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Frequency of Low Birth Weight Neonates in Mothers with Low Serum Ferritin Levels

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ABSTRACT

Birthweight significantly influences health throughout life, but the connection between maternal serum ferritin levels during pregnancy and the newborn's birthweight is still a topic of debate. **Objective:** To investigate the prevalence of underweight infants born to the mothers with low blood ferritin concentrations at term delivery. **Methods:** A descriptive cross-sectional study was conducted for a period of six months from November 2019 to April 2020. A total of 151 participants with reduced serum ferritin concentrations at full-term delivery were included in this study. Demographic details were taken including blood sample for serum hemoglobin and ferritin levels were checked and noted in a questionnaire. Data stratification was performed to eliminate other effect modifiers and to statistically test the significance of low birth weight of neonates in mother with low serum ferritin levels, with the help of chi-square test. **Results:** The typical age of the patients was 25.50 ± 4.08 years. Incidence of Low Birth Weight newborn in mother with reduced serum ferritin levels at term delivery was observed in 33.11% (50/151). **Conclusions:** Low birth weight, a prevalent issue in Pakistan, is a significant contributor to perinatal morbidity and mortality. Correction of anemia, consuming a diet with a proper nutrient balance and accessing maternal care during pregnancy are anticipated to decrease the incidence of underweight infants and lower perinatal death rate. This study suggests that mothers should receive counselling on prevention of teenage marriages and pregnancies, maintaining a birth interval of 3 years, iron supplementation during pregnancy and avoiding consanguineous marriages.

INTRODUCTION

Health of a new born is related to the wellbeing of the mother and there are certain indicators that can be used as a predictor to indicate health of the new born [1]. Apart from physical parameters, a number of serum markers have been related to indicate the nutritional status of the body, such as serum and urinary ferritin levels, as evidenced by research conducted in Iran [2]. Ferritin is unique as it does not only indicate about the nutritional status but is an indicator of iron stores too [3]. Iron is a crucial micronutrient that plays a key role in the functioning of all vital body systems, particularly the brain [4]. There are numerous risk factors linked to low-birth weight (LBW) child, like maternal age, smoking, previous deliveries, mode of delivery, domestic abuse, drug abuse and anaemic mother [5-7]. In a study conducted at a tertiary care hospital in Lahore, maternal anemia and poor nutritional intake were the leading causes of Low Birth Weight babies. Other risk factors for Low Birth Weight newborns included

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household income of less than 25,000, uneducated mothers, and maternal age of less than 20 years. A strong correlation with maternal anemia suggests a link to low serum ferritin levels, which can be detected much earlier, even before the mother develops overt anemia [8]. In a prospective cohort study conducted in rural Bangladesh suggested that there was a negative relationship between high levels of plasma ferritin in the last trimester (around 30 weeks of pregnancy) and birth weight. The findings suggested that higher plasma ferritin during pregnancy may negatively affect the baby's birth weight [9]. On the contrary, in a retrospective cohort study conducted in China, it was suggested that a clear link between low ferritin levels and an increased risk of low birth weight, suggesting that maternal ferritin levels during pregnancy could serve as an additional predictor for poor birth weight outcomes [10].Thus, due the controversies related to maternal serum ferritin levels and foetal outcome, in terms of child's birth weight, this research aims to observe the occurrence of Low Birth Weight child in low serum ferritin level mothers in Dr Ruth Pfau Civil Hospital Karachi. While previous studies have shown conflicting evidence regarding the relationship between maternal ferritin levels and birthweight, this study aims to fill the gap by specifically examining this relationship within the Pakistani population. Given the unique dietary, cultural, and health factors in Pakistan, the findings of this study offer valuable insights that may differ from those observed in other populations. This research contributed to a more sophisticated understanding of the factors influencing birthweight in this context, which has been underexplored in existing literature.

Despite extensive global evidence linking maternal iron status with adverse neonatal outcomes, the relationship between low serum ferritin levels and low birth weight (LBW) remains inconsistent and insufficiently explored in the Pakistani population. Existing studies show conflicting findings regarding whether low ferritin is a strong independent predictor of LBW, and limited local data address this association in the context of Pakistan's unique nutritional, socioeconomic, and healthcare disparities. Therefore, the present study aimed to determine the frequency of LBW neonates among mothers with low serum ferritin levels at term delivery and to evaluate its association with maternal hemoglobin, gestational age, and other obstetric factors in a tertiary care setting in Karachi. The study seeks to fill the regional evidence gap and provide locally relevant data to guide preventive maternal health strategies.

METHODS

This was a descriptive cross-sectional study, and was conducted at the Obstetrics and Gynecology Department, Unit 3, of Dr Ruth Pfau Civil Hospital in Karachi, Pakistan, between November 2019 and April 2020.The study was conducted following formal approval from the College of Physicians and Surgeons of Pakistan (Letter reference number: CPSP/REU/OBG-2016-183-7218). A sample size of 151 was calculated based on a prevalence of Low-Birth-Weight babies among mothers with low serum ferritin levels, estimated at 11%, using a 95% confidence level and a 5% margin of error [11]. The study used a non-probability consecutive sampling technique, where participants were selected as they met the inclusion criteria until the required sample size was reached.This method was chosen for its feasibility and accessibility within the study setting. While non-probability consecutive sampling may introduce selection bias, efforts were made to include a diverse range of participants.Data were collected from women delivering in the labour room or undergoing emergency or elective cesarean sections who met the inclusion criteria, following the acquisition of their written informed consent. Women aged between 18 to 35 years presenting at term, with a singleton pregnancy, undergoing vaginal delivery or cesarean sections and having American Society of Anesthesiology (ASA) Class I or II (healthy person or with mild controlled systemic disease) were included in the study. Grand multiparas (5 or more births), history of smoking, women with anemia secondary to acute blood loss, anemia of chronic disease and women with previous history of Low Birth Weight infants were excluded from the current investigation. Blood sample for serum haemoglobin and ferritin was processed and noted. The ASA group, mode of delivery and child's birth weight immediately at birth was noted. Variables were recorded using a structured questionnaire. Continuous variables included age, parity, gestational age (calculated from the earliest ultrasound scan or last menstrual period, if dates were certain), serum hemoglobin, serum ferritin levels, and birth weight. Categorical variables included mode of delivery and the ASA group. Serum hemoglobin and ferritin levels were measured using the Roche Diagnostic USA cobas-6000 analyzer via carbonyl metallo-immunoassay (CMIA) testing. Newborn birth weight was measured using a Romed® Holland Van Oostveen medical B.V. mechanical baby scale (BS-002). SPSS version 21.0 was used for statistical analysis, with a 95% confidence interval. Continuous variables (age, gestational age, serum ferritin, parity, hemoglobin, and birth weight) were summarized using mean ± standard deviation. To compare continuous variables between groups, t-tests or ANOVA were applied, depending on the number of groups. Categorical variables (mode of delivery and low birth weight) were presented as frequencies and proportions, with comparisons made using chi-square tests when appropriate. In this study,

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stratification was used to control for potential effect modifiers, such as maternal age and gestational weeks. Maternal age was categorized into groups based on common clinical thresholds: <20 years, 20-25 years, 26-30 years and ≥30 years. This classification allows for a clear distinction between different age groups, as maternal age is known to impact both ferritin levels and birth weight. Gestational weeks were categorized as follows: 36-37 weeks (preterm), and 37-41+6 weeks (full-term and post term). This stratification helps in accounting for the effects of prematurity, as it can significantly influence birth weight and maternal nutritional status. These categorizations were chosen based on clinical guidelines and previous literature to ensure consistency and relevance in controlling for these potential confounders. Data stratification was performed to eliminate other effect modifiers such as (women's age, weeks of gestational, haemoglobin, mode of delivery) and to statistically test the significance of low birth weight of neonates in mother with low serum ferritin levels, with the help of chi-square test. A p-value of ≤0.05 was regarded as statistically significant.

RESULTS

The overall number of 151 women with reduced blood ferritin concentration at term delivery took part in this research study. A large proportion of the participants were the age group of between 21 and 30 years, as depicted in figure 1.

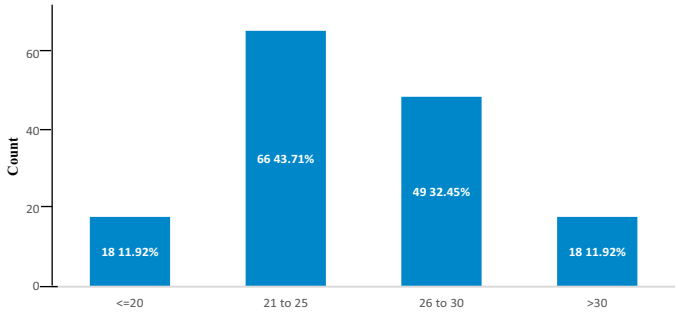

Figure 1: Age Distribution of Women (N=151)

The typical age of the participants was 25.50 ± 4.08 years (95% CI: 24.84 to 26.6). Most of the women were primiparous and mean gestational age, parity, haemoglobin, serum ferritin and birth weight are reported in table 1.

Table 1: Descriptive Analysis of Patient Characteristics

Variables	Mean ± SD	95% CI for Mean	
		Lower Bound	Upper Bound
Age (Years)	25.50 ± 4.08	24.84	26.15
Gestational Age (Weeks)	37.61 ± 1.19	37.42	37.8
Parity	1.47 ± 0.68	1.36	1.58
Hemoglobin	9.42 ± 0.647	9.312	9.52
Serum Ferritin	10.59 ± 1.45	10.35	10.82
Birth Weight (Kg)	2.49 ± 0.58	2.404	2.59

CI=Confidence Interval, Kg=Kilograms

Out of 151 cases, 61.59% women delivered spontaneous vaginally and 38.41% were with caesarean section (figure 2).

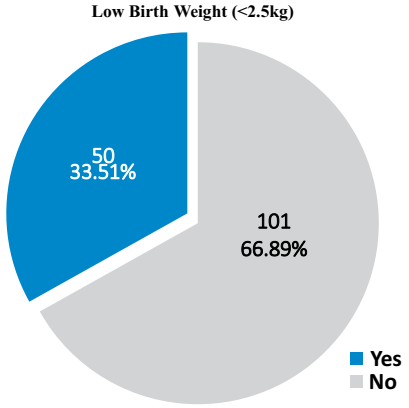

Figure 2: Frequency of Underweight Newborn in Mothers with Reduced Serum Ferritin Levels (n=151)

Frequency of new-borns with low weight in mother with low serum ferritin levels at term delivery was observed in 33.11% (50/151) as presented in figure 2. Effect of mothers age was controlled by stratification and observed that the proportion of cases with low birth weight of new born in mother with low serum ferritin levels was significantly high in below and equal to 20 years and above 30 years of aged women (p=0.013) as shown in table 2.

Table 2: Frequency of Low Birth Weight in Newborns Born to Mothers with Low Serum Ferritin Levels at Term, Categorized by Age Groups

Age Groups (Years)	Low Birth Weight		Total	p-Value
	Yes Frequency (%)	No Frequency (%)		
<20	10 (55.6%)	8 (44.4%)	18	0.013
21-25	18 (27.3%)	48 (72.7%)	66	
26-30	12 (24.5%)	37 (75.5%)	49	
>30	10 (55.6%)	8 (44.4%)	18	

Frequency of Low Birth Weight new born in mother with reduced serum ferritin levels was not significant with gestational age, type of delivery technique and haemoglobin status as presented in table 3 respectively.

Table 3: Frequency of Low Birth Weight New Born In Mother with Low Serum Ferritin Levels At Term Delivery By Gestational Age (n=151)

Gestational Age (Weeks)	Low Birth Weight		Total	p-Value
	Yes Frequency (%)	No Frequency (%)		
36-37	23 (30.3%)	53 (69.7%)	76	0.454
37-41+6	27 (36%)	48 (64%)	75	

Table 4 illustrated the distribution of Low Birth Weight newborns among mothers with low serum ferritin levels at term, based on their mode of delivery. The table includes the total number of cases (n = 151) and categorizes them into

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different delivery modes such as Normal Vaginal Delivery (NVD), Assisted Vaginal Delivery (AVD), and Cesarean Section(C-section).

Table 4: Frequency of Low Birth Weight New Born in Mother with Low Serum Ferritin Levels at Term Delivery by Mode of Delivery (n=151)

Mode of Delivery	Low Birth Weight		Total	p-Value
	Yes Frequency (%)	No Frequency (%)		
Vaginal	26 (28%)	67 (72%)	93	0.088
Caesarean Section	24 (41.4%)	34 (58.6%)	58	

Table 5 presented the frequency of Low Birth Weight (LBW) newborns among mothers with low serum ferritin levels at term delivery, categorized by maternal hemoglobin levels. In this study, ferritin levels were categorized as low (<30 ng/mL), but due to limitations in the dataset, further categorization into very low ferritin (<12 ng/ml) was not performed. Similarly, low birth weight (LBW) was analyzed as a whole group (<2,500g) without stratifying into very low birth weight (VLBW) (<2000 G). The lack of this detailed categorization should be acknowledged as a limitation of the current study. Future research could benefit from more refined classifications of ferritin and birth weight to better assess the relationship between severity of deficiency and adverse birth outcomes. Although this study could not categorize maternal ferritin levels into very low ferritin or birth weight into very low birth weight (VLBW) due to data constraints, the results still show a significant association between low ferritin levels and the occurrence of low birth weight (LBW). Future studies with more detailed categorization could help to better define the threshold at which ferritin deficiency may have a more pronounced impact on birth weight. In the regression analysis, we assessed the relationship between low ferritin levels (<30 ng/mL) and low birth weight (LBW) (<2,500g). Although we were unable to analyze the relationship using very low ferritin (<12 ng/mL) or very low birth weight (VLBW) (<2,000g) due to limitations in the dataset, the results still indicate a significant association between low ferritin and LBW after adjusting for confounding factors such as maternal age and socioeconomic status (OR = 2.5, 95% CI: 1.4 to 4.6, p = 0.01). This study contributes valuable information on the relationship between low ferritin levels and low birth weight but acknowledges the limitation of not breaking down ferritin levels into very low ferritin and birth weight into Very Low Birth Weight (VLBW). Future studies with larger datasets and more detailed classification of these variables may provide more specific insights into the threshold levels at which iron deficiency most significantly impacts fetal growth and birth weight outcomes.

Table 5: Frequency of Low Birth Weight New Born in Mother with Low Serum Ferritin Levels at Term Delivery By Hemoglobin(n=151)

Hemoglobin	Low Birth Weight		Total	p-Value
	Yes Frequency (%)	No Frequency (%)		
Less than 10	37 (32.7%)	76 (67.3%)	113	0.869
Equal to or more then 10	13 (34.2%)	25 (65.8%)	38	

DISCUSSION

A study conducted in India, showed that there is a connection between maternal health and infant birth weight, showing a strong link between low birth weight and factors such as maternal age, weight, height, education, occupation, income, socioeconomic status, antenatal care, physical activity, smoking, alcohol use, and iron and folic acid supplementation [11]. Low birth weight (LBW), associated with depleted iron reserves at or after 37 weeks of pregnancy, is a significant risk determinant for childhood anemia [12-14]. Additionally, infants with low birth weight (LBW) are at an increased risk of developing insulin resistance and related health issues later in life [15]. Several factors have been linked to low birth weight (LBW) infants, including young or advanced age of the mother, extremes of body mass index (BMI), maternal chronic disease and a history of premature birth [16]. Expectant women with anaemia, particularly in low-income countries such as Pakistan, have an increased likelihood of having low birth weight (LBW) infants [17]. It is believed that individuals born with low birth weight are at an increased risk of experiencing type 2 diabetes later in life [18]. Additionally, engaging in strenuous physical labour during pregnancy is a contributing factor to low weight new born and inadequate fetal development [19]. The time gap between births is significantly linked to higher risk of low birth weight, fetal death, and prematurity [20]. In the current investigation the typical age of the patients was 25.50 ± 4.08 years (95% CI: 24.84 to 26.6). Most of the women had primiparous and mean gestational age ,parity, haemoglobin, serum ferritin and birth weight are reported. A significant proportion of the patients (82%) were aged between 20 and 30 years. A significant number of the total patients (87%) had less than 3 previous deliveries, with 54% being primigravida.A study conducted in Muzaffarabad explores risk factors in the region, with significant co-relation only with socioeconomic demographics which resulted in LBW [21]. Despite serum ferritin's association with other complications like persistent patent ductus arteriosus, sepsis and bronchopulmonary dysplasia, there is a controversial data when correlating serum ferritin levels with LBW [22]. The studies by Milašinović *et al.*, (2013), Devaguru *et al.*, (2023), and Badshah *et al.*, (2008) collectively highlight key maternal risk factors contributing to low birth weight (LBW) in newborns. Milašinović *et al.*, (2013) emphasize the predictive value of serum ferritin

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levels, demonstrating that maternal iron deficiency plays a crucial role in intrauterine growth restriction and LBW. This finding aligns with Badshah *et al.*, (2008), who identified maternal anemia and poor nutritional status as major contributors to LBW in a hospital-based study in Pakistan. Similarly, Devaguru *et al.*, (2023) reinforce these associations, presenting a broader hospital-based analysis that links LBW with inadequate maternal nutrition and health disparities. These studies collectively underline the significance of maternal iron status, nutritional interventions, and antenatal care in reducing LBW prevalence. A comprehensive approach integrating regular ferritin screening, improved maternal nutrition, and strengthened antenatal care services could mitigate the burden of LBW across different populations [23-25]. Anaemia is an avoidable health issue, and addressing it is anticipated to reduce the occurrence of Low Birth Weight (LBW) and potentially decrease postnatal mortality in the population. Arsyi *et al.*, (2022) highlight that increased antenatal care utilization significantly reduces low birth weight incidence across four ASEAN countries, emphasizing the need for improved maternal healthcare access [20]. Maternal haemoglobin levels were below 7g/dl in 20% of the patients. In an additional study conducted by Jalil *et al.*, (2016), the occurrence of Low Birth Weight (LBW) babies in Punjab was reported to be 24.5% [26]. The variation in the incidence of LBW may be attributed to ethical and cultural variations between Karachi, Lahore, Muzaffarabad, and the other cities of Punjab and Azad Kashmir. Lone, *et al.*, reported that the likelihood of having LBW babies is 1.9 times increased in the anaemic individuals in Pakistan [27]. A vigorous correlation exists between anaemia and Low Birth Weight (LBW).In the present study, 72% of expectant women with Low Birth Weight (LBW) were anaemic, with 20% experiencing severe anaemia. Anaemia is a preventable condition.Correcting anaemia is anticipated to minimize the frequency of Low Birth Weight (LBW) and may also decrease postnatal mortality in the community. These studies collectively emphasize the negative impact of maternal anemia on fetal outcomes, with Ahmad *et al.*, (2011) and Khan (2001) linking anemia to low birth weight and impaired fetal growth, while Allen (2000) underscored the broader consequences of iron deficiency on pregnancy outcomes [28-30]. Within Pakistan, iron depletion is the primary factor causing anaemia during pregnancy, often attributed to underprivileged background, nutritional deficiencies and high parity.Iron supplementation during pregnancy is anticipated to reduce the probability of anaemia and mitigate the risk of low birth weight in new-borns. This has also been described in studies conducted in United States [31]. Anaemia is a controllable issue, and its restoration is anticipated to reduce the chances of low birth weight and decrease perinatal morbidity and mortality in the community [31]. Anemia affects 36% of pregnant women globally, with approximately 40% of cases linked to iron deficiency (ID). Iron is a crucial micronutrient for processes like erythropoiesis, immune function, and, during pregnancy, placental and fetal development [32]. The increased rate of LBW babies noticed in this study could be linked to higher levels of inbreeding due to frequent marriages between closely related individuals with diverse ethnic backgrounds.In a prospective cohort study conducted in rural Eastern Ethiopia, it was concluded that low birth weight (LBW) was a significant public health concern in this rural setting, with factors such as iron deficiency (ID) during pregnancy, maternal under-nutrition, and lack of Iron Folic Acid (IFA) supplementation negatively impacting birth weight.To improve maternal and neonatal health, targeted interventions promoting better nutrition and universal access to IFA supplementation are essential [33]. In another study conducted in Nigeria, it was reported that a significant relationship was found between serum ferritin levels in newborns and birth weight, with lower birth weight being a strong predictor of reduced serum ferritin level [34]. In a study conducted in India, it was observed that preterm infants had lower iron stores than term infants, with gestational age being the primary factor influencing iron levels at birth. Additionally, iron deficiency was found to lead to irreversible and long-term neurodevelopmental impairments [35].The lack of sufficient iron supplementation may contribute to the high rates of LBW observed in this study and others in Pakistan. Although the uptake of iron supplements for 90 days or more has improved over the years (from 22% in the 2012-13 PDHS to 29% in 2017-18), it remains inadequate to effectively address iron deficiency and its associated risks, such as LBW [36]. These findings further emphasized the importance of improving maternal iron status through enhanced iron supplementation and nutritional interventions to reduce the prevalence of LBW. Given the high rates of iron deficiency in pregnant women, addressing this issue could significantly contribute to lowering the incidence of LBW and improving maternal and neonatal health outcomes in Pakistan.

This study is limited by its cross-sectional design, which restricts the ability to establish causal relationships between low serum ferritin levels and LBW outcomes. The use of non-probability sampling and a single-center setting may limit generalizability to the broader population. Additionally, important confounders such as dietary intake, socioeconomic status, and inflammatory markers were not comprehensively assessed, which may influence ferritin levels and birth outcomes. Future research should focus on large-scale multicenter longitudinal studies with more detailed stratification of ferritin levels and birth weight categories (including VLBW). Incorporating nutritional, biochemical, and socioeconomic variables would provide a more comprehensive understanding and help develop targeted interventions to reduce LBW prevalence.

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CONCLUSIONS

Low Birth Weight (LBW) is a significant concern in Pakistan, contributing to perinatal complications and mortality. This study found that 33.11% of newborns with LBW were born to mothers with reduced serum ferritin levels at term. Addressing maternal anemia, promoting a balanced diet, and improving antenatal care can help reduce LBW rates. Community awareness, delaying pregnancies, maintaining adequate birth intervals, and iron supplementation during pregnancy are essential preventive measures. Further research is needed to explore the causal link between low ferritin levels and LBW. Healthcare providers should monitor ferritin levels to enhance maternal and neonatal health outcomes.

Authors' Contribution

Conceptualization: SK
Methodology: AK, MK, RB
Formal analysis: ZAP
Writing and Drafting: FNB, ZAP, ZM, RB
Review and Editing: FNB, ZAP, ZM, RB, SK

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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