

## Comparative Study of Serum Progesterone Levels between Women with Ongoing Pregnancies and Those with Pregnancy Loss in a Tertiary Health Center in Owerri, Nigeria

**Dr. Ekpeni Sunday Obia**

*Department of Obstetrics and Gynaecology, Federal Medical Centre, Owerri, Imo State.*

**Dr. Callistus Obinna Elegbua**

*Department of Obstetrics and Gynaecology, Nigerian Navy Reference Hospital, Calabar, Cross River State.*

**Dr. Augustine Duke Onyeabochukwu**

*Department of Obstetrics and Gynaecology, University of Nigeria Teaching Hospital Ituku Ozalla, Enugu State.*

**Dr. Kingsley Chukwu Episteme Obioha**

*Department of Obstetrics and Gynaecology, University of Nigeria Teaching Hospital Ituku Ozalla, Enugu State.*

**Correspondence:** Dr. Augustine Duke Onyeabochukwu

*Department of Obstetrics and Gynaecology, University of Nigeria Teaching Hospital Ituku Ozalla, P.M.B. 01129, Enugu State.*

*Received 04 November 2023; Accepted 16 November 2023*

### ABSTRACT

**Background:** Early pregnancy period is saddled with a lot of uncertainties. It is associated with palpable anxiety if pregnancy will be ongoing or miscarry. Various biomarkers have been evaluated to track the course of early pregnancy in order to avert pregnancy loss; one of them that has shown great promise in predicting outcome following threatened miscarriage is serum progesterone. Comparing serum progesterone levels between women with ongoing pregnancies and those with pregnancy loss will aid in making recommendations on the management of early pregnancies.

**Objectives:** To compare the serum progesterone levels between women with ongoing pregnancies and those with pregnancy loss in a Tertiary Health Center in Owerri, Nigeria.

**Study design:** A prospective cohort study of pregnant women with threatened miscarriage at 6-10 weeks gestation (Group 1) and those without threatened miscarriage (Group 2) at the same gestational age.

**Methodology:** A total of 100 parturient who satisfied the inclusion criteria were recruited for the study by systematic sampling. These were equal number of 50 participants each as subject and control. They were matched for gestational age and social status. Serum progesterone measurement obtained and the pregnancy outcomes were evaluated for each participant. The results were analysed using SPSS version 25 with appropriate tables and figures generated.

**Results:** The overall median serum progesterone levels were higher in the control group than the subject ( $p=0.228$ ). The median progesterone levels were significantly lower among those with threatened miscarriage who had pregnancy loss compared with those that had ongoing pregnancy [9.33ng/ml (4.56-14.75) vs. 20.72ng/ml (16.10-28.87) respectively,  $p<0.001$ ]. Progesterone had 77.8% sensitivity with negative predictive value of 85.2% and 92% specificity with positive predictive value of 87.5% at optimum cut-off value of 14.80ng/ml. The area under the curve for progesterone was 0.89 (95% CI, 0.764-1.000).

**Conclusion:** Serum progesterone levels were significantly higher in women with ongoing pregnancies as opposed to their counterparts with pregnancy loss.

**Recommendation:** Serum progesterone levels should be routinely evaluated to help in decision making for progesterone supplementation in the first trimester.

**KEYWORDS:** Progesterone, Pregnancy, Levels, Loss, Serum, Ongoing, Comparative.

## I. INTRODUCTION

Threatened miscarriage is the most dreaded complication of early pregnancy which is seen in approximately 20% of pregnant women.<sup>1</sup> As the outcome is difficult to predict, it is a cause of psychological trauma to the patients and also a dilemma to the managing health personnel.<sup>2</sup> Threatened miscarriage diagnosis is made through a history of vaginal bleeding, a closed cervix on clinical examination and subsequent ultrasound scan (USS) demonstrating fetal cardiac activity in early pregnancy.<sup>3,4</sup>

The worst outcome of threatened miscarriage is pregnancy loss and about 16.9% to half of women with vaginal bleeding in the first half of pregnancy will invariably miscarry<sup>5,6</sup>. The rate of pregnancy loss is less if there is fetal cardiac activity demonstrable by ultrasonography.<sup>7</sup> Pregnancy loss of 36.2% amongst women with prior threatened miscarriage has been reported by a study in North Central Nigeria.<sup>8</sup> Majority of these abortions occur in the first trimester as the rate of fetal death after 14 weeks gestation is minimal as opposed to that in lesser gestational age.<sup>9</sup>

Of all the causes of miscarriage; chromosomal abnormalities have been documented to rank first as a cause of first trimester miscarriage. It is responsible for 50% of first trimester miscarriages.<sup>10</sup>

The actual course of miscarriage is not always straight-forward. The prediction of spontaneous abortion or subsequent outcome of pregnancy have been investigated for using the following;

ultrasonography and biomarkers such as urine estrogens, urine HCG, estrone, estradiol (E2), progesterone, human placental lactogen, cortisol, serum human chorionic gonadotropin (HCG), estradiol (E2), and Cancer Antigen-125 (CA-125). Suggestions have been made that abnormal levels of one or more of these biomarkers might help to predict miscarriage. Several studies have reported that serum progesterone level in early pregnancy is the most specific predictive biomarker for distinguishing viable from non-viable pregnancies in natural conception and measurable progesterone levels in circulation in the first trimester are related to the outcome of the pregnancy<sup>11-13</sup>. There is an association between low progesterone values with miscarriages as well as high progesterone concentrations with viable pregnancies.<sup>14,15</sup>

The progesterone production by the corpus luteum and placenta which is stimulated by a viable pregnancy are responsible for serum progesterone in a pregnant woman. Although, the corpus luteum retains its capacity to secrete progesterone throughout pregnancy, its functional ability decreases drastically at approximately 7th week of gestation which is the period that the placenta takes over the function of progesterone production.<sup>16</sup> Progesterone has the following functions; preparation of the uterus for implantation of the blastocyst by promoting endometrial decidualisation and maintenance of early pregnancy by stimulating the secretion of Th2 cytokines while reducing Th1 cytokines, thus, inhibiting immune responses like those responsible for graft rejection<sup>17</sup>. Other functions of progesterone in pregnancy are to inhibit smooth muscle contractility, decrease prostaglandin formation thus maintaining myometrial quiescence and preventing the onset of uterine contractions.<sup>17-19</sup>

Laboratory progesterone assays are available at presence in most immunoassay platforms and have been of great promise in terms of assay sensitivity, specificity, accuracy and precision with rapid turnaround times.<sup>19</sup> Its ability as a single test to differentiate continuing from non-continuing intrauterine pregnancy in patients with threatened abortion will be very helpful. Studies comparing the serum progesterone levels between women with ongoing pregnancies and those with pregnancy loss in Nigeria are scarce and this in essence shows a knowledge gap which this study will fill. The reason for this study is to compare the serum progesterone levels between women with ongoing pregnancies and those with pregnancy loss in a Tertiary Health Center in Owerri, Nigeria.

## II. METHODOLOGY

**Study Area:** The study was conducted in the department of Obstetrics and Gynaecology of the Federal Medical Centre, Owerri, Imo State, South-East Nigeria. Federal Medical Centre Owerri is a tertiary health facility that trains Resident Doctors in all medical and surgical specialties and also provides health care to the people in the city of Owerri as well as nearby semi-urban settlements and neighbouring towns. It receives clients from other States in Nigeria such as Abia and River States as well. The average monthly antenatal attendance in the center are 153,580 pregnant women.

**Study Population:** The study population were pregnant women at 6-10 weeks gestational age who satisfied the inclusion criteria.

**Inclusion Criteria:** All parity, spontaneously conceived pregnancies, gestational age between 6 and 10 weeks, singleton intra-uterine pregnancy and demonstration of cardiac activity by ultrasonography.

**Study Design:** The study was a prospective cohort study; participants were pregnant women with threatened miscarriage at 6-10 weeks gestation (Group 1) and those without threatened miscarriage (Group 2) at the same gestational age.

**Study Tool:** The study tool was data collection sheets.

## *Comparative Study of Serum Progesterone Levels between Women With Ongoing Pregnancies ..*

**Sample Size:** The sample size was 100 comprising 50 eligible participants with threatened miscarriage in the 6-10 weeks gestation and 50 eligible participants with no history of threatened miscarriage in the same gestational age. It was determined by a previously validated formula for cohort study<sup>20</sup>.

**Sampling Technique:** The sampling method was systematic sampling. First, all pregnant women were screened to determine those who satisfied the inclusion criteria. Second, eligible women were screened to determine those who were having threatened miscarriage at 6-10 weeks gestation (Group 1). Those without threatened miscarriage (Group 2) were recruited after matching for gestational age and social status.

**Patients Recruitment:** Consenting and eligible pregnant women in their first trimester, between 6-10 weeks gestational age, who presented to the hospital either as their first antenatal booking or at the Gynaecological emergency unit or hospitalized for threatened miscarriage were enrolled into the study until the sample size was complete. They were categorized into two groups. Group 1 included women with threatened miscarriage in whom an ultrasonography report confirmed the presence of fetal cardiac activity and Group 2 consisting of consenting control population that were recruited from the antenatal booking clinic or general outpatient clinic after eligibility criteria were met.

Recruitments were done by the researcher with assistance from the research assistants. The research assistants were four junior resident Doctors who were trained about the study protocol (such as the contents of the information sheet, consent form, data collection sheet and also sample collection) daily for one week before commencement of the study.

**Data Collection:** Pregnant women in their first trimester between gestational ages of 6-10 weeks, who meet the criteria were given detailed explanation of the study and a written informed consent obtained. Participants were subjected to history taking and examination to determine age, parity, gestational age, any previous early pregnancy miscarriage; and to exclude general and systemic diseases.

A transvaginal or abdominal ultrasonographic scanning was done to establish gestational age, presence of intrauterine pregnancy with demonstrable embryonic or fetal cardiac activity, and to exclude multiple pregnancies, and vesicular mole. Information obtained were recorded in the data collection sheet.

Two milliliters of peripheral venous blood was taken once, at recruitment, for serum progesterone measurement following selection of a consenting eligible participant. While in sitting or lying position, the cubital vein was identified having prepared the required materials for the procedure. The puncture site was aseptically prepared and tourniquet applied at the upper arm. The venipuncture procedure was completed by collection of blood after removal of the tourniquet. The puncture site and the overall condition of the participant were observed for complications that could arise, and all contaminated materials were disposed of. The samples were collected at the antenatal clinic, general outpatient clinic, gynaecologic emergency unit and ward into a plain bottle and taken to the laboratory where the serum was separated by centrifugation at 2000rpm and stored at -20°C until hormonal level measurement; which were done in batches, to minimize analytical variation.

Serum progesterone was analyzed using a fully-auto chemiluminescence immunoassay (CLIA) analyzer MAGLUMI 1000 which uses competitive immunoluminometric assay principle.

**Patients Follow up:** All participants in group I who presented with threatened miscarriage were advised to have physical rest. Both groups were followed up to observe participants whose pregnancies would be on-going or abort at the end of the first trimester. The follow up information were documented in the data collection sheet.

**Data Analysis:** The data were analyzed using the Statistical Package for Social Sciences (SPSS) software version 25. Kolmogorov-Smirnov test was used to evaluate normality of Data distribution. The values of progesterone was expressed as median values and interquartile ranges as data was not normally distributed. Comparative analysis of serum progesterone in the different groups was done using Mann-Whitney test. Receiver Operator Characteristic (ROC) curve was constructed to evaluate the level of serum progesterone in distinguishing ongoing pregnancies from those that resulted in pregnancy loss. The accuracy of progesterone in predicting pregnancy loss was established by determining the area under the ROC curve; and the optimal predictive cut-off value of serum progesterone for pregnancy loss determined by the best sensitivity and specificity from the Receiver Operator Characteristic (ROC) curve analysis. In all statistical analyses,  $p < 0.05$  (95% confidence interval) was considered significant. Results were presented using tables and figures.

**Ethical Consideration:** An institutional approval for this study was obtained from the Ethical Review Committee of Federal Medical Center, Owerri. Informed written consent was obtained from each participant after adequate counselling and the data obtained from the study were treated with confidentiality and used solely for the purpose of the study.

### **Limitation of the study:**

1. Serial serum progesterone analysis would have shown the trend of progesterone changes during the course of the pregnancy than a single serum progesterone evaluation.
2. The study was a single centre study; a multicentre study with a larger number of participants may be more representative.
3. Pregnancy outcome was only followed up to the end of the first trimester. Monitoring till delivery would have been more informative.

### III. RESULTS

The study was conducted over a period of 24 months (October, 2018 to October, 2020). A total of 100 participants were enrolled comprising 50 participants in each group. Two women, one in each group, had induced termination of pregnancy while ten women; one in group 1 and 9 in group 2 were lost to follow up. Five women in the study group were excluded from the analysis because they received progesterone medication. A total of 43 women with threatened miscarriage and 40 participants without threatened miscarriage were included in the analysis.

**Table 1: Demographic profile of the participants**

	Study group Mean(SD)	Control group Mean(SD)	p- value
Age (years)	28.81 (4.98)	27.7 (5.15)	0.224
Gravidity	2.07 (0.99)	2.11 (0.92)	0.776
Parity	1.00 (1.11)	1.18 (1.09)	0.425
Gestational Age	7.77 (1.34)	7.83 (1.36)	0.848
BMI(Kg/m <sup>2</sup> )	24.31 (4.78)	27.65 (5.15)	0.750

BMI = Body mass index

Analysis by Student's t-test

The demographic profile of each group is shown in table 1. The mean ages for the maternal groups with threatened abortion and control were 28.81 (21-40) years with SD  $\pm$  4.98 and 27.70 (21-35) years with SD  $\pm$  5.15 respectively. No significant differences were noted between the maternal ages, gestational ages, BMI and parity between the two groups.

**Table 2: Pregnancy outcome of participant at gestational age of 13 weeks**

	Ongoing pregnancy n (%)	Pregnancy loss n (%)
Study group(n=43)	25 (58.1)	18 (41.9)
Control group (n=40)	38 (95.0)	2 (5.0)

Study group: women with threatened miscarriage

Table 2 illustrates the proportion of women with ongoing pregnancy or pregnancy loss in both groups by 13 weeks.

**Table 3: Comparison of median progesterone of participants with ongoing pregnancy and those with pregnancy loss**

	Ongoing pregnancy Median(IQR)	Pregnancy loss Median(IQR)	P-value
Study group	20.72 (16.10-28.87)	9.33 (4.56-14.75)	< 0.001
Control group	21.93 (17.57-30.16)	18.10*	0.352

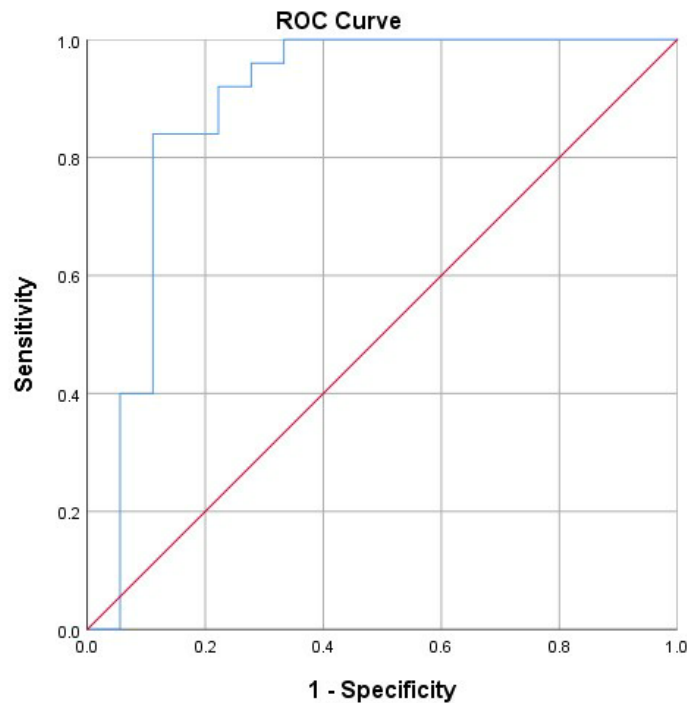
IQR: Interquartile range

Median progesterone is measured in ng/ml

\* No interquartile range because there was only two values.

Table 3 depicts the median progesterone of participants with ongoing pregnancy by 13 weeks and those with pregnancy loss in both groups as analysed by the Mann-Whitney U test.

The progesterone distribution in both groups were not normally distributed as determined by the Kolmogorov smirnov test ( $p < 0.001$ ). Progesterone values ranged from 4.25 – 64.21ng/ml and 3.21 – 68.33ng/dl with median (IQR) values of 21.55 (17.44 – 29.38)ng/ml and 16.00 (10.65 – 24.92)ng/ml for the control and study groups respectively. The overall serum progesterone median value was higher in the control group compared with those with threatened miscarriage but this difference was not statistically significant ( $p = 0.228$ ). In the threatened abortion group, median serum progesterone level was significantly lower in patients who went on to miscarry (9.32ng/ml) as compared to those who did not miscarry (20.72ng/ml) ( $p < 0.001$ ) there was no statistically significant difference between the median progesterone across the categories of gestational ages ( $p = 0.311$ ).



**Figure 1: Receiver operator characteristic (ROC) curve of progesterone concentration as a predictive test for pregnancy loss.**

Figure 1 illustrates receiver operator characteristic (ROC) curve of serum progesterone concentration in predicting pregnancy loss in women with threatened miscarriage. Single serum progesterone estimation was able to significantly discriminate between those threatened miscarriages that continued with those that failed as demonstrated by the ROC curve analysis.

The area under the curve (AUC) for progesterone as derived from the ROC curve was 0.89 (95% CI, 0.764-1.000). The optimum cut-off value of progesterone concentration from the ROC analysis of below 14.80ng/ml for the prediction of pregnancy loss established sensitivity, specificity, positive predictive and negative predictive value as shown in table 3.

#### **IV. DISCUSSION**

The demographic characteristics of the participants in this study showed no statistically significant differences in the maternal ages, gestational ages, body mass index and parity between the two groups. The number of ongoing pregnancies were higher in the participants without threatened miscarriage while participants with threatened miscarriage recorded more pregnancy loss.

Analysis of the median progesterone levels in women who went on having miscarriage with those with ongoing viable pregnancies in both groups showed that while there was no statistically significant difference in the progesterone concentration between those with threatened miscarriage and the control, it was determined that the median concentration of progesterone was significantly higher in those whose pregnancies were still viable by 13 weeks of gestation following a threatened miscarriage. These findings were in accordance with reports from other researches.<sup>14,19</sup>

The correctness of serum progesterone measurement as a predictor of pregnancy viability or failure by the end of 13 weeks of gestation in women diagnosed with first trimester threatened miscarriage was evaluated in this study. As demonstrated by the ROC curve analysis, serum progesterone concentration showed a significant ability to differentiate between pregnancies that continued and those that eventually aborted.

The ROC analysis obtained a progesterone cut-off value of 14.80ng/ml which was shown in this study to be optimum in discriminating between pregnancies that are likely to continue with those at risk of miscarriage. At this cut-off value, the highest combined sensitivity and specificity was obtained. The positive predictive value (PPV) and negative predictive value (NPV) for the prediction of pregnancy loss were 87.5% and 85.2% respectively. A similar cut-off of 14.15ng/ml was shown by another study<sup>21</sup>, in a prospective comparative study to assess the role of a single maternal serum progesterone measurement in the immediate diagnosis of early pregnancy failure and in the long-term prognosis of fetal viability, to make a distinction between threatened-continuing and non-continuing pregnancies with 87.6% sensitivity and specificity of 87.5%. This study unlike the index study included ectopic gestations and women with threatened miscarriage in the first 18 weeks of pregnancy. Lower discriminating cut-off values of 10ng/ml have been reported by some studies<sup>22,23</sup>. However, these studies did not give data on fetal heart activity at presentation and included participants with missed miscarriage, ectopic pregnancy and those with inconclusive ultrasound findings in their analysis which were all excluded in our study. This can explain the lower cut-off as compared with that obtained in the index study as serum progesterone concentrations have been noted to be lower in ectopic and non-viable pregnancies<sup>24,25</sup>. Lek et al.<sup>26</sup> in a large cohort study validated progesterone concentration of 11.0ng/ml as a cut-off for spontaneous miscarriage following a first trimester miscarriage sensitivity 92.0%, specificity 92.0%, PPV 67.7% and NPV 91.3%. The cohorts were followed up to 16 weeks as opposed to ours that were followed up to 13 weeks of pregnancy. Other studies reported higher progesterone cut-off values. In a study by Abdelazim et al.<sup>27</sup>, serum progesterone was 95.1% sensitive for diagnosing non-viable pregnancy and 98.9% specific for the diagnosis of viable pregnancy at a cut-off level of 20ng/ml. However, the study included those with abdominal pain without vaginal bleeding. This could explain the higher cut-off value reported as women with bleeding tends to have lower serum progesterone level.<sup>14</sup>

While utilizing a progesterone concentration of less than 32.7ng/ml as a cut-off value for the diagnosis of non-viable pregnancy, it was noted by Hanita et al.<sup>19</sup>, in a cross sectional study, that sensitivity was 90% , specificity 92% , while the positive predictive value was 97% and the negative predictive value 75%. The study design of this study was different from that of the index study. Differences in data collection or study design have a significant impact on the estimated discriminative capacity of serum progesterone measurement<sup>3</sup>. Variation in progesterone values among women from different geographic background may affect the outcome of a study.<sup>28</sup>

## V. CONCLUSION:

Serum progesterone levels were significantly higher in women with ongoing pregnancies as opposed to their counterparts with pregnancy loss.

## REFERENCES

- [1]. American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 150: Early pregnancy loss. *Obstet Gynecol.* 2015 May;125(5):1258–67.
- [2]. Rekha NP, Justin CK, Douglas GT, Neelam P. Role of serum biomarkers in the prediction of outcome in women with threatened miscarriage: a systematic review and diagnostic accuracy meta-analysis. *Human Reproduction Update.* 2016;22(2):228-239.
- [3]. National Institute for Health and Clinical Excellence. (2012). Ectopic pregnancy and miscarriage: Diagnosis and initial management in early pregnancy of ectopic pregnancy and miscarriage. Clinical Guideline 154. London: NICE.
- [4]. Saraswat L, Bhattacharya S, Maheshwari A. Maternal and perinatal outcome in women with threatened miscarriage in the first trimester: a systematic review. *BJOG*2010;117:245–257.
- [5]. Ahmed SR, El-Sammani ME, Al-Sheeha MA, Aitallah AS, Khan FJ. Pregnancy Outcome in Women with Threatened Miscarriage: a Year Study. *J Acad Med Sci Bos Herz.* 2012; 24(1): 26-28.
- [6]. Hasan R, Baird DD, Herring AH, Olshan AF, Jonsson Funk ML, Hartmann KE. Association between first-trimester vaginal bleeding and miscarriage. *Obstet Gynecol.* 2009;114(4):860-867.
- [7]. Cunningham FG, Leveno kj, Bloom SL, Spong CY, Dashe JS, Hoffman BL, et al editors. *Williams’s obstetrics* .24<sup>th</sup> ed. New York:McGraw-Hill;2014.
- [8]. Adeniran AS, Fawole AA, Abdul IF, Adesina KT. Spontaneous abortions (miscarriages):
- [9]. Analysis of cases at a tertiary center in North Central Nigeria. *J Med Trop.*2015;17(1):22-26.
- [10]. Kolte AM, Olsen LR, Mikkelsen EM, Christiansen OB, Nielsen HS. Depression and emotional stress is highly prevalent among women with recurrent pregnancy loss. *Oxf J.*2015;30:77–82.

---

*Comparative Study of Serum Progesterone Levels between Women With Ongoing Pregnancies ..*

---

- [11]. Keyhan S, Muasher L, Muasher S. Spontaneous abortion and recurrent pregnancy loss: etiology, diagnosis and treatment. In: Lobo RA, Gershenson DM, Lentz GM, Valea FA editors. *Comprehensive gynecology*. 7<sup>th</sup> ed. Philadelphia: Elsevier;2017.
- [12]. Elson J, Salim R, Tailor A, Banerjee S, Zosmer N, Jurkovic D. Prediction of early pregnancy viability in the absence of an ultrasonically detectable embryo. *Ultrasound Obstet Gynecol* 2003;21(1):57-61.
- [13]. Stefano L, Lucia L, Andrea RG. Endocrinology of pregnancy loss. In: Howard JA, Carp, eds. *Recurrent Pregnancy Loss*. 1st ed. US: CRC Press; 2008:79-87.
- [14]. Vicdan K, Zeki Isik A. Luteal phase hormonal profile in prediction of pregnancy outcome after assisted reproduction. *Eur J Obstet Gynecol Reprod Biol*.2001;96:98-101.
- [15]. Ku1 CW, Allen JC, Lek SM, Chia ML, Tan NS, Tan TC. Serum progesterone distribution in normal pregnancies compared to pregnancies complicated by threatened miscarriage from 5 to 13 weeks gestation: a prospective cohort study. *BMC Pregnancy and Childbirth*. 2018;18:360. doi:10.1186/s12884-018-2002-z
- [16]. Osmanağaoğlu MA, Erdoğan I, Eminağaoğlu S, Karahan SC, Özgün S, BH CG. The diagnostic value of beta-human chorionic gonadotropin, progesterone, CA125 in the prediction of abortions. *J Obs Gynaecol*. 2010;30:288–93.
- [17]. Schindler A E. Endocrinology of pregnancy. Consequences for the diagnosis and treatment of pregnancy disorders. *J Steroid Biochem Mol Biol*, 2005;97(5):386-388.
- [18]. Brar AK, Frank GR, Kessler CA, Cedars MI, Handwerker S. Progesterone-dependent decidualization of the human endometrium is mediated by cAMP. *Endocrine* 1997;6:301-7.
- [19]. Pratap K, Navneet Magon. Hormones in pregnancy. *Niger Med J*. 2012 Oct-Dec; 53(4):179-183.
- [20]. Hanita O, Hanisah AH. Potential use of single measurement of serum progesterone in detecting early pregnancy failure. *Malaysian J Pathol*. 2012;34:41-46.
- [21]. Fleiss JL. *Statistical Methods for Rates and Proportions*. John Wiley & Sons, 1981.
- [22]. Al-Sebai MA, Kingsland CR, Diver M, Hipkin L, McFadyen IR. The role of a single progesterone measurement in the diagnosis of fetal viability. *Br J Obstet Gynaecol*. 1995;102(5):364-9.
- [23]. Khosho EZ, Aiub MM, Adnan S. The value of early pregnancy single serum progesterone measurement in relation to the first trimester viability. *Thi-qar medical journal (TQMJ)*. 2011;5(2):133-141.
- [24]. Verhaegen J, Gallos ID, van Mello NM, Abdel-Aziz M, Takwoingi Y, Harb H, Deeks JJ, Mol BW, Coomarasamy A. Accuracy of single progesterone test to predict early pregnancy outcome in women with pain or bleeding: meta-analysis of cohort studies. *BMJ* 2012; 345:e6077.
- [25]. Alnakash AH, Abdulsahib Z. Role of serum progesterone in the diagnosis of ectopic pregnancy and miss abortion. *The Iraqi Postgraduate Medical Journal*. 2015;14(1):22-27.
- [26]. Selvarajan S, Ramalingam J, Vijayaraghavan J, Bobby Z. Serum progesterone measurement in diagnosis of ectopic pregnancy. *Journal of SAFOG*. 2019;11(6):353-355.
- [27]. Lek SM, Ku CW, Allen JC Jr, Malhotra R, Tan NS, Østbye TTT. Validation of serum progesterone <35nmol/L as a predictor of miscarriage among women with threatened miscarriage. *BMC Pregnancy Childbirth*. 2017;17:78.
- [28]. Abdelazim IA, Belal MM, Makhlof HH. Relation between single serum progesterone assay and viability of the first trimester pregnancy. *J Turkish-German Gynecol Assoc*. 2013;14:68-71.
- [29]. Vitzhum VJ, Bentley GR, Spielvogel H, et al. Salivary progesterone levels and rate of ovulation are significantly lower in poorer than in better off urban-dwelling Bolivian women. *Human Reprod*. 2002;17:1906-13.