IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 20, Issue 6 Ser.12 (June. 2021), PP 43-48
www.iosrjournals.org

Correlation of sonographic fetal growth evaluation with maternal serum Human Placental Lactogen levels

Efanga SA[1], Akintomide AO[1], Obiora CI[2], Okpara HC[3], Efanga I[4].
[1]*Radiology Department, University of Calabar, Calabar, Cross River State, Nigeria.*
[2]*Radiology Department, University of Calabar Teaching Hospital, Calabar, Cross-River State, Nigeria*
[3]*Chemical Pathology Department, Nnamdi Azikiwe University, Nnewi, Anambra state, Nigeria.*
[4]*Radiography Department, University of Calabar, Calabar, Cross River State, Nigeria.*

Abstract:
Background: *Human placental lactogen (HPL) is a hormone synthesized by the placenta modulates fetal growth. The concentration of HPL in the maternal circulation offers an avenue to assess the growth of the developing fetus in pregnancy and it is essential to establish the feasibility of this potential fetal growth monitoring tool in this locality. We have selected this study to evaluate the relationship that HPL has with fetal growth parameters.*
Material and Methods: *This was a prospective cross-sectional study conducted over a 6-month period in the University of Calabar Teaching Hospital that involved 100 healthy pregnant women. An ultrasound scan was done for all the subjects and blood samples were collected for the determination of serum HPL concentration. Pearson correlation was done on the data collected.*
Results: *HPL had a positive significant correlation with Estimated gestational age (P 0.000) and Estimated fetal weight (P 0.000) and a significant negative correlation with Head circumference to Abdominal circumference ratio (HC/AC) (P 0.000).*
Conclusion: *The assessment of maternal serum concentration of HPL is an invaluable tool in the detection of restricted fetal growth. HPL level is significantly related to the estimated fetal weight and consequently it shows the existence of asymmetric intra-uterine growth restriction.*
Key words *– Human placental lactogen, Intra-uterine growth restriction, Ultrasound*

Date of Submission: 15-06-2021 Date of Acceptance: 30-06-2021

I. Introduction

Human placental lactogen (HPL) is regarded as a member of the somatotropin family which also encompasses growth hormone, prolactin and placental growth hormone. [1] HPL is produced by the placenta and is detected in the umbilical blood and maternal blood from the 6th week of pregnancy and rises in concentration as the fetus and placenta develop. In fact, in the middle and late trimesters of pregnancies, HPL peaks at a range of 5000 to 7000 ng/ml. [2] A larger proportion of HPL produced is released into the maternal circulation with about 0.05% flowing into the fetal circulation and an equally small percentage remains in the amniotic fluid. [1, 3, 4]

Studies have suggested that HPL regulates fetal metabolism and fetal growth. This notion is backed by the existence of specific HPL receptors in human fetal tissues. [5] Mothers with high levels of HPL and estradiol have been demonstrated to experience the lowest risks of fetal growth restriction. [1]

Intra-Uterine Growth Restriction (IUGR) is commonly a result of varying combinations of defective placental development and vascular pathology. [6] The incidence of IUGR is 5% in the general obstetric population. [7] IUGR is defined as Estimated Fetal Weight (EFW) $\leq 10^{th}$ percentile for gestational age. It consists of symmetrical IUGR which is commonly seen in the first trimester of pregnancy and asymmetrical IUGR which is noticed in the second and the third trimesters. An elevated HC/AC ratio above 1.2 is suggestive of asymmetric IUGR. Newborns with IUGR are at a higher risk of neonatal morbidity and mortality, impaired neurodevelopment and abnormalities with the cardiovascular system. [2, 6, 7]

The Royal college of Obstetricians and Gynecologists recommend serial detailed ultrasound scan of the IUGR fetus to closely monitor the fetal growth parameters. [6, 7] Haezel et al [8] inferred from their research that calculating EFW with an ultrasound scan was the most accurate procedure for the detection of small for gestational age (SGA) babies, probably due to IUGR, at birth with a diagnostic odds ratio (DOR) of 21.3 while HPL was observed to be the most accurate biochemical test with a DOR of 4.78. They advocated for the combination of both methods for an early and reliable detection of IUGR. [8] The early identification of IUGR is of much value because proper evaluation and management of the condition can lead to a favourable outcome. [7]

This accentuates the belief that the measurement of maternal HPL is a good tool in intensive fetal monitoring for the evaluation of the risks of IUGR. [1, 9, 10]

The current study aims to evaluate the relationship of maternal HPL with fetal anthropometric parameters that are indicative of IUGR.

II. Material and Methods

This research was a prospective cross-sectional study carried out in the Radiology Department of the University of Calabar Teaching Hospital, Calabar, Nigeria, from January 2019 to June 2019. The study population was obtained from the pregnant women who attended the Antenatal clinic of the Obstetrics and Gynecology department of the University of Calabar Teaching Hospital, Calabar, Nigeria, during the period of the study. The subjects engaged in this study were 100 consenting pregnant women.

Inclusion Criteria

1. Singleton pregnancy
2. Age below 40 years

Exclusion Criteria

1. Pregestational Diabetes mellitus
2. Gestational diabetes mellitus
3. Sickle cell disease
4. Pregnancy induced hypertension
5. Chronic hypertensives
6. Fetal anomalies
7. Habitual cigarette smoker
8. Placental anomalies
9. Abnormal cord insertion
10. Abnormal placental location
11. Maternal cardiovascular disease
12. Uterine anomalies

Procedure methodology

After obtaining an informed consent from the subjects their height and weight were measured and used to calculate their Body Mass Index (BMI). They were afterwards ushered into the Radiology Department from the Antenatal clinic where the ultrasound scan procedure was conducted by two experienced Radiologists.

Ultrasound procedure

The Ultrasound machine utilized for the study was an Aloka prosound SSD–3500sx (2 Dimensional with Doppler) that has curvilinear probe with a frequency range of 3.5-5MHz (manufactured in 2008 by Aloka company limited located in Meerbusch, Germany). The anthropometric parameters of interest were the EFW, HC/AC ratio and Estimated Gestational Age (EGA).

The patients were requested to lie in a supine position on a comfortable couch. An ultrasound gel was applied on their abdomen and the probe was gently used to spread the gel to the surfaces that will be scanned. During the ultrasound scanning process, the probe was applied in the longitudinal plane, transverse plane and the coronal plane to assess the fetal parts and the intra-uterine environment.

Each subject was led into another ultrasound suite for a second scan. An average of the result obtained from the ultrasound scan procedures done by the 2 Radiologists was used as data for this study and each subject spent approximately 30 minutes for the ultrasound scan.

EFW was derived after the measurements of HC, AC and the femur length (FL) were measured, [6] HC/AC ratio was obtained by dividing the measured HC by the AC while the EGA was produced by the machine after all the fetal parameters [Bi-parietal diameter (BPD), HC, AC and FL] were measured. The landmark for the measurement of HC must include both thalami and the cavum septum pellucidum while the measurement of AC is done when the stomach and the umbilical vein are noted in the cross section of the abdomen. [7]

Serum HPL evaluation procedure

On emerging from the ultrasound suites each subject was ushered into an improvised phlebotomy space. Blood sample was collected by venous puncture using a sterile 5 ml syringe and each subject spent approximately 10 minutes for the phlebotomy procedure.

The blood sample was run into a serum separator tube/gel tube and then it was left to clot. The sample was centrifuged at 5000 rpm for 5 mins after which the serum was carefully extracted. The serum was transferred to a screw-cap polypropylene transport tube and frozen at -20^0 C until analysis. Analysis to evaluate HPL concentration was done using ELISA (Enzyme Linked Immunosorbent Assay). [11]

Statistical analysis

The data obtained from the research was analyzed using SPSS version 20 (SPSS Inc., Chicago, IL). Appropriate descriptive and inferential statistical methods were used to analyse the data while tables and charts were the means of displaying the results where applicable. Continuous variables were reported as mean and standard deviation (mean ± SD). Correlation was determined by using Pearson's correlation *P* value < 0.05 was considered statistically significant.

III. Results

The age range of the subjects that were involved in this study was from 20 years to 39 years. The age group from 20 to 24 years had 10 subjects, the age group from 25 to 29 years was the highest with 38 subjects, the age group from 30 to 34 years had 36 subjects and the age group from 35 to 39 years had 16 subjects.

Table 1 shows the range of the maternal and fetal variables that were assessed in the study. The minimum EFW noted in the fetuses of the subjects in this study was 0.350 kg and the maximum EFW was 4.100 kg with a mean value of 2.129±1.017 kg. The minimum HC/AC ratio obtained was 0.900 while the maximum value was 1.200 with the mean being 1.017±0.073. Maternal serum HPL concentration evaluated in the subjects had a minimum value of 2.700 microgram/ml and a maximum value of 8.700 microgram/ml with a mean value of 6.519±2.082 microgram/ml. The BMI of the subjects had a minimum value of 20.500 kg/m2 while the maximum value was 39.700 kg/m2 with a mean value of 29.153±4.212 kg/m2.

Table 1: Shows the key statistical analysis of the maternal and fetal variables in the study

	n	Minimum	Maximum	Mean	Standard Deviation
EGA (weeks)	100	20.000	40.290	32.644	±5.523
EFW (kg)	100	0.350	4.100	2.129	±1.017
HC/AC	100	0.900	1.200	1.017	±0.073
HPL (microgram/ml)	100	2.000	8.700	6.519	±2.082
BMI (kg/m2)	100	20.500	39.700	29.153	±4.212
AGE (years)	100	20.000	39.000	29.860	±4.318

EGA:- Estimated gestational age. EFW:- Estimated fetal weight. HC/AC:- Head circumference to Abdominal circumference ratio. HPL:- Human placental lactogen. BMI:- Body mass index.

Table 2 shows the correlation between maternal HPL and the maternal and fetal variables of the subjects that were involved in the study. EGA, EFW, HC/AC ratio values obtained following the assessment of the fetus and the maternal BMI were all seen to be correlated to maternal serum HPL.

Table 2: Shows the correlation between maternal HPL and the maternal and fetal variables

HPL

	Correlation coefficient ®	P value
EGA (weeks)	+ 0.986	0.000*
EFW (kg)	+0.952	0.000*
HC/AC	-0.479	0.000*
BMI (kg/m2)	+0.239	0.017*
AGE (years)	+0.048	0.635

P value <0.05 is significant. EGA:- Estimated gestational age. EFW:- Estimated fetal weight. HC/AC:- Head circumference to Abdominal circumference ratio. HPL:- Human placental lactogen. BMI:- Body mass index.

Figure 1 shows the maternal serum concentration of HPL at different gestational age groups in this study. In the gestational age groups 21 to 25 weeks, 26 to 30 weeks, 31 to 35 weeks and 36 to 40 weeks the corresponding mean values of HPL measured were as follows respectively, 2.94 microgram/ml, 4.50 microgram/ml, 7.18 microgram/ml and 8.25 microgram/ml.

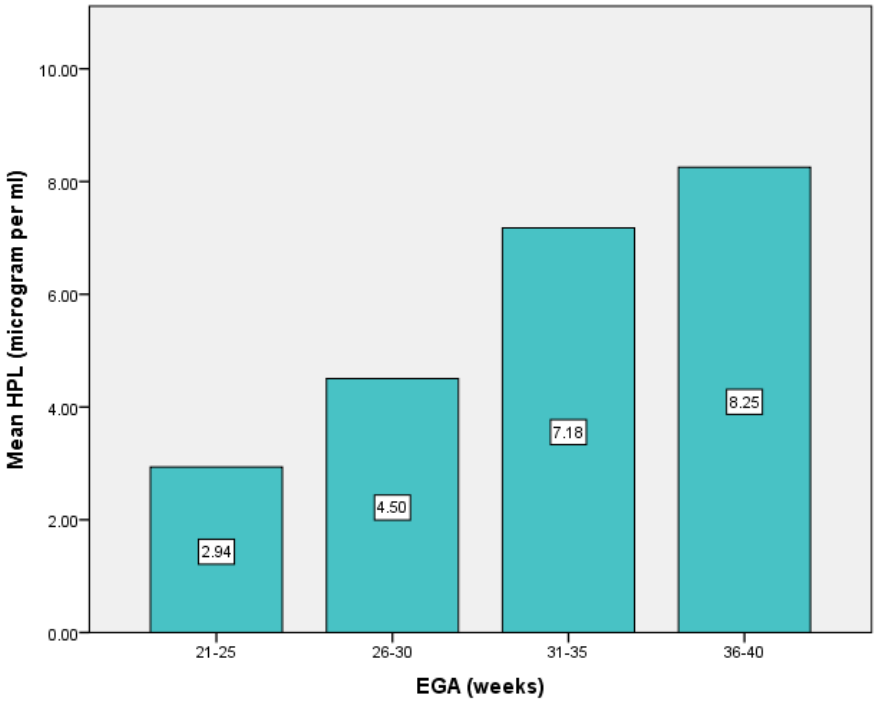

Figure 1: Shows the progressive increase in the serum concentration of HPL as the EGA increases

Figure 2 shows a linear increase in the EFW of the fetus in direct proportion with an increase in the serum level of maternal HPL. The correlation coefficient between the two variables (EFW and HPL) has a positive value indicating that a change in their quantity occurs in the same direction.

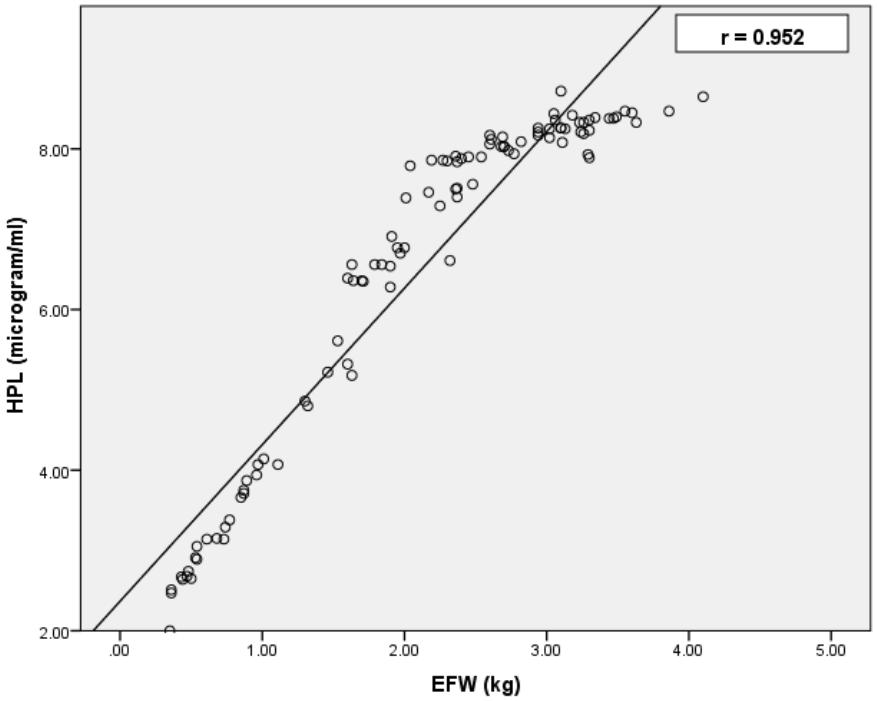

Figure 2: Shows a proportional increase in the fetal weight as the maternal HPL concentration rises

Figure 3 shows that a reduction in the serum concentration of maternal HPL is associated with an increase of the HC/AC ratio and consequently, the risk of IUGR of the fetus becomes high. The correlation coefficient has a negative value demonstrating the inverse relationship between the two variables (HPL and HC/AC ratio).

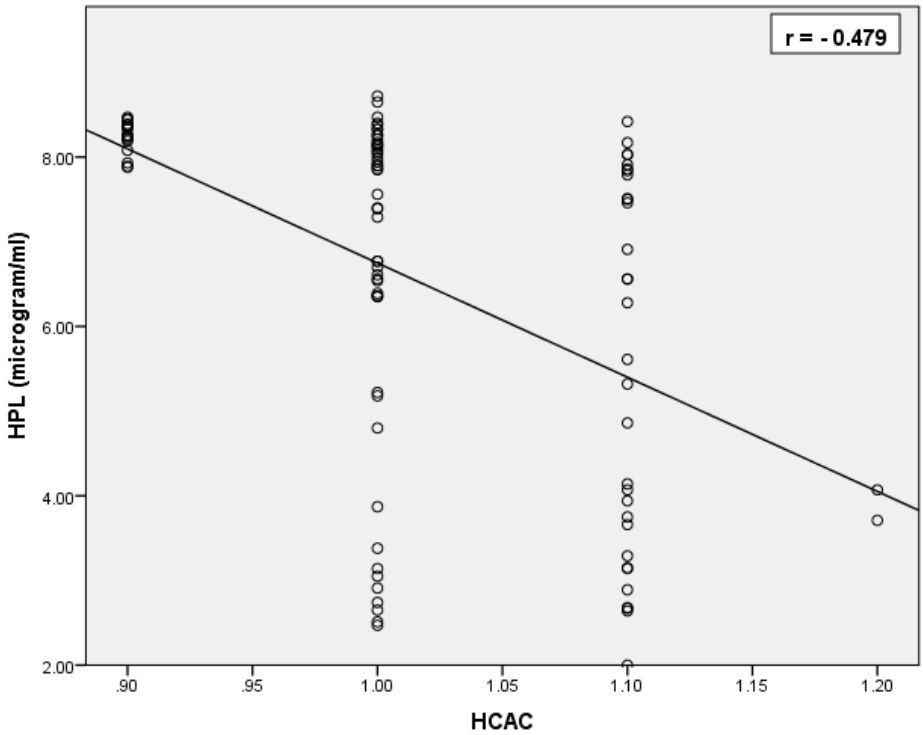

Figure 3: Shows a gradual elevation of the HC/AC ratio as the serum concentration of the maternal HPL drops

IV. Discussion

HPL is regarded as an essential component of the processes that regulate fetal growth and is a clinical biomarker of the maternal and fetal metabolic status. [1] We found out from this study that the serum concentration of HPL had a significant positive correlation with EGA (*P* 0.000) which was actually in congruence with earlier documented studies. In agreement with this study, Dutton et al [1] inferred that the circulating concentration of maternal HPL increases as the gestation (EGA) advances and further noticed that HPL is a reliable marker for the determination of gestational age in early pregnancy because they realized that the quantified HPL was similar to the result obtained from Crown-rump length measurement. [1]

A useful surveillance means of fetal growth is the estimation of fetal weight and furthermore, the demonstration of a progressive increment through the course of pregnancy. EFW was seen to exhibit a significant positive correlation with HPL (*P* 0.000) suggesting that the rise in HPL is indicative of a favourable state in terms of the fetal weight. This buttresses the overwhelming opinion held on the influential role that HPL plays in the determination of fetal weight and by implication, the birth weight. Knopp et al [1] also discovered a significant positive correlation between maternal HPL and both birth length and weight while Houghton et al [1] noticed a correlation between maternal HPL and infant weight. However, it was reported in another study where the maternal blood and cord blood HPL were collected at term, that there was no correlation between them and fetal growth parameters. [1] Spellacy et al [12] and Singer et al [12] also did not observe any correlation between maternal blood concentration of HPL and fetal weight at birth. Spellacy et al [12] opined that there is always a wide variation of HPL levels during labour and parturition, thus nullifying the diagnostic efficacy of assessing HPL concentration during delivery and after delivery. Gennazani et al [12] decided to obtain the maternal serum HPL 10 days before parturition and found out that there was a correlation between it and the birth weight on delivery.

Asymmetrical IUGR is predominantly seen in the 2nd and 3rd trimesters of pregnancy and it is suggested when the value of HC/AC ratio increases significantly above 1.2. The disproportional growth or the restricted growth of the intra-abdominal structures when related to the growth of the fetal head is the basis for the abnormal values of HC/AC ratio. [6, 7] This study demonstrated a significant negative correlation between HPL and HC/AC ratio (*P* 0.000) highlighting the importance of a serial assessment of maternal serum HPL values because when it persistently drops the impairment of fetal growth is highly likely to occur. In consonance

with this study, Niven et al [12] observed that in 141 pregnant women admitted for threatened miscarriage the serum level of HPL was significantly below the normal range and kept on dropping until they lost their babies. Conversely, Pedersen et al [3] could not establish any relationship between HPL and the probability of the occurrence of IUGR in their research which mainly involved the assessment of first trimester pregnancies.

Poor pregnancy outcome initiated by reduced fetal movement is independently related to maternal serum HPL. [13] Dutton et al [1] noticed a significant reduction of the serum levels of HPL in women exhibiting reduced fetal movement and poor perinatal outcomes.

It has been observed that maternal nutrition has an essential role in modulating the gene expression of HPL which further regulates fetal growth, The index of a good nutrition is maternal weight which is manifested in the body mass index (BMI) and it is important to note that the maternal height as well as the paternal height and weight has no effect on the birth weight. [2] This study observed a significant correlation between the serum concentration of HPL and maternal BMI (*P* 0.017) and this finding dovetails with the suggestion that fetal wellbeing is a reflection of the healthy maternal weight gain during pregnancy.

The limitation of this study was that the sample size was small and thus, the results may not be used to support the presence of the relationships demonstrated. Further studies are required for it to be adopted for use clinically.

V. Conclusion

The assessment of maternal serum concentration of HPL is an invaluable tool in the detection of restricted fetal growth. HPL level is significantly related to the estimated fetal weight and consequently it shows the existence of asymmetric intra-uterine growth restriction. Maternal weight gain during pregnancy contributes to the process that regulate HPL concentration.

References

[1]. Sibiak R, Jankowski M, Gutaj P, Mozdziak P, Kempisty B, Wender-Ożegowska E. Placental Lactogen as a Marker of Maternal Obesity, Diabetes, and Fetal Growth Abnormalities: Current Knowledge and Clinical Perspectives. *J Clin Med*. 2020;9(4):1142. doi:10.3390/jcm9041142

[2]. Michael Freemark. Placental Hormones and the Control of Fetal Growth. *J Clin Endocrinology & Metabolism* 2010;95(5):2054–2057. doi.org/10.1210/jc.2010-0517

[3]. Pedersen NG, Juul A, Christiansen M, Wøjdemann KR, Tabor A. Maternal serum placental growth hormone, but not human placental lactogen or insulin growth factor-1, is positively associated with fetal growth in the first half of pregnancy. *Ultrasound Obstet Gynecol*. 2010;36(5):534-541.. doi:10.1002/uog.7727

[4]. Gueneuc A, Deloron P, Bertin GI. Usefulness of a biomarker to identify placental dysfunction in the context of malaria. *Malar J* 2017;16(11):1-7. doi.org/10.1186/s12936-016-1664-0.

[5]. Walker WH, Fitzpatrick SL, Saunders GF. Human placental lactogen transcriptional enhancer. Tissue specificity and binding with specific proteins. *J Biol Chem*. 1990;265(22):12940-12948.

[6]. Riyami NA, Walker MG, Proctor LK, Yinon Y, Windrim RC, Kingdom JCP. Utility of head/abdomen circumference ratio in the evaluation of severe early-onset intrauterine growth restriction. *J Obstet Gynaecol Can*. 2011;33(7):715-719. doi:10.1016/S1701-2163(16)34956-8.

[7]. Peleg D, Kennedy CM, Hunter SK. Intrauterine growth restriction: identification and management. *American Family Physician*. 1998;58(2):453-60, 466-7.

[8]. Heazell AE, Hayes DJ, Whitworth M, Takwoingi Y, Bayliss SE, Davenport C. Biochemical tests of placental function versus ultrasound assessment of fetal size for stillbirth and small-for-gestational-age infants. *Cochrane Database Syst Rev*. 2019;5(5):CD012245. doi:10.1002/14651858.CD012245.pub2

[9]. Reis FM, D'Antona D, Petraglia F. Predictive value of hormone measurements in maternal and fetal complications of pregnancy. *Endocr Rev*. 2002;23(2):230-257. doi:10.1210/edrv.23.2.0459

[10]. Chard T, Sturdee J, Cockrill B, Obiekwe BC. Which is the best placental function test? A comparison of placental lactogen and unconjugated oestriol in the prediction of intrauterine growth retardation. *Eur J Obstet Gynecol Reprod Biol*. 1985;19(1):13-17. doi:10.1016/0028-2243(85)90159-5.

[11]. Human Placental Lactogen ELISA kit insert from Biovendor: Biovendor Laboratorni Medicina a.s, Karasek, Brno, Czech Republic. Wilde CE, Oakey RE; Scientific and Technical Committee; Association of Clinical Biochemists. Biochemical tests for the assessment of feto-placental function. *Ann Clin Biochem*. 1975;12(3):83-118. doi:10.1177/000456327501200124

[12]. Dutton PJ, Warrander LK, Roberts SA, et al. Predictors of poor perinatal outcome following maternal perception of reduced fetal movements--a prospective cohort study. *PLoS One*. 2012;7(7):e39784. doi:10.1371/journal.pone.0039784

Efanga SA. et. al. "Correlation of sonographic fetal growth evaluation with maternal serum Human Placental Lactogen levels."*IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 20(06), 2021, pp. 43-48.