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Maternal anaemia, intra uterine growth restriction and neonatal outcomes

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Abstract

Background: Anaemia with intra uterine growth restriction (IUGR) may aggravate adverse neonatal outcomes like preterm birth, low birth weight, high perinatal morbidity and mortality along with negative long-term sequelae.

Objective: The objective of this study was to find an association between maternal anaemia in clinically diagnosed IUGR pregnancies with neonatal outcomes.

Materials and methods: A prospective study was conducted in a tertiary care hospital in which one hundred and twenty consecutive clinically suspected cases of singleton IUGR pregnancies at 34-40 weeks of gestation were enrolled. Their sociodemographic profile and hemoglobin levels were recorded. A descriptive analysis of the data was performed.

Results: Of 120 study subjects with IUGR at 34-40 weeks, 68% were anaemic, (47% had mild, 20% had moderate, 1% had severe anaemia) while 32% were not anaemic. Significantly, the ratio of anaemic to non anaemic in antenatal IUGR pregnancies was 2.1:1. A birth weight of less than 2.5 kgs was recorded in 94.44% of pregnancies with moderate anaemia and 73.68% pregnancies with mild anaemia. Forty-three babies required admission to NICU with a duration of 2-7 days of which 46.51% (n=20) were born to mothers with Hb less than 11g/dl.

Conclusion: Moderate to severe anaemia in IUGR may increase the chances of low birth weight and adverse neonatal outcomes but larger studies with standardized definitions and measurements of exposure outcomes to bring about uniformity are required to determine an accurate assessment of association between low maternal hemoglobin and IUGR.

Keywords: Anaemia, intrauterine growth restriction, neonatal outcomes

Introduction

Anaemia during pregnancy is an important public health problem especially in developing countries, due to its association in increasing morbidity in any complication associated with pregnancy [1]. According to population studies a prevalence of anaemia $\geq 40\%$ is considered a severe public health problem [2]. Globally, 56% of pregnant women in low- and middle-income countries have anaemia [1]. In Southeast Asia, the prevalence of anaemia in pregnant women is 48%. India, according to the National Family Health Survey - 4 (NFHS 2015-16) amongst pregnant women in the 15-49 years age group, has a prevalence of anaemia at 50.4% [3]. The World Health Organization (WHO) has defined anaemia in pregnancy as the haemoglobin (Hb) concentration of less than 11 g/dl [4,5]. The WHO grading of anaemia; mild, moderate and severe on the basis of haemoglobin concentration is shown in Table 1.

Anemia has been hypothesized to be a predisposing risk factor for intrauterine growth retardation (IUGR) increasing the chances of adverse neonatal outcomes and perinatal death [6]. IUGR is a clinical definition applied to neonates born with features of malnutrition and in-utero growth retardation. Globally, it is estimated that IUGR affects 24% of the newborns, which accounts for around 30 million infants born annually [7]. Approximately 75% of all infants in the Asian continent are IUGR closely followed by the African and Latin American countries [8]. In India, the National Neonatal Perinatal database reports the incidence of IUGR to be 9.65% among hospital born live infants while a recent UNICEF survey pens the incidence to be about 25-30% [9].

The causes of IUGR are varied and may relate to placental insufficiency with the placenta unable to keep up with the growing demands of the fetus [10]. A possible mechanism suggested for IUGR in women with anaemia is that low hemoglobin levels restrict oxygen circulation in

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the body, thus creating an environment of oxidative stress or chronic hypoxia, which could then cause fetal growth restriction. Another reason, specific to iron deficiency anaemia pertains to an increased production of norepinephrine in iron deficient states, stimulating the production of corticotropin-releasing hormone. This in turn increases cortisol production which may possibly restrict fetal growth [11].

Aims and objectives: The objective of this study was to find an association between maternal anaemia in clinically diagnosed IUGR pregnancies with neonatal outcomes.

Material and Methods: This was a prospective, observational study conducted in Department of Obstetrics and Gynaecology, Kamla Nehru State Hospital for Mother and Child, IGMC Shimla over a period of one year from August, 2017 to July, 2018. A total of 120 consecutive clinically suspected cases of IUGR with singleton pregnancies at 34-40 weeks of gestation were included in the study after taking an informed consent. A detailed antenatal history, socio-demographic factors and obstetric history was obtained. The socio-economic status was calculated based on modified Kuppuswamy scale 2019 [12]. The BMI was calculated based on the weight and height recorded using standard calibrated weighing scale and wall mounted stadiometer. The hemoglobin levels were estimated by the cyanmethemoglobin method and recorded. The classification of anaemia was based on the WHO criteria; hemoglobin (Hb) concentration of <11 g/dl during pregnancy was considered as anemia and graded as mild, moderate, and severe anemia depending upon the Hb concentration in the range of 10–10.9, 7–9.9, and <7 g/dl respectively. The gestational age was determined on the basis of last menstrual period if patient was sure of her dates or by first trimester ultrasound if available. The clinical diagnosis of IUGR was made on the basis of poor maternal weight gain and a non- correspondence with the period of gestation (fundal height less than the period of gestation) and an ultrasound. All the subjects were followed up until delivery. After delivery, the birth weight, APGAR score after 5 minutes and any adverse perinatal outcome in terms of asphyxia, hypoglycaemia, perinatal death or admission & stay in NICU were noted. The data was collected, compiled, analysed and descriptive analysis performed. The study was approved by the college protocol committee.

Results: Out of the 120 clinically diagnosed cases of IUGR who enrolled in the study 70% (n=83) were from the rural background and 44% (n=51) were primigravida. The mean age of the subjects was 21.8 years \pm 3.1 SD. Forty two percent of the antenatal mothers were in the age group of 20-25 years (n=50) followed by 41% in the age group of 26-30 years. The sociodemographic characteristics are shown in Table 2. All 120 study participants were non-smokers and non- alcoholics while 67.5% (n=81) were non-vegetarians. Anaemia was reported in 68% of antenatal mothers while 32% had no anaemia. Out of these 68%, 47% had mild, 20% had moderate, and 1% had severe anaemia (Fig1). The ratio of anaemic to non-anaemic

IUGR pregnancies was 2.1:1. The distribution of anemia in relation to the urban vs rural showed that 68.6% from the rural background were anaemic as compared to 62.1% from urban background as shown in Table 3. The birth weight of less than 2.5 kgs was recorded in 94.4% of pregnancies with moderate anaemia and 73.68% pregnancies with mild anaemia. The BMI ranged from 14.2 kg/m² to 25.5 kg/m² with the average BMI being 19.93 kg/m². Out of the 120 antenatal mothers evaluated, 90 subjects (75.8%) had a normal BMI, 29 subjects (24.1%) were underweight with a BMI of <18.5 kg/m² whereas only one of the subjects (1%) evaluated was overweight with a BMI of 25.5 kg/m². The average height of the subjects was 153.72 cm \pm 4.07 SD and the average pre-pregnancy weight was 47.17kg \pm 5.82 SD. The mean birth weight was 1.92 kg. The minimum birth weight was 900 gm and the maximum birth weight was 3 kg. The association of birth weight in IUGR babies with the degree of anaemia is shown in table 4. Out of the 56 IUGR babies with a birthweight <2.5 Kgs 78.5% (n=44) had mild anaemia and 83.3%(n=20) had moderate anaemia. Forty-three babies required admission to NICU with a duration of 2-7 days of which 20 (46.51%) were born to mothers with Hb less than 11g/dl. The reasons for NICU admission was mainly respiratory distress. The other causes included hypoglycaemia, neonatal jaundice and meconium aspiration syndrome.

Table 1: Hemoglobin levels to diagnose anemia at sea level (WHO criteria)

So. No.	Pregnancy Status	Non-Anemia (g/dl)	Anaemia g/dl		
			Mild	Moderate	Severe
1.	Pregnant women (15 to 49 years)	≥ 11	10–10.9	7–9.9	< 7
2.	Non-pregnant women (15 years or above)	≥ 12	11–11.9	8–10.9	< 8

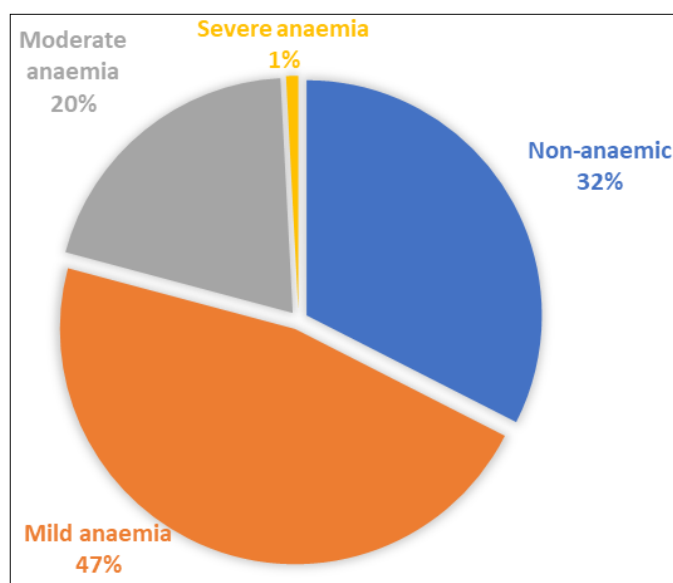


Fig 1: Association of Anaemia in IUGR pregnancies

Table 2: Sociodemographic Characteristics

Variable	Frequency	Percentage
Age Group		
<19	10	8%
$\geq 20-25$	50	42%
$\geq 26-30$	48	41%
≥ 31	12	9%

Religion		
Hindu	112	93.3%
Muslim	8	6.6%
Dietary Habits		
Vegetarian	39	32.5%
Non vegetarian	81	67.5%
Smoking Habits		
Smoker	0	0%
Nonsmoker	120	100%
Education		
<12 th Standard	20	16.7%
Graduate	64	53.3%
Postgraduate	36	30%
Occupation		
Housewife	77	64.2%
Working	43	35.8%
Socioeconomic Class		
Upper middle	36	30%
Lower Middle	54	45%
Upper lower	30	25%

Table 3: Maternal Anaemia and residential status

Variable	Non-anaemic	Anaemia			Total
		Mild	Moderate	Severe	
Urban	13	14	10	0	37(62.1%)
Rural	26	42	14	1	83(68.6%)
Total	39	56	24	1	120(100%)

Table 4: Association of maternal Anaemia in clinically diagnosed cases of IUGR and birthweight.

S. No	Birth weight	Anaemia			No Anaemia 11g/dl or higher	Total (N, %)
		Mild 10-10.9 g/dl	Moderate 7-9.9 g/dl	Severe <7 gm/dl		
1.	≥ 2.5Kgs	12	4	0	4	20(16.6%)
2.	<2.5 Kgs	44	20	1	23	100(83.3%)
3.	Total	56	24	1	39	120(100%)

Discussion

The literature on the correlation of maternal anemia in IUGR pregnancies and neonatal mortality and morbidities is limited. Both anaemia and IUGR individually are responsible for adverse neonatal outcomes. Hence, the aim of this study was to decipher any significant association between maternal anaemia in clinically diagnosed IUGR pregnancies and neonatal outcomes. In our study, anaemia was classified according to the WHO criteria [5]. The ratio of anaemic to non-anaemic IUGR pregnancies was 2.1:1. In our study 68% were anaemic, (47% had mild, 20% had moderate, 1% had severe anaemia) while 32% were not anaemic. In antenatal women with IUGR from rural areas, anaemia was noted in 68.6% which corresponds to several studies done in rural Karnataka that report a prevalence of 64% in Kolar [13] and 72.5% in Belagavi [14]. However, in urban areas the burden of anaemia was 62.1% which was higher than the prevalence rate of 50.1% found in urban Udupi [15].

Several factors contribute to causation of anaemia during pregnancy; geographical location, dietary practice, access to medical services, pre-pregnancy haemoglobin levels and cultural practices. In our study, socio-demographic factors did not appear to be significantly associated with anaemia although a younger age and a lower socio-economic status are known to be associated with anaemia as revealed in other studies.

The effect of maternal anaemia on the foetus show that with varying degree of anaemia the level of decompensation in the fetus also varies. Maternal haemoglobin below 8.0 g/dl [16] is associated with significant fall in birth weight due to increase in prematurity rate and intrauterine growth retardation. Besides Hb level 11.0 g/dl is associated with a significant rise in perinatal

mortality rate [17]. In our study the mean birth weight was 1.92 kg, minimum being 900 grams. A birth weight of less than 2.5 kgs was recorded in 94.44% of pregnancies with moderate anaemia and 73.68% pregnancies with mild anaemia. Some studies report that maternal anaemia diagnosed at entry to prenatal care was associated with low dietary energy and iron, inadequate gestational weight gain, and two fold or greater increase in the risk of preterm delivery and LBW [18, 19]. A few studies have looked into the effects of anaemia, IUGR and neonatal outcomes. In a meta-analysis, maternal anemia determined in the first and second trimesters is significantly associated with preterm birth but not with low birthweight [20]. In yet another meta-analysis, which included just three studies no association between hemoglobin <100-110 g/l and IUGR was found [21]. The meta-analysis revealed that moderate to severe anemia (<90 or <80 g/L) was significantly associated with SGA, whereas there was no relationship with milder anemia. The associations reported in this meta-analysis are to be viewed with great care, as there is heterogeneity in methods and definitions.

Conclusion

Both anemia and IUGR are a multifactorial disease condition. Individually both have reported to have negative maternal and child health effects. Both are associated with increased risk of preterm births and low birth weight babies. In order to accurately determine the association between maternal anaemia, IUGR and neonatal outcomes, large multicentric prospective studies with standardization of definitions and measurement of exposure outcomes are required to interpret the results uniformly.

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