (3.4)</td>
<td>18 (9.8)</td>
<td>8.22</td>
<td>0.004a</td>
</tr>
<tr>
<td>Low birth weight</td>
<td>35 (12.1)</td>
<td>34 (18.6)</td>
<td>3.817</td>
<td>0.051a</td>
</tr>
<tr>
<td>Intrauterine growth restriction</td>
<td>7 (2.4)</td>
<td>6 (3.3)</td>
<td>0.314</td>
<td>0.575a</td>
</tr>
</tbody>
</table>

Discussion

Anaemia complicating pregnancy is a known menace to both mother and fetus. It is not only a global pandemic but also instigates a multitude of complications such as maternal infection, prematurity, IUGR and low birth weight [17]. Nutritional Iron Deficiency Anaemia is the commonest cause of anaemia during pregnancy and hence our study population involved all pregnant mothers suffering from IDA. In the present study, the prevalence of maternal anaemia secondary to IDA during the study period was 14.3%. A local study in South-ease of Peninsular Malaysia reported that 35% of Malaysian mothers were inflicted by anemia in pregnancy and mostly of the mild type and more prevalent in the Indian and Malays communities [16]. This difference may possibly attributed by the difference geographical distribution whereby our study was conducted in urban area and the later was undertaken in rural district region. All patients in this study received oral iron supplementation of ferrous fumarate 200 mg daily along with folic acid 5 mg daily as per the government antenatal care protocol. These prescriptions are freely available in all our health care centers and prescribed to all pregnant women as early as 14 weeks period of gestation. Nonetheless, patient's compliance towards iron supplementation was uncertain as the data were retrieved from the electronic medical database. In the present study, maternal anemia was detected at late second trimester and early third trimester. Majority (85.4%) of the anaemic mother were of Malay ethnicity which is the predominant race in Malaysia, followed by Chinese (4.4%) and Indian (3.8%). 61.3% (290/473) of the mothers suffered from mild anaemia, 38.5% (182/473) had moderate anaemia and 0.2% (1/473) had severe anaemia. These findings are comparable with other Asian country. Baig-Ansari found that 0.7% mothers were severely anaemic in an urban setting in Pakistan [18]. Likewise, Bentley and Griffiths has discovered that 2.2% pregnant women suffered from severe anaemia in Andhra Pardesh [19] whereas 4% of severely anemic mother were reported in Vietnam [5].

Maternal Outcome

Postpartum haemorrhage (PPH) is recognized as one of the leading cause of maternal mortality worldwide. WHO defined PPH as an estimated blood loss of greater than 500 mL in vaginal deliveries and greater than 1000 mL in cesarean deliveries [17]. Severe anaemia may impair myometrial contractility resulting from impaired oxygen-carrying capacity leading to enzyme and cellular dysfunction. WHO statistical data shows that 25% of maternal deaths occur due to PPH [20]. The result obtained from this study demonstrated that PPH was seen in 7.9% cases of mild anaemia and 15.3% in cases of moderate to severe anaemia. In addition, PPH were significantly associated with the varying degree of severity of anaemia. Frass in her observational studies explained that relationship between PPH and severe anaemia accounting for about 90% in most studies [21]. Pregnant women with moderate-to-severe anaemia had a significantly greater total blood loss of an average 91 mL [21] as compared to non-anaemic women (p<0.01). Kavle found that blood loss at delivery was slightly elevated in mild anaemic women as compared to non-anaemic women [22]. He also observed strong association between the severity of anaemia with blood loss at delivery and in the postpartum period [22].

The susceptibility of women with severe anaemia to preeclampsia has been linked to deficiency of micronutrients and antioxidants. The reduction in serum levels of calcium, magnesium and zinc during pregnancy have been linked to the development of preeclampsia [23]. The present study revealed a non-significant association between severities of maternal anaemia with preeclampsia. Nonetheless, we believe a larger population group would yield an otherwise significant association as in a study conducted by Ali et al. where they revealed that women suffered from antenatal anaemia had 3.6 times higher risk of preeclampsia as compared to non-anaemic mothers [12]. They proved that the greater the severity of maternal anemia, the greater the risk of preeclampsia (OR 1.6 (0.8-3.4), P 0.1). Similarly, Uzan discovered that the risk of preeclampsia was 2 to 5 fold higher in pregnant women with anaemia [24].

Numerous studies have attempted to explore the association of severity of maternal anaemia and placental abnormality. Bencaiova and Breymann reported frequency of placenta abnormality in association with maternal anaemia in Zurich was 3.6% [1]. Conversely, our study revealed 23.9% of the mothers with IDA suffered from placental abnormality in association with mild anaemia whereas 0% [22]. He also observed strong association between the severity of anaemia with blood loss at delivery and in the postpartum period [22].

Severe anaemia in pregnancy requires urgent medical treatment and Hb<4 g/dl is an emergency carrying a risk of congestive cardiac failure, sepsis and death. Jaled and Khan observed a high frequency of cesarean section or episiotomy wound infection in severely anaemic pregnant women as compared with non-anaemic pregnant women [25]. Rukuni et al. had showed that anaemic mothers were more susceptible to postpartum infection and sepsis (adjusted OR 1.89, 95% CI 1.39–2.57) [26]. These results differ from our findings in which the association of severity of anaemia with sepsis was not statistically significant.

Perinatal Outcome

Maternal anaemia causes a substantial reduction in oxygen carrying capacity and hence impairment of oxygen delivery to placenta and
fetus. This later resulted in a significant impact to perinatal health particularly SGA and IUGR. SGA has been found to have significant association with severity of anaemia as compared to preterm birth and LBW [27]. On contrary, study on Finnish women has revealed no correlation between maternal anaemia in the first trimester with SGA [28]. This is could be due to the population involved in the later study are known to have low prevalence of severe anaemia in pregnancy. Yi et al. [27] had demonstrated an association between SGA and severity of anaemia in large retrospective cohort study among anaeimic Korean women. Study conducted in University Hospital of Zurich, Swiss found that pregnant women with an Hb level between 8.0 and 9.9 g/dl having significantly higher risk for SGA [1] compare with pregnant women with Hb level between 10.0 and 11.9 g/dl.

Several studies have reported that maternal anaemia during pregnancy is associated with low birth weight (LBW). WHO defines LBW as baby weight of less than 2500 g. According to Ali et al. [12], women with mild/moderate anaemia having 2.5 times higher of LBW as compared to women with no anaemia (95% CI: 1.1-5.7). Women with severe anaemia having 8.0 times higher risk of LBW (95% CI: 3.8-16.0). Kidanto [29] found that risk of low birth weight and preterm delivery were significantly increased with severity of maternal anaemia. Furthermore, Sangeeta have found that the risk of preterm delivery increases with severity of anaemia [30]. They also found that IUGR had a statistically significant association with severity of anaemia [30]. Similarly, Kalavani in her study also reported that prematurity delivery rate and IUGR escalates when maternal Hb levels were below 8.0 g/dl [31]. In contrary, the present study revealed only 5.9% of the fetus born as LBW and 15.6% cases of premature delivery. These two outcomes were not statistically significantly associated with severity of maternal anaemia.

Study Limitation and Recommendation

A larger cohort study would be ideal in order to generate a more significant clinical exposure and outcome for which an effective interventional program could be designed to improve the overall outcome of maternal anaemia. Researchers recommend future studies with larger sample size, supported by a grant and longer study period and inclusion of dietary intake among antenatal mothers as potential confounder.

Conclusion

Anaemia amongst pregnant women imposed a significant spectrum of health problems to both, mother and child. Prevention is not unsurmountable; hence active intervention by all level of health care provider is imperative in order to decrease poor maternal and perinatal outcome and hence the overall economic burden.

Acknowledgement

We gratefully acknowledge the Director of Hospital Serdang and all the members of the Department of Obstetrics and Gynaecology, for their assistance in the study. In addition, we thank all lecturers who have assisted us to complete this study. This work was supported by the Faculty of Medicine and Health Sciences, University Putra Malaysia.

References


