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MATERNAL ANAEMIA-AN INDEPENDENT RISK FACTOR FOR PERINATAL MORTALITY

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ABSTRACT

Low birth weight from intrauterine growth restriction (IUGR) and prematurity was reportedly the major cause of perinatal mortality. The aim of this study was to investigate if maternal anaemia ([Hb] < 10gdl) increases perinatal mortality after controlling for low birth weight and prematurity in low resource setting. It was a population-based cohort study using data from Ladoke Akintola University of Technology Teaching Hospital, Osogbo perinatal database. Patients with haemoglobinopathies as well as chronic medical illnesses were excluded. Multiple logistic regression analysis was performed to control for confounders. Anaemic patients were found to have higher rates of previous caesarean deliveries, IUGR, labour induction, placenta praevia, abruption placenta and breech presentation than their non-anaemic controls. There were higher rates of caesarean births in the anaemic group, as well as higher rates of birth asphyxia and perinatal mortality. The significant association of maternal anaemia with increased perinatal mortality remains significant after adjusting for IUGR and prematurity. Moreover, anaemia remains an independent predictor of perinatal mortality from the logistic regression model. In conclusion, perinatal mortality is increased by maternal anaemia, independent of IUGR or prematurity.

KEYWORDS: Anaemia, Prematurity, Intrauterine Growth Restriction, Perinatal Mortality

INTRODUCTION

Anaemia in pregnancy is defined as haemoglobin concentration < 10g/dl, with an incidence as high as 40% in developing countries (Lao 1996; Bondevik 2001; Malhotra 2002). The influence of maternal anaemia on pregnancy outcome suffers from controversy. While some studies have reported suboptimal perinatal outcome relating to low birth weight from intrauterine growth restriction and prematurity (Hamalainen 2003, Garn 1981, Murphy 1986, Aimakhu 2003, Lieberman 1988, Klebanoff 1991, Lone 2004), others have not documented any association between maternal anaemia and adverse perinatal outcomes (Scholl 1992, Scanlon 2000, Fareh 2005, Xiong 2000).

The mechanism by which maternal anaemia causes perinatal mortality is reportedly mediated by the occurrence of IUGR and prematurity (Zhang 2009). However, this assertion has been challenged by Levy and colleagues (2005) who reported that some women with anaemia in pregnancy still had good perinatal outcomes. Therefore we design the present study to elucidate if maternal anaemia is associated with adverse perinatal outcome independent of low birth weight in a resource-constrained setting where anaemia is prevalent.

MATERIALS AND METHODS

This is a retrospective cohort study of patients with or without anaemia in pregnancy in Ladoke Akintola University of Technology Teaching Hospital, Osogbo over a three year period (2012 – 2014). For the purpose of this study,

maternal anaemia was defined as haemoglobin concentration lower than 10g/dl during pregnancy. Inclusion criteria were women who were anaemic in the first half of pregnancy and had singleton gestation. Exclusion criteria were women with haemoglobinopathies and chronic medical illness. The study was considered as exempt research by the institutional review committee.

Data were retrieved from the perinatal database comprising information collected uniformly according to pre-defined criteria. Demographic characteristics examined were maternal age, parity, gestational age at delivery, gender and birth weight. Obstetric characteristics analyzed were previous caesarean delivery, recurrent miscarriages, IUGR in index pregnancy, labour induction, placenta abruption, placenta praevia, malpresentation and fetal distress in labour. Delivery characteristics examined were mode of delivery, postpartum haemorrhage and need for blood transfusions. Neonatal outcomes studied were Apgar scores, need for neonatal intensive care unit admission for >24hours, and perinatal mortality.

An initial univariate analysis was carried out, with chi-square test for comparison of qualitative variables and Student's t-test for continuous variables. Test of association between maternal anaemia and perinatal mortality was conducted with the Mantel-Haenszel test, adjusting for low birth weight and prematurity. Subsequently, a multivariate logistic regression model was constructed to adjust for variables that were significantly associated with maternal anaemia on univariate analysis. Statistical significance was set at $P < 0.05$, and Odds Ratios (OR) with 95% confidence intervals (CI) excluding 1.00. Statistical analysis was performed using the SPSS-12 package (SPSS, Chicago, IL).

RESULTS

A total of 2207 pregnant women who underwent haemoglobin estimation in the first half of pregnancy were studied. The median maternal age was 27years (interquartile range [IQR] 23-31), and 1039 (47.1%) were nulliparous. The median gestational age at delivery was 39 weeks plus 5days (IQR 38weeks + 4days to 40weeks + 6days), and the median birth weight was 3,157g (IQR 2,799 – 3,440g).

Table 1 shows the demographic variables in anaemic versus non-anaemic women. There were higher rates of older women, grand multiparty, underweight, premature delivery and low birth weight infants in the anaemic group. Table 2 shows the obstetric characteristics of anaemic and non-anaemic women. Again, there were higher rates of previous caesarean delivery, IUGR, labour induction, placenta praevia, abruption placenta and malpresentations in the anaemic group. In addition, the risk of caesarean delivery, birth asphyxia and perinatal mortality was increased in the anaemic group.

Controlling for prematurity and low birth weight, both of which are associated with increased perinatal mortality, did not change the significant association between maternal anaemia (both overall and severe) and perinatal mortality. Moreover, controlling for confounding factors with significance on multiple logistic regression models (table 3) showed maternal anaemia to be an independent risk factor for perinatal mortality (Odds Ratio 1.3, 95% Confidence interval 1.1 – 1.6).

Table1: Demographic and Clinical Variables

Clinical Variables	Anaemic Patients	Non-Anaemic	P-Value
Maternal Age	28.5 ± 5.7	27.8 ± 5.9	< 0.001
Parity			
1	47.2	46.9	
2- 4	26.8	33.7	< 0.001

5+	26.0	19.4	
BMI			
Underweight	14.5	20.4	
Normal weight	62.3	61.9	< 0.001
Overweight	23.2	17.7	
Birth weight(g)			
< 2500	22.7	14.4	
2500 – 4000	76.0	78.2	< 0.001
>4000	1.3	7.4	
Foetal gender			
Male	51.5	50.7	
Female	48.5	49.3	0.90

Table 2: Obstetric Risk Factors, Maternal and Neonatal Outcomes. Values Expressed As Percentages

	Anaemic Patients	Non- Anaemic	P-Value
Previous CS	16.5	11.0	< 0.001
IUGR	6.6	3.3	< 0.001
Labour induction	15.0	11.4	0.003
Placenta praevia	0.7	0.4	< 0.001
Abruptio placenta	1.4	0.7	< 0.001
Malpresentation	7.1	5.0	0.028
Caesarean section	21.2	10.9	< 0.001
Forceps/vacuum	16.0	15.8	0.0832
Spontaneous delivery	63.8	73.3	< 0.001
Apgar score <4 at 5min	7.2	3.1	< 0.001
Perinatal mortality	18.3	5.0	< 0.001

Table 3: The Association between Maternal Anaemia and Perinatal Mortality (PM)

Variable in Analysis	OR	95% CI	P-Value
Anaemia overall ([Hb] < 10g/dl)			
Crude OR for PM	1.9	1.7 – 2.3	< 0.001
ORs for PM adjusted for			
Prematurity	1.6	1.4 – 1.7	< 0.001
Low birth weight	1.5	1.4 – 1.6	< 0.001
Severe anaemia ([Hb] < 8g/dl)			
Crude OR for PM	2.7	2.5 -2.9	< 0.001
ORs for PM adjusted for			
Prematurity	1.8	1.7 – 1.9	< 0.001
Low birth weight	1.5	1.3 – 1.6	< 0.001

DISCUSSIONS

The main findings of this study are that both anaemia overall, and severe anaemia, during the first half of pregnancy are significantly associated with increased rates of premature delivery, low birth weight as well as perinatal mortality. And that the association with perinatal mortality was not mediated by the prematurity or low birth weight seen in the anaemic arm of the study.

Several studies have already documented the associations observed above (Hamalainen 2003, Garn 1981, Murphy 1986, Aimakhu 2003, Lieberman 1988, Klebanoff 1991, Lone 2004), but did not show the independence association with perinatal mortality in spite of low birth weight or prematurity. The traditional view has been that maternal anaemia results in adverse pregnancy outcome as a result of low birth weight and preterm delivery. However, recent report noted that

although maternal anaemia resulted in low birth weight and prematurity, the perinatal outcome is still good in developed countries, suggesting that sophisticated functional special baby care facilities could have played a major role in higher salvage rate compared to what obtains in the developing world.

The strength of our study was that we specifically adjusted for the confounding effects of prematurity and low birth weight, as well as significant demographic and obstetric factors associated with maternal anaemia. Thus we are able to specifically state the dependence or otherwise of the association between anaemia in pregnancy and pregnancy outcome.

The limitation of this study was the unavailability of data on the duration of anaemia and the haemoglobin concentration used was not at the same gestational age for all the patients, even though all were in the first half of pregnancy.

The implication of our study is that strategies to prevent anaemia in pregnancy such as iron and micronutrient supplementation (Goonewardene 2012) and use of antimalarial prophylaxis in pregnancy (Achidi 2005) should be encouraged especially in developing countries. Although, previous report(Io Lao 2000) showed lack of benefit from routine iron supplementation in developed countries, and a metananalysis of 20 randomized trials also did not report significant benefit from iron supplementation(Mahomed 2004), for settings with high prevalence of anaemia as is obtained in developing countries, routine supplementation should not be discouraged. Also, even if IUGR and prematurity do not complicate an anaemic pregnancy, the perinatal care should be optimised. Our study also raised the need for further research into the mechanism by which maternal anaemia causes perinatal mortality. Although, the perinatal outcome is different between countries, the poor availability of functioning facility for perinatal care has been alluded to above.

CONCLUSIONS

Anaemia in pregnancy is associated with prematurity, low birth weight and perinatal mortality, but the association with the latter is not mediated by the former. This call for the need for further antenatal surveillance, which should not be relaxed simply because of demonstrable satisfactory fetal growth. Furthermore, such fetuses will benefit from special care from delivery. Finally, studies should address the exact mechanism for the increased perinatal mortality rate associated with maternal anaemia.

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