

## Original Article

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# Serum ferritin and red blood cell indices in infants of diabetic mothers

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### Abstract

**Background:** Fetal iron stores are affected by maternal diabetes and it is lower at birth in infants of diabetic mothers (IDMs). Risks for developing iron deficiency and neurocognitive impairment are reported in IDMs. This study was done to assess serum ferritin and red cell indices in IDMs and to compare the values with infants born to mothers without diabetes mellitus.

**Methods:** This cross-sectional study was carried out at BIRDEM General Hospital from March to October, 2018. Total 102 full term neonates were included in this study. Among them 70 neonates were IDMs and 32 were infants born to mother without diabetes mellitus. Serum ferritin and red cell indices like hemoglobin (Hb), packed cell volume (PCV), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW) were measured within 48 hours of birth. Comparison of red cell indices and serum ferritin level were done between IDMs and infants of non-diabetes mothers. Statistical analysis was performed by using Epi info, and p value of <0.05 was considered statistically significant.

**Results:** IDMs had significantly higher value of Hb% (19.00 vs 17.47 g/dl), PCV (57.60 vs 52.67 %) and RDW (20.09 vs 17.77 %) than infant of non-diabetic mother ( $p < 0.05$ ). But there was no significant difference regarding the values of MCV, MCH and MCHC between IDMs and infants of non-diabetic mothers ( $p > 0.05$ ). Serum ferritin level was found significantly low in IDMs (94.51 vs 307.50 ng/ml,  $p < 0.001$ ).

**Conclusion:** Iron stores of IDMs were found significantly lower at birth despite higher hemoglobin content, as indicated by lower serum ferritin level. Further studies and long-term follow up are needed to determine whether these infants are at risk for developing iron deficiency anemia or iron-deficient neurocognitive disorder.

**Key words:** red cell indices, infant of diabetic mother, iron deficiency, serum ferritin.

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### Introduction

Diabetes mellitus is the most common metabolic disorder complicating pregnancy. About 2-10% of all pregnancies are complicated by diabetes mellitus.<sup>1</sup> Infants born to diabetic mothers have been at significantly higher risks for spontaneous abortions, stillbirths, congenital malformations and perinatal morbidity and mortality.<sup>2,3</sup> Fetal iron stores are also affected by maternal diabetes and is lower at birth in IDMs.<sup>4</sup> Poorly controlled diabetes mellitus during pregnancy is associated with maternal and fetal hyperglycemia, fetal hyperinsulinemia, increased fetal metabolic rate and oxygen consumption. Increased fetal oxygen consumption causes relatively hypoxic intrauterine environment which stimulates

erythropoiesis and expands the fetal red cell mass. Subsequently placental transferrin receptor expression is increased but the affinity of the receptor to maternal transferrin is decreased. Furthermore, placental vascular disease in mothers with longstanding, poorly controlled diabetes further limits iron transport across the placenta, resulting in no apparent increase in iron transport in spite of increased fetal iron demand. The fetus then draws iron from its liver. Redistribution of iron supports growth of the red cell mass, at the expense of other developing organs, including the heart and brain, which become iron deficient.<sup>5,6</sup> An autopsy study of IDM's with severe islet cell hyperplasia demonstrated a 55% reduction in heart iron concentration and a 40% reduction in brain iron concentration.<sup>7</sup> Iron plays a significant role in structural and functional development of brain because it forms an important component of enzymes involved in cell replication, myelinogenesis, neurotransmitter synthesis and cellular energy metabolism.<sup>8,9</sup> Risks for developing iron deficiency and neurocognitive impairment are reported in IDM's in several studies.<sup>10,11</sup> But no study was done in Bangladesh regarding the impact of maternal diabetes on neonatal iron store. Direct measurement of tissue iron in newborn infants is not currently feasible. Serum ferritin concentration has been used as a measurement of iron stores in infants, children and adults. So, this study was done to evaluate Red cell indices and serum ferritin in IDM's and was compared with infants born to mother without diabetes mellitus.

## Methods

This cross-sectional study was carried out in Special Care Baby Unit (SCABU), BIRDEM General Hospital from March to October 2018. Full term neonate born to mother with gestational diabetes mellitus (GDM) and pre-gestational diabetes mellitus (PGDM) admitted consecutively in this unit were included and categorized as Group A. Full term neonate born to mother without diabetes mellitus were taken as Group B. After inclusion babies were examined thoroughly. Gestational ages of babies were calculated from last menstrual period (LMP) and weight was measured by electronic weighing scale. Maternal history was taken regarding maternal age, parity, mode of delivery and past medical illness. Any congenital anomalies, early onset sepsis, asphyxia and infant born to mother with anemia were excluded. Within 48 hours of birth two venous blood samples, consisting of 1 ml each, were collected. One sample

was sent for measurement of red cell indices at hematology laboratory. Another sample was sent for measurement of serum ferritin level at biochemistry laboratory. All the reports were collected and recorded. Normal ferritin level in neonate is 36-400 ng/ml and any level <36 ng/ml was categorized as low ferritin level in this study. Comparison of red cell indices and serum ferritin level were done between IDM's and infants born to mother without diabetes mellitus. Statistical analysis was performed by using Epi info version 3.4.5 and *p* value <0.05 was considered statistically significant.

## Results

Total 102 neonates were included in this study. Seventy were IDM's (group A) and 32 were infants of non-diabetic mothers (group B). Among the group A neonates, 39 babies' mother had GDM and 31 babies' mother had PGDM. Maternal and neonatal characteristics of groups A and group B were shown in Table I. There was no significant difference regarding the maternal age and parity. Gestational age was similar but mean birth weight was significantly higher in group A (*p* < 0.05) than group B. Twenty-one (30.6%) neonates had birth weight > 90 percentile (Large for Gestational Age, LGA) in group A, and no baby was found LGA in group B (*p* < 0.05).

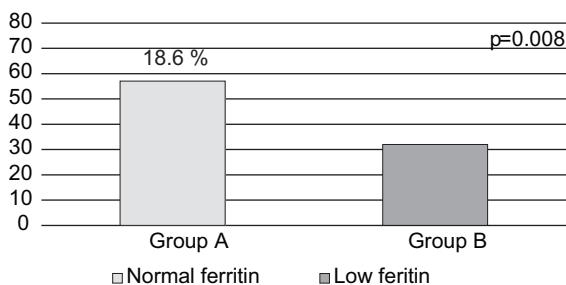
**Table I** Maternal and neonatal characteristics of study neonate (N = 102)

Maternal and neonatal characteristic	Group A (n=70)	Group B (n=32)	<i>p</i> value
Maternal age (years)	30.75 ± 4.64	29.53 ± 6.51	0.22
Parity, n (%)			
Primipara	14 (20.0 %)	11 (34.4 %)	0.14
Multipara	56 (80.0 %)	21 (65.6 %)	
Sex, n (%)			
Male	47 (67.1%)	17 (53.1 %)	0.51
Female	23 (33.9 %)	15 (46.9 %)	
Gestational age (weeks)	37.45 ± 0.58	37.78 ± 1.0	0.23
Birth weight (gram)	3296 ± 62	2714 ± 32	0.01
LGA, n (%)	21 (30.4%)	0 (0)	0.001

Comparison of red cell indices and serum ferritin level were done between group A and group B (Table II). Mean values of Hb, PCV and RDW were significantly higher in group A than the group B (*p* < 0.05), but no significant difference was found in MCV, MCH and MCHC (*p* > 0.05) values between two groups. Serum ferritin level was significantly low in group A than group B (*p* < 0.05).

**Table II** Comparison of red cell indices and serum ferritin level between two groups (N = 102)

RBC indices and ferritin	Group A (n=70) Mean ± SD	Group B (n=32) Mean ± SD	p value
Hb (g/dl)	19.00 ± 1.39	17.47 ± 1.6	0.001
PCV (%)	57.60 ± 4.33	52.67 (5.30)	0.001
MCV (fl)	100.49 ± 12.80	104.69 ± 7.12	0.07
MCH (pg)	34.03 ± 1.81	34.66 ± 1.50	0.09
MCHC (g/dl)	33.23 ± 1.18	33.53 ± 0.15	
RDW (%)	20.09 ± 2.19	17.77 ± 1.73	0.001
Ferritin (ng/ml)	94.51 ± 56.84	307.50 ± 127.88	0.001

**Figure 1** Hypoferritinemia in study neonates (N = 102)

Among the neonates in group A, 13 (18.6%) babies had low (<36 ng/ml) serum ferritin level, but none among group B had low serum ferritin level ( $p = 0.008$ )

Comparison of red cell indices and serum ferritin levels was also done between neonates born to mother with GDM and PGDM and no significant difference was found in any values among these two groups ( $p > 0.05$ ) (Table III).

**Table III** Comparison of red cell indices and serum ferritin level between neonate born to mother with GDM and PGDM (N = 70)

RBC indices and ferritin	GDM (n=39) Mean ± sd	PGDM(n=31) Mean ± sd	p value
Hb% (g/dl)	18.94 ± 1.38	19.06 ± 1.43	0.64
PCV (%)	57.04 ± 4.52	58.29 ± 4.03	0.26
MCV (fl)	98.34 ± 16.07	103.17 ± 7.12	0.13
MCH (pg)	33.92 ± 1.95	34.16 ± 1.66	0.62
MCHC (g/dl)	33.22 ± 1.46	33.23 ± 0.72	0.65
RDW (%)	19.82 ± 1.81	20.44 ± 2.58	0.39
Ferritin (ng/ml)	95.56 ± 53.81	93.19 ± 61.32	0.69

## Discussion

Iron deficiency is the commonest nutritional disorder worldwide. It is an essential micronutrient that plays a significant role in structural and functional development of brain in early stages.<sup>8,12</sup> Deficiency of dietary iron during infancy and childhood is associated with long-term effects on cognitive development that persist after treatment of iron deficiency.<sup>13</sup> Iron deficiency also may occur earlier in life, during the fetal period in IDMs.<sup>14,15</sup> This study was done to assess the effect of maternal diabetes on neonatal iron stores by using serum ferritin level. A significant difference was found in this study between IDMs and control group regarding birth weights at same gestational ages. The mean birth weight of IDMs was  $3296 \pm 62$  gram, while that of the infants of non-diabetic mothers was  $2714 \pm 32$  gram ( $p < 0.05$ ). Twenty-one (30.6%) infants of diabetic mothers had birth weights > 90 percentile that is large for gestational age (LGA) and no baby was found LGA in infants of non-diabetic mothers ( $p < 0.05$ ). LGA and macrosomia (birth weight e" 4000 gm) in IDMs is due to excess body fat, an increased muscle mass and organomegaly without increase in brain size. Fetal overgrowth is related to increased transplacental transfer of maternal glucose, which stimulates the release of insulin by fetal pancreatic beta cells. Insulin is a major factor of fetal growth and it up-regulates the insulin-like growth factor (IGF), subsequently leading to fetal macrosomia. Different studies also found higher incidence of LGA and macrosomia among IDMs.<sup>16-18</sup> This study showed a significant increase in hemoglobin and venous PCV values in IDMs as compared to infants of non-diabetic mothers ( $p < 0.05$ ). Diabetes mellitus during gestation leads to relative hypoxia in intrauterine environment, stimulating erythropoiesis, which results in expansion of fetal RBC mass. Significantly increased values of hemoglobin and PCV were found in infants of diabetic mother in different studies.<sup>18-21</sup>

Values of RDW was found significantly higher among IDMs in this study (20.09 vs 17.77,  $p < 0.05$ ). RDW is a parameter reflecting the heterogeneity of the peripheral red blood volume and is helpful in differentiating iron deficiency anemia from other microcytic anemia. It can be a useful tool to assess the iron status as it is the first parameter to increase in response to iron depletion followed by decrease in MCH and MCV. Sadwitz PD prospectively evaluated 90 term infants to establish

normal values for the RDW. Among them 16 infants were IDMs. He found RDW value was significantly higher in IDMs than other neonates.<sup>22</sup> Raggal NI also found significantly increased values of RDW in infants of diabetic mother than the control in his study but Hashim and Ameer found no significant difference between IDMs and the controls regarding RDW ( $p > 0.05$ ) level in their study.<sup>21,23</sup>

In the present study IDMs had significantly lower iron stores as represented by lower serum ferritin ( $p < 0.05$ ). Thirteen (18.6%) IDMs were found to have low serum ferritin level (<36 ng/dl). This result is similar to that of Verner et al. who found that maternal diabetes caused depletion of fetal iron stores and was associated with higher fetal iron demands as indicated by higher serum transferring receptor ( $p < 0.01$ ) level and transferring receptors ferritin index in cord blood ( $P < 0.01$ ) of IDM compared to infants of non-diabetic mothers.<sup>24</sup> Hashim and Ameer also documented that cord blood serum ferritin level was lower in IDMs compared to infants of non-diabetic mothers ( $p < 0.05$ ).<sup>23</sup>

Comparison of red cell indices and serum ferritin level was also done between neonates born to mothers with GDM and PGDM in this study and no significant difference was found in any parameters ( $p > 0.05$ ). This indicates that both groups are vulnerable to develop iron deficiency and this finding was also compatible with EI-Raggal's study.<sup>21</sup>

### Conclusion

Iron stores of IDMs were found significantly lower at birth despite higher hemoglobin content, as indicated by lower serum ferritin level in this study. In all IDMs iron profile should be checked routinely at follow up as iron supplementation may be considered. Further studies are needed to determine whether these infants are at risk for developing iron deficiency anemia or iron-deficient neurocognitive delay.

**Conflicts of interest:** Nothing to declare.

### References

1. Hunt KJ, Schuller KL. The increasing prevalence of diabetes in pregnancy. *Obstet Gynecol Clin North Am* 2007; 34(2):173 - 99.
2. Nold JL, Georgieff MK. Infant of Diabetic mothers. *Pediatr Clin N Am* 2004; 51:619-37.
3. Lucas MJ. Medical complications of pregnancy: diabetes complicating pregnancy. *Obstet Gynecol Clin North Am* 2001; 28(3):513-36.
4. Murata K, Toyoda N, Ichio T, Ida M, Sugiyama Y. Cord transferrin and ferritin values for erythropoiesis in newborn infants of diabetic mothers. *Endocrinol Jpn* 1989; 36:827 - 32.
5. Philipps AF, Porte PJ, Strabinsky S, Rosenkranz TS, Raye JR. Effects of chronic fetal hyperglycemia upon oxygen consumption in the ovine uterus and conceptus. *J Clin Invest* 1984; 74:279-86.
6. Milley JR, Papacostas JS, Tabata BK. Effect of insulin on uptake of metabolic substrates by the sheep fetus. *Am J Physiol* 1986; 251:349-56.
7. Georgieff MK, Landon MB, Mills MM, Hedlund BE, Faassen AE, Schmidt RL, et al. Abnormal iron distribution in infants of diabetic mothers: spectrum and maternal antecedents. *J Pediatr* 1990; 117:455-61.
8. Wigglesworth JM, Baum H. Iron dependent enzymes in the brain. In: Youdim MBH (ed) *Brain iron: neurochemical and behavioral aspects*. Taylor & Francis, New York. 1988, pp 25 - 66.
9. Kretchmer N, Beard JL, Carlson S. The role of nutrition in the development of normal cognition. *Am J Clin Nutr* 1996; 63:997-1001.
10. Yu GSM, Steinkirchner TM, Rao GA, Larkin EC. Effect of prenatal iron deficiency on myelination in rat pups. *Am J Pathol* 1986; 125:620-24.
11. Riggins T, Miller NC, Bauer PJ, Georgieff MK, Nelson CA. Consequences of Low Neonatal Iron Status due to Maternal Diabetes Mellitus on Explicit Memory Performance in Childhood. *Dev Neuropsychol* 2009; 34(6): 762-79.
12. Lozoff B, Georgieff MK. Iron deficiency and brain development. *Semin Pediatr Neurol* 2006; 13:158-65.
13. Lozoff B, Jimenez E, Hagen J, Mollen E, Wolf AW. Poorer behavioral and developmental outcome more than 10 years after treatment for iron deficiency in infancy. *Pediatrics* 2000; 105(4):1-11.
14. Chockalingam UM, Murphy E, Ophoven JC, Weisdorf SA, Georgieff MK. Cord transferrin and ferritin values in newborn infants at risk for prenatal uteroplacental insufficiency and chronic hypoxia. *J Pediatr* 1987; 111:283-86.
15. Petry CD, Eaton MA, Wobken JD, Mills MM, Johnson DE, Georgieff MK. Iron deficiency of liver, heart and brain in newborn infants of diabetic mothers. *J Pediatr* 1992; 121:109 -14
16. Hussain M, Irshad M. Frequency of various neonatal complications in infants born to diabetic mothers: a hospital-based study. *JPMI* 2001; 25(3):227-32.
17. Shirazi H, Raiz S. Neonatal outcome of diabetic pregnancy. *Ann Pak Inst Med Sci* 2010; 6 (2):107-12.
18. Anjum SK, Yashodha HT. A study of neonatal outcome in infants born to diabetic mothers at a tertiary care hospital. *Int J Contemp Pediatr* 2018; 5(2):489-92.

19. Cetin H, Yalaz M, Akisu M, Kultursay N. Polycythaemia in infants of diabetic mothers:  $\alpha$ -hydroxybutyrate stimulates erythropoietic activity. *The Journal of International Medical Research* 2011; 39: 815 - 21.
20. Aziz A, Annamalai T, Ahmed SM. Morbidity and mortality of infant of diabetic mothers, *Int J Contemp Pediatr* 2018; 5(4):1419-22.
21. El-Raggal NM, Abdou RM, Hamza MT, Hasan SM. Effect of Maternal Diabetes on Cord Blood Concentrations of Iron Status Parameters. *The Egyptian Journal of Hospital Medicine* 2017; 69 (3): 2109-14.
22. Sadwoitz PD, Osaki FA. Red cell Distribution Width (RDW) in the newborn abnormalities in the infants of diabetic mothers. *Pediatric Research* 1985; 19: 361.
23. Hashim JM, Ameer S. Cord Blood Serum Ferritin of Infants of Diabetic Mothers. *Iranian Journal of Neonatology* 2014; 5(1): 1-6.
24. Verner AM, Manderson J, Lappin RJ, McCance DR, Halliday HL, Sweet DG. Influence of maternal diabetes mellitus on fetal iron status. *Arch. Dis. Child. Fetal & Neonatal* 2007; 92:399 - 404.