

## Serum progesterone and serum $\beta$ -HCG levels in first trimester threatened abortion

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### ABSTRACT

**Background:** Spontaneous threatened abortion is a painful or painless vaginal bleeding from a closed cervix in the condition of positive embryo cardiac pulsations in the first 20 weeks of pregnancy. Most of pregnant women look for urgent obstetrician consultation in early pregnancy because of sudden abdominal pain with or without vaginal bleeding .

**Aim of the work:** aimed to declare the relation between maternal serum progesterone level and serum BHCG level in case of threatened abortion and their prediction role of the end result of that abortion.

**Patients and Methods:** : The study was carried out at El Hussien and Om El Masreen hospitals. 200 patients on the 5<sup>th</sup> - 12<sup>th</sup> week of gestation with first trimester threatened abortion were included in our study

**Results:** Regarding patient's age, GA, HB and BMI, there is showed no significant difference between the groups. In our study, BHCG and progesterone are markedly acceptable to anticipate abortion end result with a cutoff value of B-HCG and Progesterone which was (18153 mIU/ml ,23.5 ng/ml). The sensitivity, specificity for B\_HCG at 18153 mIU/ml were 100% and 98.2%, respectively, for Progesterone at 23.5 ng/ml 83% and 89% respectively.

**Conclusion:** In case of threatened abortion, using BHCG to anticipate the end result is more reliable than progesterone. Moreover, The assaying of BHCG and progesterone together does not add any benefits on sensitivity ,while specificity increased from 98.2% to 100%.

**Keywords:** Progesterone; B\_H.C.G; Threatened abortion

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### INTRODUCTION

Abortion is a fetus delivery before reaching 500 g or the age of viability. The age of viability differs between countries according to accompanying resources and supplies. The threatened abortion is detected, if pregnant woman has a vaginal bleeding in case of a closed cervix during the first 20 weeks of pregnancy.<sup>1</sup> Progesterone facilitates implantation by preparing and supporting endometrial building process and it is helpful in quieting the uterus or minimizing the bleeding that occur with implantation and provide an important environmental support for implantation. Increased Progesterone production has a great effect on uterine smooth muscle by suppressing its activity and contractility. Furthermore, its significant role in suppressing the rejection of the trophoblasts by inhibit the immunological rejection of newly implanted embryo.<sup>2</sup> B\_HCG secreted mainly by the syncytiotrophoblasts of the placenta after successful implantation and it is responsible for continuation of pregnancy. It has a main role in support and maintenance of the function of the corpus luteum by maintain progesterone release from the day after

implantation, by that time serum B\_HCG test may be positive.<sup>3</sup>

This study aimed to declare the relation between maternal serum progesterone level and serum B\_H.C.G level in patients with threatened abortion at gestational age 5-12 weeks and their relation to outcome of abortion.

### PATIENTS AND METHODS

The study was carried out at El Hussien and Om El Masreen hospitals during the period from June 2017 to November 2019. 200 patients on the 5<sup>th</sup> - 12<sup>th</sup> week of gestation with first trimester threatened abortion were included in our study. All pregnant women who were included in our study signed an informed written consent to clarify their agreement to be enrolled in our study. Pregnant women who were diagnosed with twin pregnancy, ectopic pregnancy, embryonic demise, induced abortion, prior treatment with progesterone or B\_HCG, diabetic patient , vesicular mole and bleeding tendency diseases were excluded in our study. All cases were subjected to history taking including personal history (name, age, parity and educational level), menstrual history (L.M.P, menarche , nature of menses), Obstetric

history (number of parity, abortion, living children and history of previous sections). General examination was done to exclude general causes of bleeding while pelvic and speculum examination was done to exclude other local causes of vaginal bleeding as cervical erosion and to examine cervix opened or closed. Trans\_ vaginal ultrasonographic scanning was done at the first presentation to check fetal viability, assess measurements, retroplacental hemorrhage and placenta previa. We assay progesterone and B\_HCG levels at the time of presentation by venous blood samples collection from all cases. All cases were followed up every two weeks by ultrasound to assess fetal viability and measurements till 20<sup>th</sup> week gestation and according the outcome they were divided in two groups the aborted group and the continued group.

Statistical analysis:

SPSS version 24 was our chosen version . MD and SD were used to analyze data , while frequency and percentage were used with qualitative data. We compare between the continued and aborted group by Student t test, while comparing non parametric data corrected chi square was used. Our cutoff value of serum progesterone and serum beta HCG was detected by receiver operator characteristic curve (ROC) analysis.

**RESULTS**

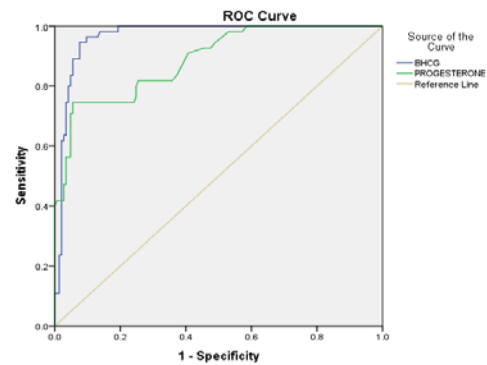
This prospective study was conducted on two hundred pregnant women on the 5- th 12th week of gestation with threatened abortion. The abortion rate is 27.5% (55 aborted cases ) till the 20th week of gestation. We divided the patients into two groups aborted group and continued group.

Variables	Aborted (n=55)	Continued (n=139)	T	P
<b>Age (years)</b> Mean ±SD	29.62 ± 3.82	29.12 ± 4.12	.781	.436
<b>GA (weeks)</b> Mean ±SD	10.28 ± 1.87	10.64 ± 1.03	1.03	.302
<b>Hb (g/dl)</b> Mean ±SD	9.89 ± 1.75	10.12 ± 1.25	1.73	.085
<b>BMI (kg/m<sup>2</sup>)</b> Mean ±SD	28.85 ± 3.66	29.3 ± 3.39	.819	.413

**Table 1:** Demographic and clinical variables distribution according to aborted or continued. This table revealed no considerable difference found regarding age, GA, hemoglobin and BMI between the aborted and continued groups.

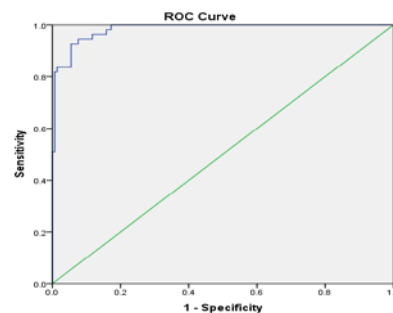
Variables	Aborted (n=55)	Continued (n=139)	T	P
<b>β-hCG (mIU/ml)</b> Median Range	7950 1287 – 216506	112253 17982 – 218801	<b>261.5</b>	<b>&lt;0.001</b>
<b>Progesterone (ng/mL)</b> Mean ±SD	25.14 ± 8.33	27.87 ± 5.12	<b>2.57</b>	<b>.012</b>

**Table 2:** B\_hCG and Progesterone distribution according to aborted or continued. Regarding median B\_hCG levels were significantly lower among aborted women compared to those who continued pregnancy. Meanwhile, mean progesterone levels were low significant between the groups.



Variable(s)	Cutoff f	AU C	S. E.	Sensitivity	Specificity	95% Confidence Interval
β-HCG	<18153	.967	.012	100%	98.2%	.943 - .990
Progesterone	<23.5	.702	.021	83%	89%	.760 - .843

**Fig 1:** ROC curve for β-HCG and Progesterone for predicting abortion. The ROC curve showed that the cut off level of β-HCG 18153 gave 100% sensitivity and specificity was 98.2% and cut off level of Progesterone 23.5 gave 83% sensitivity and specificity was 89%.



Variable	AU C	S. E.	Sig.	Sensitivity	Specificity	95% Confidence Interval
β-hCG & Progesterone	.983	.007	<0.001	100%	100%	.970 - .997

**Fig 2:** ROC curve for investigated B\_H.C.G and Progesterone together for predicting abortion. The ROC curve showed that progesterone and β-H.C.G combined together rises specificity up to 100%.

	β	S.E	Sig.	B	95% C.I. for B	
					Lower	Upper
Age (by increasing 5 yr)	.098	.047	.185	1.132	.052	1.041
BMI	.056	.056	.315	1.058	.948	1.181
β-hCG (<18153)	.969	.158	<0.001	1.951	1.732	3.012
Progesterone (<23.5)	.481	.144	.094	1.618	1.375	1.904
Constant	-13.710	2.229	<0.001	.000		

**Table (3):** Logistic Regression model for abortion. The table showed that there is significant risk for abortion in case of patients with decreasing in B\_H.C.G level.

### DISCUSSION

Miscarriage is an anxious thought faced by women who look for to be a mother. Miscarriage is pregnancy termination before fetus reach the age of viability. Up to 20% of all pregnant women, their pregnancy would ended by miscarriage and most of them occurred during the first trimester.<sup>4</sup> Early vaginal bleeding could be a predictor for miscarriage. However, there were different risk of miscarriage based on reported duration and amount of bleeding and accompanying pain symptoms.<sup>5</sup>

Progesterone and B\_HCG were consider as reliable single markers because of their potential prediction of miscarriage. Progesterone is one of ovarian steroid hormones secreted by the ovary and markedly related to the continuation and stabilization of pregnancy. This hormone plays important role for preparing uterus for embryo implantation. The other

importance of progesterone is inhibition of uterus contraction and suppression of the maternal immune system.<sup>6</sup> HCG promotes progesterone production by corpus luteal cells, promotes angiogenesis in uterine hypertrophy; aids in suppressing maternal immunity and cripples phagocytes action on implanted embryo and placental formation; increases uterine growth parallel to fetal growth; Facilitates implantation and enhances maturation of fetus organs during fetal life.<sup>7</sup> Increased progesterone levels means a well functional corpus luteum and a healthy growing placenta. Viable pregnancy have been associated with more than 55 nmol/L serum progesterone levels, meanwhile low levels less than 30 nmol/L signals to incoming pregnancy failure.<sup>8</sup>

Serum progesterone concentration < 5ng/ml reflect ongoing pregnancy failure, whilst healthy pregnancy is more related to values > 20 ng /ml.<sup>9</sup> In our study we found that β-HCG levels were significantly lower among aborted women compared to those who continued pregnancy, meanwhile progesterone levels were low significant between the groups. In agreement with Osmanağaoğlu et al.<sup>10</sup> study, who revealed that β-HCG levels were detected significantly lower in the aborted women than that of the group where no abortion was detected. Also, we revealed that B\_HCG and progesterone are significant in predicting pregnancy outcome with a cutoff value of B\_HCG and Progesterone which was (18153 mIU/ml ,23.5 ng/ml). for B\_HCG at 18153 mIU/ml were 100% and 98.2%, respectively meanwhile, for Progesterone at 23.5 ng/ml 83% and 89% respectively. and this is supported by the results of by (Maged and Mostafa<sup>11</sup>; Kim et al.<sup>12</sup>; Darwish et al.<sup>13</sup>; Duan et al.<sup>14</sup>, and Al-Sebai et al.<sup>15</sup>).

Moreover, we warranted that β-HCG is considered as an independent factor on miscarriage. Also, we have noticed a significant positive correlation between β-HCG and progesterone. This result agreed with that reported by Al-Sebai et al.<sup>15</sup> who studied the role of B\_HCG measurement in normal pregnant women and women who complained of vaginal bleeding in their first eighteen weeks of pregnancy revealed that a single serum B\_HCG measurement is greatly acceptable in the prediction of prognosis of vaginal bleeding in early 18 weeks of gestation.

In study of Darwish et al.<sup>13</sup> who investigated using progesterone in cases with recurrent abortions to predict pregnancy outcome, they revealed that no relevant relation between progesterone and pregnancy outcome with a 43% sensitivity and 50% specificity. Also, Kim et al.<sup>12</sup> in comparison between B\_HCG, progesterone and inhibin A for prediction of threatened abortion outcome found that the single measurement of serum HCG is sufficient meanwhile, the ordinary assessment of inhibin A serum and progesterone levels seems to be unjustifiable in these patients to predict pregnancy outcomes. Meanwhile, Verhaegen et al.<sup>16</sup> in their recent meta-analysis study revealed that the single marker strategy for predicting the prognosis of threatened miscarriage is not preferred rather than the combination of serum progesterone with serum B\_H.C.G which is more reliable. In the contrary, Lo and Rajuddin<sup>17</sup> use the cut-off point of progesterone

to a level of 19.5 ng/dl gave the best sensitivity and specificity. Also Abdelazim et al.<sup>18</sup> which found a 20 ng/dl as a cut-off point had 95.1% sensitivity and 98.9% specificity to predict viable and non-viable pregnancy. Duan et al.<sup>14</sup> concluded that there is significant relation between measuring B\_HCG and progesterone in predicting outcome of threatened abortion and when using together shows great improvement over a single test. Depend on our findings, the single measurement of B\_H.C.G give the best sensitivity, specificity and the best prognosis rather than progesterone. Moreover, The Combination does not add any benefit on sensitivity ,while specificity increased from 98.2% to 100%.

### CONCLUSION

We revealed that B\_HCG is considered as an independent factor on miscarriage. Also, we have noticed a significant positive correlation between B\_HCG and progesterone . In case of threatened abortion, using B\_HCG to anticipate the end result is more reliable than progesterone with a cutoff value of B\_HCG 18153 mIU/ml (with sensitivity 100% and specificity 98.2%), Progesterone 23.5 ng/ml (with sensitivity 83% and specificity 89%). Depend on our results, the single measurement of B\_HCG gave the best sensitivity, specificity and the best prognosis rather than progesterone. Moreover, The Combination of B\_HCG and progesterone does not add any benefits on sensitivity ,while specificity increased from 98.2% to 100%.

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