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Maternal Serum Ferritin Level in Prediction of Mothers with Appropriate-For-Gestational-Age (AGA), Small-For-Gestational Age (SGA), and Intrauterine Growth Restriction (IUGR)

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Abstract

Background

Fetal growth restriction is one of the main causes of perinatal mortality that can be predicted by ferritin. We aimed to evaluate the role of ferritin in prediction of mothers with Appropriate-for-gestational-age (AGA), Small-for-gestational age (SGA) and intrauterine growth restriction (IUGR).

Materials and Methods: In this cohort study, we screened 73 mothers with gestational ages of 32-34 weeks. If amniotic fluid index (AFI) was normal and there was no circulation defect, the fetuses were classified in SGA group and in case of presence of oligohydramnios or circulation defect; they were classified in IUGR group. Also, fetuses with normal growth were classified in AGA group. We evaluated the serum ferritin, hemoglobin, and iron of the mothers. Moreover, we evaluated the levels of placenta ferritin, Hb, and hematocrit in the delivery room.

Results: In this study, 28 patients were categorized in AGA group, 15 patients in SGA group and 30 patients in IUGR group. Mean weight of all infants was 2210.60 ± 932.77 grams. Also, the mean AFI of all infants was 9.81 ± 3.59. The mean ferritin level of all mothers was 30.29 ± 10.80 and IUGR group had the highest and AGA group had the lowest ferritin levels (P=0.015). Maternal ferritin (µg/l) (Sen: 67.9%, Sp: 61.9%), maternal hematocrit (%) (Sen: 70%; Sp: 62.8%,) and maternal Hb (Sen: 70%, Sp: 65.1%,) could predict IUGR.

Conclusion

Increased (>34 µg/l) and decreased (<26 µg/l) levels of maternal serum ferritin level may be correlated with IUGR and SGA fetuses, respectively. Thus, measurement of maternal serum ferritin level in addition to sonography can be a useful marker in differentiating SGA and IUGR fetuses.

Key Words: Ferritin, Hemoglobin, Fetal growth restriction, Small fetus.

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1- INTRODUCTION

In fetuses with growth restriction, mortality around birth is 6-10 times more common and 35% of stillbirths occur in preterm fetuses. Also, the rate of asphyxia reaches 50%, however the prevention of these events can be achieved by recognizing cases of growth restriction and optimal care (1). Fetal weight gain is 5 gr per day at 15 weeks, 15-20 gr per day at 24 weeks and 30-35 gr per day at 34 weeks and depends on the genetics of the fetus and occurs with the transfer of material from mother to placenta and from placenta to fetus. Fetus weighing less than 10% is in the SGA group (1). These fetuses have an increased risk of intrauterine death, so that the risk of intrauterine death of small fetuses at 38 weeks is 1%, while in fetuses of appropriate weight is 0.2%. Importantly, many fetuses weighing less than 10% have no pathological growth restriction, and 70% of these fetuses have normal pregnancy outcomes. Factors such as maternal race, parity, and maternal height and weight will appear to be proportional to their growth (2).

There are various causes for fetal growth restriction, which are divided into three categories: maternal (maternal hypertension, diabetes, heart disease, connective tissue diseases), fetal (exposure to teratogens, viral and anoploid infections of the fetus, fetal abnormalities), and placental (placental diseases such as heart attack and placental abruption and placenta previa). Therefore, small fetuses with pathological growth restriction are in the group below 10% by weight. Amniotic fluid volume and Doppler studies can help differentiate between the two AGA (Appropriate-for-gestational-age), and SGA (Small-for-gestational age) groups (3, 4). In some studies, the role of maternal serum ferritin in differentiating between normal small group and small fetuses with pathological growth restriction was found (5-10). Ferritin levels are higher in fetuses with pathological growth restriction, which can indicate inflammation and placental dysfunction. Serum ferritin level is an indicator of the body's iron stores and at levels below 12 ng / ml indicates iron deficiency. On the other hand, ferritin is an acute inflammatory marker and rises in conditions such as inflammation, fever, infection and other stresses (11). We intend to compare maternal serum ferritin levels in small fetuses and AGA. On the other hand, the role of ferritin in differentiating normal small fetuses and fetuses with growth restriction was investigated. According to the studies on the role of ferritin in differentiating small and growth-restricted fetuses, in this study we evaluated the role of ferritin in prediction of mothers with Appropriate-for-gestational-age (AGA), Small-for-gestational age (SGA), and intrauterine growth restriction (IUGR).

2- MATERIALS AND METHODS

2-1. Study design and population

In this cohort study, 73 mothers who were diagnosed with fetal growth restriction and referred to the perinatology clinic of Shahid Motahari medical center in Urmia, Iran to be followed by the delivery time (termination of pregnancy). Based on the previous studies (10), and values of $\mu1=11.11$, $\mu2=17.54$, $SD1=3.24$, $SD2=7.84$, taking into account 99% accuracy ($Z1-\alpha/2 = 2.575$), and power 90% ($Z1-\beta = 1.28$), 73 patients were selected.

2-2. Methods

The sampling method was convenient provided that the inclusion and exclusion criteria were met. Fetal growth restriction screening is performed as part of prenatal care at 32-34 weeks. On the other hand, during the study period, some mothers were referred to a high-risk pregnancy clinic with an initial diagnosis of fetal growth restriction during ultrasound

examinations. In mothers who went to the perinatology clinic, we screened fetal growth restriction at 32-34 weeks (gestational age was determined based on the first trimester, under 14 weeks ultrasound and based on Crown-rump length [CRL]). In singleton pregnancies where fetal growth restriction is diagnosed, we further examined amniotic fluid volume and fetal circulation. If the amniotic fluid volume was normal and there was no circulatory defect, the fetus was in the SGA group, and if oligohydramnios was present or circulatory defect were observed in the fetus, the fetus was in the fetal growth-restricted (FGR) group. Fetuses that were weighted according to gestational age were also considered as a control group.

A perinatologist using a Medison AccuvixV10 ultrasound machine performed ultrasound examinations. SGA/FGR was defined if fetal weight was less than 10% of the weight percentile (according to Callen´s 2017 weight percentile table) for gestational age. Oligohydramnios was defined as AFI≤5cm or Deepest pocket < 2 cm and fetal circulation disorder was defined based on the following findings: Umbilical artery PI > 95th percentile for gestational age, absent/reversed end diastolic flow in umbilical artery and reversed α-wave in ductus venosus/ umbilical vein pulsatility.

2-3. Measuring tools

Three ml of venous blood was collected from all three groups of mothers to assess serum ferritin, Hb, Hct and serum iron levels. Pregnancy was controlled by Non-Stress Test (NST is an electronic tool to check fetal heart rate), biophysical and Doppler tests due to the severity of growth restriction. At delivery, 3 ml of blood was taken from the fetal umbilical cord and the levels of ferritin, Hb and Hct in the umbilical cord were assessed. All tests were done at Motahari laboratory in Urmia. Hb, ferritin and Hct were evaluated by complete blood count (CBC) test.

2-4. Ethical consideration

This study was reviewed and approved by the committee of Urmia University of Medical Sciences, Iran (IR.UMSU.REC.1397.189). This study was extracted from residential thesis of Mahdiyeh Mortazavi, at the department of gynecology of Urmia University of Medical Sciences. We adhered to the principles of Helsinki and the informed consent of the mothers was obtained.

2-5. Inclusion and exclusion criteria

Inclusion criteria were satisfaction to participate and mothers who diagnosed with fetal growth restriction. Excluding criteria were multiple pregnancies, maternal anemia (hemoglobin below 11 g / dl in the first and third trimesters and hemoglobin below 10.5 g / dl in the second trimester) (2), fetal aneuploidy and fetal anomalies.

2-6. Data Analyses

Quantitative variables were reported as mean and standard deviation and qualitative variables were reported as frequency and percentage. To compare the mean of ferritin, Hb and Hct between small fetuses and growth-restricted fetuses, independent t-test and Mann-Whitney U test were used. Pearson correlation test was used to evaluate the relationship between each of the maternal indices with ferritin, Hb and Hct of the umbilical cord. Fisher's exact test was used to compare neonatal diseases across three groups. To diagnostic purposes, Receiver-Operating Characteristic (ROC), and its statistic Area under curve (AUC) was performed in which AUC more than 0.5 is considered as positive prediction. The data analysis was performed using SPSS (version 20.0), and the significance level was considered less than 0.05.

3- RESULTS

In this study, 28 patients were categorized in AGA group, 15 patients in SGA group and 30 patients in IUGR group. The mean age of all mothers was 28.71±6.58 years. According to the results of ANOVA test in **Table.1**, the mean age of mothers in the three groups showed no significant difference (P=0.171). The mean total weight of the studied neonates was 2210.60± 932.77 gr and the mean birth weight of newborns in three groups were significantly different (P=0.001). The mean estimated fetal weight at the time of admission in the study was 1649.68± 557.55 gr. The mean estimated fetal weight was significantly different in the three groups (P<0.001). The mean amniotic fluid index (AFI) in all cases was 9.81±3.59. The mean amniotic fluid index was significantly different in the three groups (P<0.002).

Table 1: Mean age of mothers, neonatal weight, estimated fetal weight, and amniotic fluid index in the studied groups, n=73.

Variables		Frequency	Mean	SD	P- value
Age (year)	AGA	28	29.32	6.64	0.171
	SGA	15	25.87	5.95	
	IUGR	30	29.57	6.64	
Weight of neonates (gr)	AGA	28	3186.79	446.77	0.001
	SGA	15	2167.33	376.36	
	IUGR	30	1321.13	407.96	
Estimated weight of fetus (gr)	AGA	28	2006.85	426.69	0.001
	SGA	15	1926.93	391.61	
	IUGR	30	1201.50	396.79	
AFI	AGA	28	11.75	2.73	0.002
	SGA	15	8.83	2.73	
	IUGR	30	8.62	3.48	

AFI: Amniotic fluid index, IUGR: Intrauterine growth restriction, AGA: Appropriate-for-gestational-age, SGA: Small-for-gestational age.

Table.2 shows the types of deliveries of mothers in each group. According to the results of Chi-square test, the type of maternal delivery in the three groups was significantly different from each other (P=0.031), and the number of cesarean deliveries in all groups was more than vaginal deliveries. According to Fisher's exact test, the status of the neonates in the three groups was significantly different (P=0.002), and the number of alive neonates in all groups was higher than the expired neonates and totally 8 neonates in the IUGR group in the days after birth died due to low weight and immaturity. There was no stillborn in this study.

According to Fisher's exact test, neonatal diseases were significantly different in the three groups (P=0.029), and the number of neonates without disease was higher in all groups than neonates with the disease. At follow-up, 3 infants in the IUGR group had low growth and 2 infants in this group had kidney stones. Regarding umbilical artery pulsatility index (UAPI) in each group, UAPI was significantly different in the three groups (P<0.001). In respect of middle cerebral artery pulsatility index (MCAPI) in each group, MCAPI was significantly different in the three groups (P<0.001) and there was a decrease in MCAPI in the IUGR group.

Table-2: The types of deliveries of mothers, status of neonates, comorbidity, UAPI and MCAPI, n=73.

Variables		AGA Number (%)	SGA Number (%)	IUGR Number (%)	P-value
Types of delivery	Vaginal	11 (39.3%)	5 (33.3%)	3 (10%)	0.031
	Cesarean	17 (60.7%)	10 (66.7%)	27 (90%)	
	Total	28 (100%)	15 (100%)	30 (100%)	
Status of neonates	Alive	28 (100%)	15 (100%)	22 (73.33%)	0.002
	Expired	0 (0%)	0 (0%)	8 (27.6%)	
	Total	28 (100%)	15 (100%)	30 (100%)	
Comorbidity of neonates	No disease	28 (100%)	15 (100%)	25 (83.33%)	0029
	Low growth	0 (0%)	0 (0%)	3 (10%)	
	Nephrolithiasis	0 (0%)	0 (0%)	2 (6.6%)	
	Total	28 (100%)	15 (100%)	30 (100%)	
UAPI	Normal	28 (100%)	15 (100%)	0 (0%)	0.001
	Absente	0 (0%)	0 (0%)	12 (42.9%)	
	Reversed	0 (0%)	0 (0%)	5 (10.7%)	
	Increased	0 (0%)	0 (0%)	13 (46.4%)	
	Total	28 (100%)	15 (100%)	30 (100%)	
MCAPI	Normal	28 (100%)	15 (100%)	0 (0%)	0.001
	Decreased	0 (0%)	0 (0%)	30 (100%)	
	Total	28 (100%)	15 (100%)	30 (100%)	

MCAPI: Middle cerebral artery pulsatility index, UAPI: Umbilical artery pulsatility index, IUGR: Intrauterine growth restriction, AGA: Appropriate-for-gestational-age, SGA: Small-for-gestational age.

The mean total ferritin of the studied mothers was 30.29±10.80. According to **Table.3**, the mean ferritin of mothers was shown in three groups and the three groups were different in this regard (P = 0.015). The mean hematocrit of all mothers was 37.23±2.78 and the three groups were different in this regard (P = 0.020). The mean total hemoglobin of the mothers was 12.65± 0.83 without significant difference across groups (P=0.150).

Table-3: Comparison of the ferritin, hematocrit and hemoglobin across the groups.

Variables		Frequency	Mean	SD	P-value
Ferritin (µg/l)	AGA	28	26.33	9.67	0.015
	SGA	15	29.72	8.76	
	IUGR	30	34.52	11.52	
Hematocrit (%)	AGA	28	36.33	2.31	0.020
	SGA	15	36.80	3.44	
	IUGR	30	38.28	2.54	
Hemoglobin (g/dl)	AGA	28	12.33	0.72	0.150
	SGA	15	12.68	0.76	
	IUGR	30	12.93	0.89	

IUGR: Intrauterine growth restriction, AGA: Appropriate-for-gestational-age, SGA: Small-for-gestational age.

According to the results obtained from the receiver operating characteristic (ROC) curves in **Table.4**, maternal ferritin with a cutoff of 30.48 was able to predict IUGR with a sensitivity of 67.9% and a specificity of 61.9% (AUC= 0.679) (**Figure.1**). Also, maternal hematocrit with a cutoff of 37.25 can predict fetal growth restriction with a sensitivity of 0.70% and a specificity of 62.8% (AUC= 0.690) (**Figure.2**). Finally, the maternal hemoglobin with a cutoff of 12.55 was able to predict IUGR with a sensitivity of 0.70% and a specificity of 65.1% (AUC= 0.667) (**Figure.3**).

Table-4: Cutoff point of maternal ferritin, hemoglobin and hematocrit in predicting IUGR.

Variables	Cutoff point	AUC	Sensitivity	specificity
Maternal ferritin	30.48	0.679	67.9%	61.9%
Maternal hemoglobin	37.25	0.690	70%	62.8%
Maternal hematocrit	12.55	0.667	70%	65.1%

AUC: Area under curve (a measure of the accuracy of a quantitative diagnostic test).

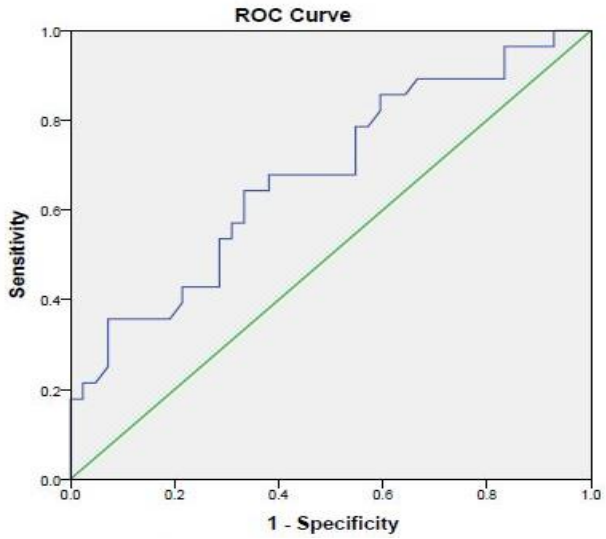

Fig.1: ROC of maternal ferritin for IUGR prediction.
IUGR: Intrauterine growth restriction.

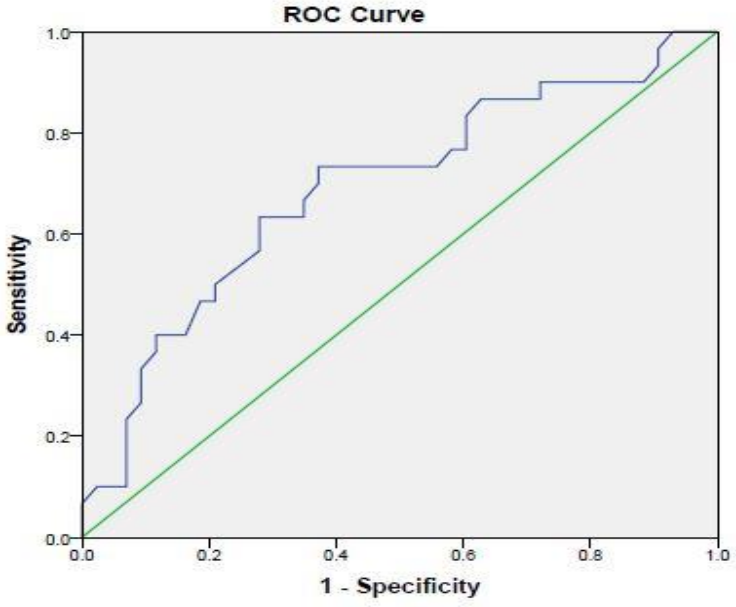

Fig.2: ROC of maternal hematocrit for IUGR prediction.
IUGR: Intrauterine growth restriction.

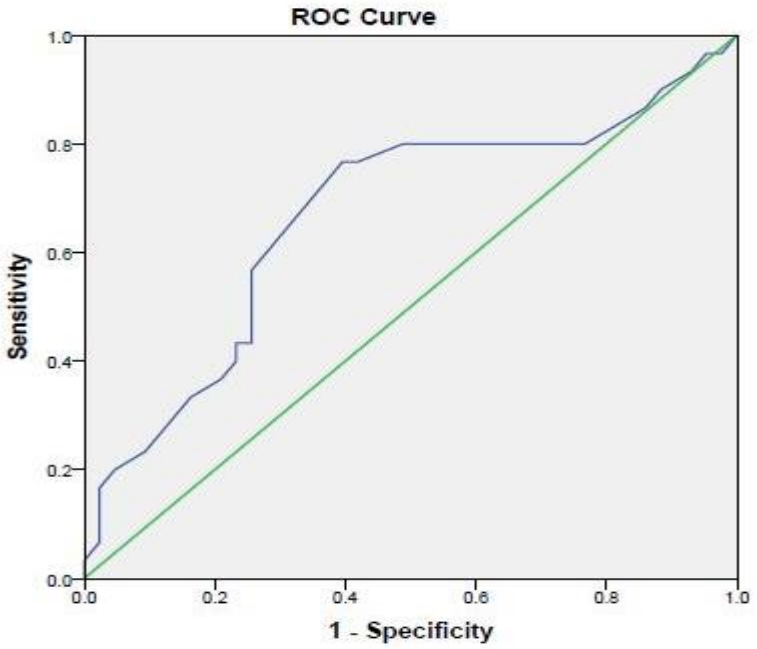

Fig.3: ROC of maternal hemoglobin for IUGR prediction.
IUGR: Intrauterine growth restriction.

4- DISCUSSION

In this study we evaluated the role of ferritin among fetuses suffering from growth restriction and we found that maternal serum ferritin >34 µg/l and <26 µg/l may be correlated with IUGR and SGA fetuses, respectively. Several markers in serum and amniotic fluid have been studied in previous studies to predict fetal growth restriction. Although various markers such as alpha-fetoprotein and chorionic gonadotropin were associated with IUGR during the second trimester screening, due to their low sensitivity, there are no promising markers for predicting IUGR (13, 14). The concentration of ferritin in the mother's blood depends on the amount of extraction by the fetus. Pregnant women with fetuses with IUGR have higher blood ferritin levels due to decreased placental intake of iron and ferritin (15). Some authors believe that fetal IUGR reduces placental perfusion, small placental abruption, and other placental damage, so that damage to the placental parenchyma, which is significantly rich in ferritin, leads to an increase in maternal serum ferritin and reduces the intake of ferritin by the placenta and the fetus (16, 17). High levels of ferritin in the mother may decrease uterine blood flow by increasing blood concentration. In addition, increased free iron appears to lead to DNA damage due to oxidative stress in the fetus. Therefore, increased blood concentration and oxidative stress can be an acceptable biological justification for the association between high ferritin levels and IUGR (18). Our findings show that maternal serum ferritin levels are increased in fetuses with growth restriction. In other words, high serum ferritin levels were associated with IUGR and low serum ferritin levels were observed in AGA fetuses, which is similar to the findings of previous studies (19, 20). In a study by Hill et al, higher concentrations of renin and lower concentrations of leptin were observed in IUGR infants with abnormal waves on umbilical artery using Doppler ultrasound. However, during the second trimester, Haedersdal et al found no

differences in inflammatory markers including CRP and interferon between IUGR and AGA embryos (21). The effect of maternal iron status on fetal iron is controversial. O'Brien et al showed that maternal ferritin levels were the strongest predictor of iron status in the infant (22). However, others have stated that fetal iron status is not affected by maternal iron deficiency due to the active transfer of iron from mother to placenta (23). Iron deficiency has a known adverse effect during pregnancy. Various studies have shown that lower levels of transferrin receptor expression in the placenta are associated with preeclampsia and IUGR, which can reduce placental iron uptake and increase maternal serum ferritin. In addition, in some studies, placental isoferritin levels are reduced in IUGR and preeclampsia. This iron deficiency can increase fetal corticotrophin and cortisol and inhibit fetal growth (24).

In our study, no significant difference was observed between the studied groups in the mean hemoglobin and hematocrit of umbilical cord blood. Therefore, our study supports the hypothesis that fetal iron status is independent of maternal iron. In IUGR, umbilical cord blood flow is significantly reduced, mainly due to changes in the vascular resistance of the placenta (25, 26). In our study, maternal ferritin with a cutoff of 30.48 is able to predict IUGR with a sensitivity of 67.9% and a specificity of 61.9% (AUC=0.679). Also, maternal hematocrit with a cutoff of 37.25 can predict fetal growth restriction with a sensitivity of 70.0% and a specificity of 62.8% (AUC=0.690). Finally, the maternal hemoglobin with a cutoff of 12.55 can predict IUGR with a sensitivity of 0.70% and a specificity of 65.1% (AUC=0.667). In a study by Bindal et al., maternal ferritin with a cutoff of 20.2 can predict IUGR with a sensitivity of 64.7% and a specificity of 91.7% (27). Also, in a study by Vinjevac et al, the maternal hemoglobin with a cutoff of 13.7 was able to predict IUGR with a sensitivity of 64.7% and a specificity of 91.75% (28). Nowadays ferritin biomarker has wide use in other disorders like beta-thalassemia (29, 30). In addition, our study examined the sensitivity and specificity of hemoglobin and hematocrit, which has not been done in other studies. A parameter that has not been studied in previous studies is cord blood ferritin level, wich the highest mean cord blood ferritin belonged to the AGA group (177.06 ± 79.72) and the lowest mean belonged to the SGA group (109 ±70 07). Only significant differences were observed between AGA and SGA groups (P=0.003) but no significant difference was observed between IUGR and AGA (P= 0.063) and SGA and IUGR (P=0.101). The results of this study show that cord blood ferritin is more likely to be lower in fetuses with growth restriction than in normal-growth fetuses.

4-1. Study Limitations

Considering that the present study was conducted in Motahhari hospital and in a referral center, it seems that a sufficient number of samples were available for inclusion in the study. The cost of tests performed on the mother's serum and umbilical cord required financial support from the university's research department, which followed up. Compared to the other designs of studies, our sample size was not large.

5- CONCLUSION

Based on the results, increased (>34 µg/l), and decreased (<26 µg/l) levels of maternal serum ferritin as cut off points are associated with the possibility of IUGR and SGA, respectively. Therefore, measurement of maternal serum ferritin in addition to ultrasound can be a useful marker in differentiating SGA and IUGR. Our study was a cohort study. Therefore, our results may not show exactly a

causality relationship between maternal ferritin levels and fetal growth. Prospective cohort studies will be required to demonstrate an independent relationship in serum ferritin and IUGR measurements.

6- ABBREVIATIONS

AFI: Amniotic fluid index,

MCAPI: Middle cerebral artery pulsatility index,

UAPI: Umbilical artery pulsatility index,

IUGR: Intrauterine growth restriction,

AGA: Appropriate-for-gestational-age,

SGA: Small-for-gestational age,

NST: Non-Stress test,

Hb: Hemoglobin,

CRL: Crown-rump length,

FGR: fetal growth-restricted.

7- CONFLICT OF INTEREST: None.

8- REFERENCES

1. Gabbe SG, Niebyl JR, Simpson JL, Landon MB, Galan HL, Jauniaux ER, et al. Obstetrics: normal and problem pregnancies e-book: Elsevier Health Sciences; 2016.

2. Cunningham FG. Williams obstetrics 2018;37(1):77-8.

3. Zur RL, Parks WT, Hobson SR. The placental basis of fetal growth restriction. Obstetrics and Gynecology Clinics. 2020 Mar 1;47(1):81-98.

4. Waters T, McNulty J, Wylie B, Sciscione A, Iriye B. Society for Maternal-Fetal Medicine Special Statement: Society for Maternal-Fetal Medicine's conflict of interest policy. American Journal of Obstetrics and Gynecology. 2020;223(6):47-57.

5. Akkurt MO, Akkurt I, Altay M, Coskun B, Erkaya S, Sezik M. Maternal serum ferritin as a clinical tool at 34-36 weeks' gestation for distinguishing subgroups of fetal growth restriction. J Matern Fetal Neonatal Med 2017;30:452-56.

6. Bindal N, Godha Z, Kohli R, Kadam VK. Role of maternal serum ferritin as a predictive marker in intrauterine growth restriction. Int J Reprod Contracept Obstet Gynaecol 2017;4: 804-8.

7. Ozgu-Erdinc AS, Cavkaytar S, Aktulay A, Buyukkagnici U, Erkaya S, Danisman N. Mid-trimester maternal serum and amniotic fluid biomarkers for the prediction of preterm delivery and intrauterine growth retardation. J Obstet Gynaecol Res 2014;40:1540-46.

8. Saha B, Jeeva Sankar M, Gupta S, Agarwal R, Gupta N, Deorari A, et al. Iron Stores in Term and Late Preterm Small for Gestational Age and Appropriate for Gestational Age Neonates at Birth and in Early Infancy. Indian J Pediatr 2016;83:622-27.

9. Soubasi V, Petridou S, Sarafidis K, Tsantali C, Diamanti E, Buonocore G, et al. Association of increased maternal ferritin levels with gestational diabetes and intra-uterine growth retardation. Diabetes Metab 2010;36: 58-63.

10. Akkurt MO, Akkurt I, Altay M, Coskun B, Erkaya S, Sezik M. Maternal serum ferritin as a clinical tool at 34–36 weeks' gestation for distinguishing subgroups of fetal growth restriction. The Journal of Maternal-Fetal & Neonatal Medicine. 2017;30(4):452-6.

11. Goldman L, Schafer AI. Cecil medicine: Elsevier; 25 edition; 2016.

12. Leon-Fuenmayor L, Reyna-Villasmil E, Mejia-Montilla J, Santos-Bolivar J, Torres-Cepeda D, Reyna-Villasmil N, et al. Maternal plasma ferritin during the third trimester of pregnancy and foetal growth. Clin Invest Ginecol Obstet 2018; 45:7-11.

13. Ozgu-Erdinc AS, Cavkaytar S, Aktulay A, Buyukkagnici U, Erkaya S, Danisman N. Mid-trimester maternal serum and amniotic fluid biomarkers for the prediction of preterm delivery and intrauterine growth retardation. J Obstet Gynaecol Res 2014; 40:1540-46.

14. Krantz D, Hallahan T, Janik D, Carmichael J. Maternal serum screening markers and adverse outcome: a new perspective. J Clin Med 2014;3: 693-712.

15. Uberos J, Molina A, Munoz A. Blood ferritin levels in pregnant women as an estimator of low birth weight? Prenat Neonatal Med 2000; 5: 177-81.

16. Bothwell TH. Iron requirements in pregnancy and strategies to meet them. Am J Clin Nutr 2000;72: 257S-64S.

17. Hubel CA, Bodnar LM, Many A, Harger G, Ness RB, Roberts JM. Nonglycosylated ferritin predominates in the circulation of women with preeclampsia but not intrauterine growth restriction. Clin Chem 2004;50: 948-51.

18. Çakmak BD, Türker ÜA, Öztaş S, Arık M, Üstünyurt E. The effect of first trimester hemoglobin levels on pregnancy outcomes. Turkish journal of obstetrics and gynecology. 2018 Sep;15(3):165.

19. Akkurt MO, Akkurt I, Altay M, Coskun B, Erkaya S, Sezik M. Maternal serum ferritin as a clinical tool at 34–36 weeks' gestation for distinguishing subgroups of fetal growth restriction. J Matern Fetal Neonatal Med 2017;30:452-56.

20. Lausten-Thomsen U, Olsen M, Greisen G, Schmiegelow K. Inflammatory markers in umbilical cord blood from small-for-gestational-age newborns. Fetal Pediatr Pathol 2014;33:114-18.

21. Haedersdal S, Salvig JD, Aabye M, Thorball CW, Ruhwald M, Ladelund S, et al. Inflammatory markers in the second trimester prior to clinical onset of preeclampsia, intrauterine growth restriction, and spontaneous preterm birth. Inflammation 2013;36: 907-13.

22. O'Brien KO, Zavaleta N, Abrams SA, Caulfield LE. Maternal iron status influences iron transfer to the fetus during the third trimester of pregnancy. Am J Clin Nutr 2003;77: 924-30.

23. Soubasi V, Petridou S, Sarafidis K, Tsantali C, Diamanti E, Buonocore G, et al. Association of increased maternal ferritin levels with gestational diabetes and intra-uterine growth retardation. Diabetes Metab 2010;36: 58-63.

24. Hubel CA, Kozlov AV, Kagan VE, Evans RW, Davidge ST, McLaughlin MK, et al. Decreased transferrin and increased transferrin saturation in sera of women with preeclampsia: implications for oxidative stress. Am J Obstet Gynaecol 1996;175: 692-700.

25. Giles WB, Trudinger BJ, Baird PJ. Fetal umbilical artery flow velocity waveforms and placental resistance: pathological correlation. Br J Obstet Gynaecol 1985; 92:31.

26. Fleischer A, Schulman H, Farmakides G, Bracero L, Blattner P, Randolph G. Umbilical artery velocity waveforms and intrauterine growth retardation. Am J Obstet Gynaecol 1985; 151: 502-5.

27. Bindal N, Godha Z, Kohli R, Kadam V. Role of maternal serum ferritin as a predictive marker in intrauterine growth restriction. Int J Reprod Contracept Obstet Gynaecol 2015;4: 804-8.

28. Visnjevac N, Segedi L, Curcic A, a Visnjevac J, Stajic D. Blood ferritin levels in pregnant women and prediction of the development of fetal intrauterine growth restriction. J Med Biochem 2011;30: 317.

29. Taghizadeh Sarvestani R, Moradveisi B, Kompany F, Ghaderi E. Correlation between heart and liver iron levels measured by MRI T2 and serum ferritin in patients with β-thalassemia major. International Journal of Pediatrics. 2016 Mar 1; 4(3):1559-67.

30. Shooriabi, M., Zareyee, A., Gilavand, A., Mansoori, B., Keykhaei Dehdezi, B. Investigating DMFT Indicator and its Correlation with the amount of Serum Ferritin and Hemoglobin in Students with Beta-thalassemia Major in Ahvaz, South West of Iran. International Journal of Pediatrics, 2016; 4(3): 1519-27.