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Original Article

Prediction of fetal growth restriction using combined fetal biometry and maternal serum [Inhibin A] in pregnant women with type 1 diabetes

Gynecology and Obstetric

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ABSTRACT

Background: Fetal growth restriction is a main contributing factor of perinatal morbidity and mortality. Screening for fetal growth restriction is a major component of prenatal care but it is known to be problematic. One approach to create evolution is to convalesce screening by emerging new sensitive and specific test.

Objective: To detect the predictive value of using combined fetal biometry and maternal serum inhibin A in fetal growth restriction detection, in type 1 diabetic patients.

Methodology: A prospective cohort study on 100 type1 diabetic pregnant women. At Gestational age after12 weeks, Singleton pregnancy, age 20-40 years. For all patients Serial fetal ultrasound biometry was done and umbilical artery Doppler study were performed, fasting glucose serum levels, Hemoglobin A1C , Maternal Serum Inhibin A were also assessed.

Results: Incidence of IUGR was [66%] in a group of cases with high maternal serum Inhibin A level and non-IUGR was [34%] in a group of cases with normal maternal serum Inhibin A level. Receiver operator characteristics [ROC] curves were constructed for serum inhibin A level, pulsitility index PI of umbilical artery UA by average visit and resuscitative index RI of umbilical artery UA by average visit as predictors of intrauterine growth restriction IUGR in included women. It shows that, pulsitility index of umbilical artery PIUA by average visit and serum inhibin A level the most significant predictors. Serum inhibin A level Cut-off >240, Sensitivity 86.8%, Specificity 76.5%, Accuracy 85.8%, pulsitility index of umbilical artery PIUA by Average visit Cut-off >1.39, Sensitivity 92.4% ,Specificity 91.2% Accuracy 89.3%, resuscitative index of umbilical artery RI UA by Average visit Cut-off >0.62, Sensitivity 69.7% ,Specificity 61.8% Accuracy 68.4% .

Conclusion: In type 1 diabetic women serum levels of inhibin A, and umbilical artery pulsitility index were highly significantly increased in a status of fetal growth restriction. measurement of maternal serum inhibin A ,in type 1 diabetic pregnant women is reliable as a single test for diagnosis of fetal growth restriction.

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Keywords: Diabetes, fetal biometry, fetal growth restriction, inhibin A

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INTRODUCTION

Diabetes mellitus influence on fetus development and placenta plays a crucial role in maintaining normal fetal growth and development, in uncontrolled diabetes hyperglycemia exceed the placental homeostatic capacity, leading to placental insufficiency. As placenta is an organ composed entirely of vessels, maternal vasculopathy complicating type 1 diabetes linked to placental malfunction and hence fetal growth restriction [1].

Fetal growth in diabetic pregnancy might be altered in two contradictory ways, maternal vasculopathy accompanied with placental insufficiency leading to modified nutrient transport and IUGR which is common in type1 diabetes. In reverse maternal hyperglycemia, that provokes fetal overgrowth common in other types of diabetes [2]. Fetal growth restriction is a dynamic process and its estimation requires many ultrasound biometric

and Doppler assessments over period of pregnancy, the rationale of application of Doppler velocimetry in fetal growth estimation of FGR is that it can recognize uteroplacental function through evaluation of the umbilical arteries [3].

Currently, the birth weight <10th centile, either by population-based or customized charts, is the most accepted definition for FGR [4]. IUGR associated with diabetic vasculopathy and resultant placental insufficiency is typically asymmetric and does not manifest before the third trimester (late onset IUGR) [5]. Biomarker measurements of placental functioning-related substances like Inhibin A is crucial in IUGR prediction as during pregnancy, inhibin A synthesized and secreted by placenta, which is involved in the placental local regulatory axis, Multiple studies report the association between increase inhibin A, and adverse pregnancy outcome and fetal growth restriction [6].Reduced placental blood flow and insufficiency can be the cause of fetal growth restriction and higher inhibin A [7]. Combination of ultrasound parameters and serum inhibin A strengthen the predictive tests for IUGR [8]. Therefore, this study was carried out to detect the predictive value of using combined fetal biometry and maternal serum inhibin A in fetal growth restriction detection, in type 1 diabetic women.

PATIENTS AND METHODS

This is a prospective cohort **s**tudy was carried out at the obstetrics and gynecology outpatient clinic at Suez General Hospital, all the laboratory tests were done in the Suez general hospital laboratory unit, in the period from April 2019 to July 2020.

Sample size

Before the study, the number of patients required in each group was determined after a power calculation according to data obtained [6]. In the study, FGR in Normal Inhibin A was (3.3%) and in high inhibin A was (10.2%), and a large effect size (f = 0.343095). A sample size of 100 patients in the study group was determined to provide 80% power for independent samples T test at the level of 5% significant and Confidence interval 95% using G. Power 3.19.2 software.

Inclusion criteria: 1) Gestational age after12 weeks, 2) singleton pregnancy, 3) type 1 diabetic patient. 4) maternal age between 20-40 years.

During the study period, 136 pregnancies undergoing fetal growth restriction screening with fetal biometry and inhibin A testing were recruited. Of this number, (15) were excluded because of medical conditions, such as chronic hypertension, heart disease, (14) excluded as they did not complete their antenatal visit, and (7) was excluded as they were multifetal pregnancies. The remaining 100 pregnancies met the inclusion criteria and were available for analysis presented in figure (1).

The exclusion criteria were as follow: 1) Multiple pregnancy, 2) Non-diabetic pregnant patients, or gestational diabetic patients, 3) Chronic hypertension and kidney disease, Presence of immune disease, 4) Consanguinity between pregnant women and her husband.

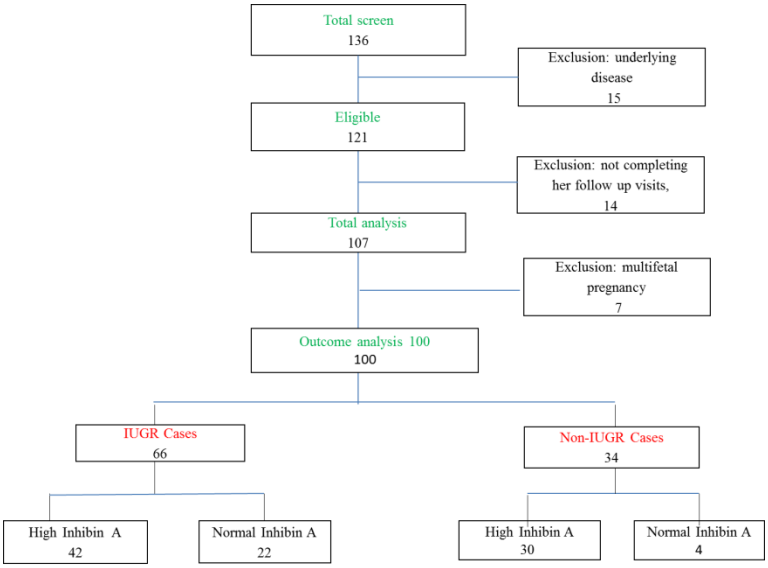

Figure (1): Flow chart of participant recruitment

The study was ethically approved by institutional review board (IRB 202101596) committee of faculty of medicine for "girls" Al-Azhar University. The women were recruited and submitted a written informed consent.

Diabetes diagnosis was based on the criteria of the American Diabetes Association guidelines [9].

Detailed history was including Personal, Menstrual, obstetric, past, and family histories were noted. Clinical

examination including general and local examinations was performed. Ultrasound examination was done for fetus growth evaluation as an estimated fetal weight (EFW) which is derived from ultrasonic measurements of head size, abdominal circumference, and femur length, then an EFW centile is calculated using a reference standard formula. While a single measurement of fetal size and the EFW below 10th centile, Cut- off inadequate to differentiate between fetal growth restriction (FGR) and constitutionally small fetus. Serial fetal biometry reveals the growth retardation of the fetus, and this helps differentiate between healthy SGA and IUGR (in three antenatal visits). Using fetal growth chart (Figure 2) serial Doppler assessment. Of umbilical artery pulsitility index, (P.I) and resuscitative index (R.I) were performed (High-resistance patterns of flow in the umbilical arteries in IUGR).

After aseptic circumstances, samples from venous blood were collected in serum separator tubes (SST) clotted for 10-20 minutes at room temperature after that centrifuged for 20 minutes at 2000-3000 RPM Serum was aspirated and stored at -80◦ c until the test. Estimation of inhibin A was done in the serum of all women in this study in the early second trimester using enzyme linked immunosorbent assay (ELIZA) kit. The kit is for quantitative level of human INH-A, adopt purified INH-A antibody to coat micro titer plate, make solid-base antibody, then add INH-A to wells, combine INH-A antibody with labeled HRP to form antigen antibody enzyme antibody complex after washing completely, add TMB substrate solution (sandwich technique). The normal range of maternal serum inhibin A is 4pg/ml-240pg/ml Measurement of maternal serum (inhibin A) done once in second trimester and not serially assessed as it could be conclusive from single measurement in contrast to fetal biometry it must be noted serially at least in three visits 3-5 weeks apart to be presented on fetal growth chart (figure 2)

Measurement of maternal fasting glucose serum level, Hemoglobin AIC serum level done for each patient once in second trimester by blood sampling.

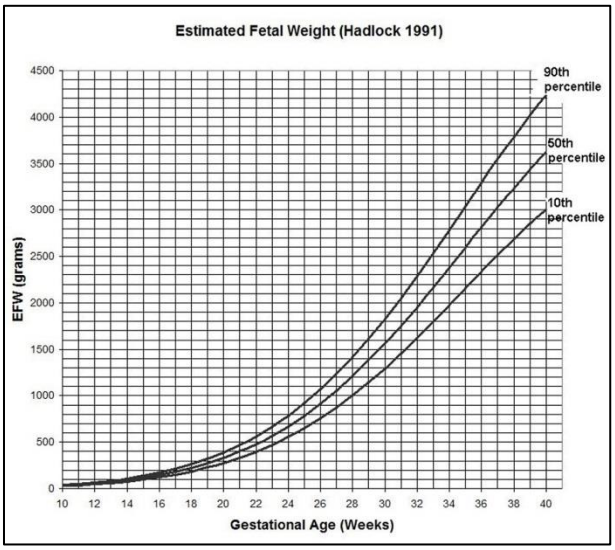

Figure (2): Estimated fetal growth weight

Statistical analysis

Data were collected then fed to the computer and analyzed using IBM SPSS software package version 22.0 qualitative data were described using number and percent, tables and figures were prescribed as range, mean and standard deviation. The qualitative variables were presented as number, (SD >50% of the mean), P value > 0.05 were considered non-significant and p-value < 0.05 was considered significant. Receiver operating characteristic curve (ROC) was used to estimate the best cut off value with its sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and area under curve (AUC) of); with PI of UA, RI of UA by average visit and serum inhibin A level, the most significant predictor.

RESULTS

Distribution of women according to serum Inhibin A measurement done in early second trimester to predict IUGR Incidence in late pregnancy, (table 1and figure 3) in this table serum Inhibin A ranged 33-1300 with mean 479.43±472.41 and median 105 (883) in all cases. There was highly statistically significant higher mean in IUGR **(66%)** 673.83±470.43, compared to non-IUGR (34%) 102.06±106.29. There was no statistically difference regarding maternal gravity, parity, and maternal. Age of diabetes affection (Table 2).

There was statistically significant difference between groups according to fetal weight, abdominal circumference, RI of UA and PI of UA at average visit trimester. Fasting glucose serum level, Hemoglobin A1C level, amniotic fluid index AFI, and no statistically

significant mean maternal systolic and diastolic blood pressure, as presented in table (3).

Receiver operator characteristics [ROC] curves were constructed for serum inhibin A level, PI of UA by average visit and RI of UA by average visit as predictors of IUGR in included women. All items indices were significant predictors as denoted by the significantly large area under the curves [AUCs]; with PI of UA by average visit and serum inhibin A level the most significant predictor,

Serum inhibin A level Cut-off >240, Sensitivity 86.8%, Specificity 76.5%, Accuracy 85.8%, PI of UA by Average visit Cut-off >1.39, Sensitivity 92.4% ,Specificity 91.2% Accuracy 89.3%, RI of UA by Average visit Cut-off >0.62, Sensitivity 69.7% ,Specificity 61.8% Accuracy 68.4% as demonstrated in (table 4 and figure 4).

Logistic regression of factors affecting IUGR versus NON-IUGR shows that HbA1C level, Serum inhibin A level, Fetal weight (gm) by average visit and R. I of UA by average visit, and P. I of UA by average visit, have significant effect on the IUGR rate, the higher the serum inhibin A level and PI and RI of UA by average visit the higher the IUGR, the lower the fasting glucose serum level and amniotic fluid index, by average visit as presented in table (5).

Table (1): This table shows Distribution of women according to their serum inhibin A level (n=100) and Comparison between IUGR and non-IUGR according to serum inhibin A level

Serum inhibin A Level	In total (n=100)	IUGR (n=66)	Non-IUGR (n=34)	z-test	p-value
Mean ± SD	479.43±472.41	673.83±470.43	102.06±106.29	8.717	0.001*
Median (IQR)	105 (883)	840 (940)	67 (35)		
Range	33-1300	37-1300	33-418		

z-Mann-Whitney test; **p-value 0.001 HS

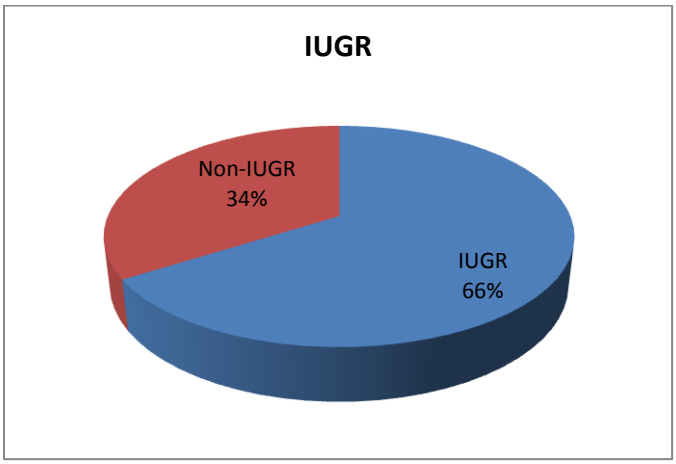

Figure (3): Pie chart distribution of women according to their IUGR (high inhibin),and NON-IUGR (normal inhibin).

Table (2): Distribution of women according to their baseline characteristics in IUGR and NON-IUGR cases

Baseline characteristics	Total (n=100)	IUGR (n=66)	Non-IUGR (n=34)	t/x2#	p-value
Age (years)					
Mean ± SD Range	30.50±4.16 21-40	30.67±4.34 21-40	30.18±3.83 22-38	0.309	0.579
No. of Gravity					
Mean ± SD Range	0-4 2(1)	2.18±0.88 0-4	2.15±0.86 0-3	0.036	0.850
No. of parity					
Mean ± SD Range	0-2 1(1)	1.05±0.64 0-2	0.94±0.81 0-2	0.491	0.485
Age of Diabetes Affection (years)					
Mean ± SD Range	6-18 11.45±2.63	11.30±2.57 6-18	11.74±2.76 7-18	0.606	0.438

t-Independent Sample t-test; #x^2: Chi-square test

Table (3): Comparison between IUGR and non-IUGR according to average visit regarding systolic (mmHg), diastolic (mmHg), GA (wks), Fetal weight (gm), RI of UA and PI of UA

Average visit	IUGR (n=66)	Non-IUGR (n=34)	t-test	p-value
Systolic blood pressure (mmHg)				
Mean ± SD Range	116.90±7.67 110-148.3	115.09±5.41 110-130	1.493	0.225
Diastolic blood pressure (mmHg)				
Mean ± SD Range	75.20±4.16 70-88.3	75.21±3.91 70-85.7	0.001	0.982
Gestational age (wks)				
Mean ± SD Range	32.44±1.17 28-34	32.65±0.92 29-34	0.817	0.368
Fetal weight (gm)				
Mean ± SD Range	1562.17±172.02 866.7-1890	2337.74±248.10 1533.3-2666.7	6.497	0.001*
Resuscitative index of umbilical artery				
Mean ± SD Range	0.68±0.10 0.54-0.93	0.61±0.05 0.47-0.74	11.593	0.001*
Pulsitility index of umbilical artery				
Mean ± SD Range	1.26±0.19 0.91-1.74	0.64±0.16 0.45-0.96	7.496	0.001*
Abdominal circumference (mm)				
Mean ± SD Range	279.11±81.22 240.67-922.67	291.11±12.30 274-322.33	0.729	0.395
Fasting glucose level				
Mean ± SD Range	249.09±52.94 120-350	176.38±21.14 150-250	9.045	0.001*
Amniotic fluid index				
Mean ± SD Range	6.30±1.43 4-11.5	10.06±1.22 8-13	7.731	0.001*
Haemoglobin A1C level				
Mean ± SD Range	7.88±0.45 6.5-9	6.84±0.66 6-9	5.846	0.001*

t-Independent Sample t-test; S; *p-value <0.05

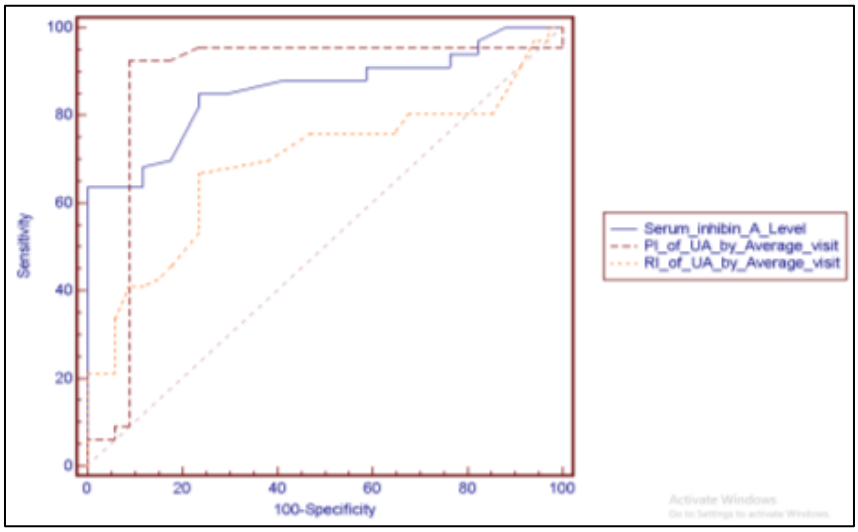

Figure (4): Receiver-operating characteristic (ROC) curve for prediction of IUGR using the serum inhibin A, PI of UA and RI of UA by average visit

Table (4): Cut-off value of inhibin A, PI of UA,RI of UA

Item	Cut-off	Sen.	Spe.	PPV	NPV	Accuracy
Serum inhibin A Level	>240	86.8%	76.5%	87.5%	72.2%	85.8%
PI of UA by Average visit	>1.39	92.4%	91.2%	95.3%	86.1%	89.3%
RI of UA by Average visit	>0.62	69.7%	61.8%	78.0%	51.1%	68.4%

Table (5): Logistic regression of factors affecting IUGR versus non-IUGR.

Parameters	B	S.E.	p value	Odds ratio	95% C.I.	
					Lower	Upper
Fasting Glucose Serum Level	-0.04	0.01	0.106	0.96	0.94	0.98
HbA1C Level	-1.14	0.06	0.045*	0.04	0.01	0.14
Serum inhibin A Level	0.03	0.02	0.001*	1.00	0.99	1.00
Fetal weight (gm) by Average visit	0.08	0.02	0.032*	1.02	1.01	1.02
RI of UA by Average visit	-10.71	3.62	0.003*	0.82	0.55	2.68
PI of UA by Average visit	-34.87	14.41	0.001*	0.98	0.49	3.13
AFI by Average two trimester	1.65	0.34	0.115	2.19	0.68	4.07

*: Significant p value

DISCUSSION

Fetal growth restriction is a main contributing factor of perinatal morbidity and mortality. Screening for fetal growth restriction is a major component of prenatal care but it is known to be problematic. One approach to create evolution is to convalesce screening by emerging new sensitive and specific tests. As abnormal placentation is assumed to be the main cause of fetal growth restriction, one strategy is to combine fetal biometry with a marker of placental dysfunction [10]. multiple studies report the association between increase inhibin A, and fetal growth restriction as type 1 diabetes usually result in defective placentation and vasulopathy, and as the incidence of type 1 diabetes is expanding at an alarming rate, mostly in younger age groups it was remarkable to specify our study in type 1 diabetic women [2]. So, this study was designed to evaluate the predictive value of combining early maternal serum (inhibin A) in second trimester and fetal ultrasound biometry (in type 1 diabetic women) on IUGR incidence. Distribution of women according to serum Inhibin A measurement done in early second trimester to predict IUGR incidence in late pregnancy, show high correlation between high serum inhibin A, in early second trimester and incidence of IUGR (66٪) in reverse normal inhibin serum level in NON-IUGR cases (34 ٪). This conclusion in agreement with Fitzgerald et al. [11] who reported that increased inhibin-A levels may be caused by premature accelerated differentiation of the villous cytotrophoblast, resulting in marked alterations in the syncytiotrophoblast morphology and concurrent villous cytotrophoblast depletion increasing the pregnancy at risk of fetal growth restriction, and also in consistence with Zongji Shen [12] who found positive correlation in inhibin A concentrations between the serum and placental extract ($r = 0.57$, $P < 0.001$). Both maternal serum and placental inhibin A in FGR and Preeclampsia groups were significantly higher than in controls, Serum inhibin A level might be a useful for diagnosis and monitoring of FGR and preeclampsia [12], and agreed with ladfors et al [13] who conducted a retrospective chart review study, medical files of pregnant women with T1DM and T2DM were analyzed at Skåne University Hospital during the years 2006 to 2016. Maternal weight in early pregnancy and at term was registered *the* rates of light-for-dates infants were 50% among women with T1DM and 23% among women with T2DM. In contrast with Gutaj et al. [2] who reported an association between large for gestational age (LGA) being the most typical one and diabetes LGA may be associated with maternal hyperglycemia, in spite other factors such as gestational weight gain and maternal lipids can have a role between diabetes and fetal abnormalities.

Regarding ultrasound fetal biometry and Doppler assessments, in this study ultrasound fetal biometry and Doppler was statistically highly significant with predictive value < 0.001.the most significant parameters were, EFW, FL, P. I, and R. I of UA.. EFW positive correlation agree with a retrospective cohort study done by *Lunshof* et al[14] Who found that, the EFW gave a better sensitivity than the AC in IUGR diagnosis. Also in consistence with a study done by Warrander et al. [15] who found that Hadlock HCACFL is the most precise model presently available to evaluate fetal weight in early onset fetal growth restriction whatever fetal size, or presentation, *and disagree with* Mailath-Pokorny et al. [16] , who shows that there is a significant relation between short FL and IUGR and poor perinatal outcome, as supported by recent literature. This conclusion in contrary to our study as we approve the use of combined ultrasound parameters in IUGR prediction more dependable than rely on single ultrasound parameter.

Regarding umbilical artery Doppler highly significant predictive value < 0.001. Agreed with study done by lees et al. [17] ,who concluded that progressively increasing PI in the UA corresponds to decrease in the placental surface area which reduce its nutrient exchange capacity, and is associated with placental vascular insufficiency reflected by, reversed end diastolic flow (EDF) in the UA, and also in consistence with Khadija et al. [18] who conducted observational case-control study of singletons with intra-uterine growth restriction (fetal weight <10th percentile). Intra-uterine growth restricted fetuses (cases) and normal (controls) were examined for the umbilical artery. Fetal umbilical artery Doppler ultrasound is an effective tool in the detection of early intra-uterine growth restriction fetuses. In disagreement with Macdonald et al.[19] who found Pulsatility Indices (PI) of the uterine arteries (UtA), umbilical artery (UA) and fetal vessels were analyzed, individually and in combination, for prediction of fetal weight found abnormal umbilical Doppler patterns in a few rate in contrast cerebral–placental–uterine ratio (CPUR).

This study concluded that. Mean serum inhibin A level was 673.83± 470.43 in IUGR cases and 102.06 ± 106.29 in NON-IUGR cases, [P value <0.001]. with a cutoff point >240 pg. / ml with high sensitivity and specificity (86.8% and 76.5%) respectively). So, increased level of Inhibin-A is associated with fetal growth restriction. Most of previous studies support this concern and in agreement with our study as Singnoi et al. [6] who concluded that, the rates of preterm birth, preeclampsia, fetal growth restriction, and low birth weight were crucially elevated in the group of high levels than those in the normal group; (12.2% vs 8.3%, *p*-value 0.049, 7.3% vs 2.0%, *p*-value < 0.001; 10.2% vs 3.3%, *p*-value < 0.001; and 15.1% vs 9.5%, p-value 0.008 respectively), but Low levels of serum Inhibin-A were not remarkably associated with any unfavorable outcomes. In agreement with D'Anna et al. [20] who found that elevated maternal inhibin-A concentrations in the second trimester are strongly associated with intrauterine growth restriction in a retrospective analysis of serum samples from a bank of stored serum, originally taken for Down's syndrome screening over 15-18 weeks, was performed. In disagreement with Morris et al. [21] who found that Down's screening serum biomarkers have low screening value in pre-eclampsia and small for gestational age prediction. when combined with other tests. Five serum screening markers were evaluated (alpha feto protein, Inhibin-A, human chorionic gonadotropin, unconjugated estrogen,human placental lactogen , 44 studies, testing pre-eclampsia cases and 86 studies, testing fetal growth restriction cases met the selection criteria. The results revealed low predictive accuracy overall.

In this study, logistic regression analysis of the IUGR showed that the rate of IUGR was significantly associated with serum inhibin A Level <0.001**,P.I of UA<0.001** , R.I of UA 0.003* Fetal weight (gm) by Average visit 0.032* HbA1C 0.045* but neither Fasting Glucose Serum Level nor amniotic fluid index by Average visit, as presented in (table 5). Our findings that elevated inhibin-A in the second trimester might be reflective of an abnormal development of the placenta in early gestation which could cause serious clinical adverse outcome (fetal growth restriction and preeclampsia) in late pregnancy. So high inhibin-A with in the second trimester could be considered one of the risk factors of abnormal placentation these conclusions. In consistence with study done Singnoi, et al. [6] who theorize that the high incidence of preterm birth in cases of high inhibin A levels shown in previous studies [22,23] could be a sequel of preeclampsia or fetal growth restriction rather than spontaneous preterm birth and also in agreement with Yue et al. [24] in there multivariate regression analysis was accustomed to assess the influence of confounding variables, including age, parity, gravidity and pre-pregnancy BMI. And Inhibin A. and the result was, Inhibin A risk factor for: preeclampsia, gestational hypertension, gestational diabetes, macrosomia, low birth weight, preterm delivery.

CONCLUSION

In type 1 diabetic women serum levels of inhibin A, and umbilical artery pulsitility index were significantly high in a status of fetal growth restriction. Measurement of maternal serum inhibin A in type 1 diabetic pregnant women is a reliable as single test for diagnosis of fetal growth restriction .therefore, combining both assessments strongly predictive for IUGR. In addition, help in establishing an integrated efficient model of IUGR screening.

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Conflict of interest: The Authors declare that there is no conflict of interest

REFERENCES

1. **Desoye G.** The Human Placenta in Diabetes and Obesity: Friend or Foe? The 2017 Norbert Freinkel Award Lecture. Diabetes Care. 41: 1362–1369, 2018.
2. **Gutaj P, Wender-Ozegowska E, Iciek R, Zawiejska A, Pietryga M, and Brazert J.** Maternal serum placental growth factor and fetal SGA in pregnancy complicated by type 1 diabetes mellitus. J Perinat Med. 42(5):629–33, 2014.
3. **Salomon LJ, Alfirvic Z, Da Silva Costa F, and Deter RL.** ISUOG Practical Guidelines ultrasound assessment of fetal biometry and growth. Ultrasound Obstet Gynecol.53: 715-723, 2019.
4. **Mc Cowan LM, Figueras F, Anderson NH.** "Evidence-based national guidelines for the management of suspected fetal growth restriction: comparison, consensus, and controversy," American Journal of Obstetrics and Gynecology. 218 (2): S855–S868, 2018.

5. **Sharma D, Farahbakhsh N, Shastri S, and Sharma P.** Intrauterine growth restriction – part 2. J Matern Fetal Neonatal Me. 0(0): 1-12, 2016.
6. **Singnoi W, Wanapirak C, Sekararithi R, Tongsong T.** A cohort study of the association between maternal serum Inhibin-A and adverse pregnancy outcomes: a population-based study. BMC Pregnancy Childb. 19[1]:124, 2019.
7. **El-Gharib MN, and Morad M.** Maternal serum inhibin-A for predicting preeclampsia. J Matern Fetal Neonatal Med. 24(4):595–9, 2011.
8. **Gaccioli F, Aye ILMH, Sovio U, Charnock-Jones DS, and Smith GCS.** Screening for fetal growth restriction using fetal biometry combined with maternal biomarkers. Am J Obstet Gynecol, 218: S725-S737, 2018.
9. **American Diabetes Association.** Older Adults: Standards of Medical Care in Diabetes—2018. Diabetes Care. 41; S119–S125, 2018.
10. **American College of Obstetricians and Gynecologists.** Fetal growth restriction. Practice bulletin no. 134. Obstet Gynecol.121: 1122-33, 2013.
11. **Fitzgerald B, Levytska K, Kingdom J, Walker M, Baczyk D, and Keating S.** Villous trophoblast abnormalities in extremely preterm deliveries with elevated second trimester maternal serum hCG or inhibin-a. Placenta. 32(4): 339-45, 2011.
12. **Zongji Sh , Li-Yi C, Iwan-Satyagraha S, Pooja Sh,** and **Xiping Z.** Placental and maternal serum inhibin A in patients with preeclampsia and small-for-gestational-age. J Obstet Gynaecol Res. 37(10):1290-6, 2011.
13. **Ladfors L, Shaat N, Wiberg N, Katasarou A, Berntorp K, and Kristensen K.** Fetal overgrowth in women with type 1 and type 2 diabetes mellitus. PLoS One.12: e0187917, 2017.
14. **Lunshof S, Friese A, Grijseels E, and Laudy J.** Validity of ultrasound estimated fetal weight and abdominal circumference for assessment of IUGR from 35 weeks of gestation. Ultrasound in Obstetrics and Gynecology. 54 (S1):171-172, 2019.
15. **Warrander LK, Ingram E, Heazell AE, and Johnstone ED.** Evaluating the accuracy and precision of sonographic fetal weight estimation models in extremely early onset fetal growth restriction. Acta Obstetricia et Gynecologica Scandinavica. 99 (3): 364-73, 2020
16. **Mailath-Pokorny M, Polterauer S, Worda K, Springer S, and Bettelheim D.** Isolated short fetal femur length in the second trimester and the association with adverse perinatal outcome: experiences from a tertiary referral center. PLoS One. 10(6): e0128820, 2015.
17. **Lees T. Stampalija A. Baschat F. da Silva CE. and Ferrazzi F, Figueras F, et al.** ISUOG Practice Guidelines: diagnosis and management of small for gestational age fetus and fetal growth restriction. The official journal of the International Society of Ultrasound in Obstetrics and Gynecology. 56 (2), 298-312, 2020.
18. **Khadija S, Gilani SA, Butt S, Yousaf M, and Bacha R.** The efficacy of Doppler Indices in Third Trimester of IUGR Pregnancies. Obstetrics and Gynecology Research. 001-009, 2020.
19. **Macdonald TM, McCarthy EA, and Walker SP.** Shining light in dark corners: diagnosis and management of late-onset fetal growth restriction. Australian and New Zealand Journal of Obstetrics and Gynaecology. 55(1):3–10, 2015.
20. **D'Anna R, Baviera G, Corrado F, Leonardi I, Buemi M, and Jasonni V.** Is mid-trimester maternal serum inhibin-A a marker of preeclampsia or intrauterine growth restriction?. Acta obstetricia et gynecologica Scandinavica. 81(6): 540-543M, 2002.
21. **Morris RK, Cnossen JS, Langejans M, Robson SC, Kleijnen J, Ter Riet G, et al.** Serum screening with Down's syndrome markers to predict pre-eclampsia and small for gestational age: systematic review and meta-analysis. BMC pregnancy and childbirth. 8(1): 1-19, 2008.
22. **Jelliffe-Pawlowski LL, Baer RJ, Blumenfeld YJ, Ryckman KK, O'Brodovich HM, Gould JB.** Maternal characteristics and mid-pregnancy serum biomarkers as risk factors for subtypes of preterm birth. BJOG. 122 (11):1484–93, 2015.
23. **Dugoff L, Hobbins JC, Malone FD, Vidaver J, Sullivan L, and Canick JA.** Quad screen as a predictor of adverse pregnancy outcome. Obstet Gynecol. 106 (2):260-7, 2005.
24. **Yue, C. Y., Zhang, C. Y., Ni, Y. H., & Ying, C. M**. Are serum levels of inhibin A in second trimester predictors of adverse pregnancy outcome?. Plos one. 15(5), e0232634, 2020.

الملخص العربي

الاكتشاف المبكر لتأخر نمو الجنين داخل الرحم بالاستخدام المزدوج للقياسات البيومتريه للجنين والمصل الحيوي للأم (إنهيبن أ) في الحوامل المصابة بمرض السكري من النوع الأول.

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ملخص البحث

الخلفية: يعد تأخر نمو الجنين عاملا رئيسيا يساهم في معدلات الاعتلال والوفيات التي تحدث في الفترة المحيطة بالولادة ويعد فحص تأخر نمو الجنين مكونًا رئيسيًا في رعاية ما قبل الولادة ولكن من المعروف أنه يمثل مشكلة. تتمثل إحدى طرق إحداث التطور في تحري النقاهة من خلال ظهور اختبار جديد حساس ومحدد.

الهدف : الكشف عن القيمة التنبؤية للاستخدام المزدوج القياسات البيومتريه للجنين والمصل الحيوي للام (إنهبين أ) في الكشف عن تا خر نمو الجنين، في الحوامل مرضى السكري من النوع الأول.

الطرق : شملت دراستنا 100 امرأة حامل مصابة بداء السكري من النوع الاول تتراوح اعمارهن 20-40 عامًا ووعلي ان يكون الحمل بجنين واحد، عمر الحمل بعد 12 أسبوعًا وبالنسبة لجميع المرضى ، تم إجراء القياسات البيومتريه للجنين بالموجات فوق الصوتية بشكل تسلسلي و ايضا دراسة دوبلر للشريان السري للجنين، وتم قياس مستويات مصل الجلوكوز الصائم للام، وقياس نسبة السكر التراكمي للام، والمصل الحيوي للام انهيبين ا.

النتائج:خلصت هذه الدراسة إلى أن حدوث تأخر النمو داخل الرحم كان [66٪] في مجموعة الحالات ذات مستوى الإنهيبين أ المرتفع في مصل الأم وعدم تأخر النمو داخل الرحم كان [34٪] في مجموعة الحالات ذات مستوى الإنهيبين أ الطبيعي في مصل الأم. تم إنشاء منحنيات مشغل المستقبل لمستوى مصل االانهيبين أ، ومؤشر النبض للشريان السري من خلال متوسط الزيارات ومؤشر الإنعاش للشريان السري عن طريق متوسط الزيارة كمتنبئات لتأخر النمو داخل الرحم في النساء المشمولات. يُظهر أن مؤشر النبض للشريان السري حسب متوسط الزيارة ومستوى مصل الانهيبين أ هما أهم المؤشرات التنبؤية

المصل الحيوي للام انهيبين أ: مستوى القطع> 240، الحساسية 86.8٪، الخصوصية 76.5٪، الدقة 85.8٪، مؤشر النبض للشريان السري حسب متوسط الزيارات: مستوى القطع> 1.39 ، الحساسية 92.4٪، الخصوصية 91.2٪ الدقة 89.3٪، و مؤشر الإنعاش من الشريان السري حسب متوسط الزيارات: مستوى القطع> 0.62، الحساسية 69.7٪، الدقة 61.8٪ الدقة 68.4٪.

الاستنتاجات: انه في النساء المصابات بداء السكري من انوع الاول، لوحظ ارتفاع مستويات المصل الحيوي للام الإنهيبين أ، ومؤشر النبض في الشريان السري بشكل كبير في حالات تأخر نمو الجنين. ويمكن الاعتماد على المصل الحيوي للام الإنهيبين أ بمفرده في تشخيص تأخر نمو الجنين.

الكلمات المفتاحية: داء السكري، القياسات الحيوية للجنين، تأخر نمو الجنين، الإنهيبين أ.

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