International Journal of Clinical Obstetrics and Gynaecology

ISSN (P): 2522-6614
ISSN (E): 2522-6622

www.gynaecologyjournal.com
2019; 3(3): 141-144
Received: 07-03-2019
Accepted: 09-04-2019

Meena Dr. Priyanka
Sr. Demonstrator, Department of Biochemistry, SMS Medical College& attached Hospital, Jaipur, Rajasthan, India

Mathur Dr. Rati
Sr. Professor, Department of Biochemistry, SMS Medical College& attached Hospital, Jaipur, Rajasthan, India

Meena Dr. Mohan Lal
Professor, Department of Obstetrics & Gynecology, SMS Medical College& attached Hospital, Jaipur, Rajasthan, India

Simlot Dr. Anita
Sr. Professor, Department of Obstetrics & Gynecology, SMS Medical College& attached Hospital, Jaipur, Rajasthan, India

Correspondence
Meena Dr. Mohan Lal
Professor, Department of Obstetrics & Gynecology, SMS Medical College& attached Hospital, Jaipur, Rajasthan, India

Association of serum hCG level with miscarriage in early pregnancy

Meena Dr. Priyanka, Mathur Dr. Rati, Meena Dr. Mohan Lal and Simlot Dr. Anita

DOI: https://doi.org/10.33545/gynae.2019.v3.i3c.273

Abstract
The aim and objective of the study was the measurement of hCG level in asymptomatic pregnant women and to determine the efficacy of hCG in preventing miscarriage in asymptomatic pregnant women. It was descriptive type longitudinal study including 178 asymptomatic pregnant women with a gestation age of 6 to 16weeks attending routine antenatal booking visit in the Department of Obstetrics and Gynaecology, S.M.S. Medical College and Attached Hospitals, Jaipur, India. Participants presented from June 2017 to November 2018. After initial clinical examination of every participants a single blood sample was taken for the measurement of serum hCG. Serum hCG measurement was performed by chemiluminescent method by using the Siemens Immulite 2000 and result were expressed as mIU/ml. Pregnancy outcome was recorded prospectively. Data were expressed in mean±SD. The median level for hCG was 87351.00 mIU/ml (range 12836.00 - 269800.00). The mean level of serum hCG in women without miscarriage (N=165) 97137.53±53745.46 mIU/ml and women with miscarriage (N=13) 48725.31±21933.20 mIU/ml (P<0.002). Further distribution of women with miscarriage (N=13) according to time to diagnosis (days) into three group [<10days (N=3) 44016.67±28495.53, 10-20days (N=8)45903.25±21413.01,>20days (N=2) 67076.50±11636.86] (P value 0.473). Therefore, in our study serum levels of hCG have been suggested as a biomarker for miscarriage and for early pregnancy viability.

Keywords: hCG, biomarker, miscarriage, asymptomatic pregnant women

Introduction
Miscarriage is defined as spontaneous pregnancy loss prior to 24 weeks of gestation [1]. Miscarriage affects 10 to 20% of all clinically recognized pregnancies which end in miscarriage [2, 3]. Prior to 6 weeks' gestation, most miscarriages result from cytogenetic abnormalities in the embryo such as chromosomal trisomy [4]. However, later during gestation, other causes of miscarriage, such as placental insufficiency, intrauterine infection, and thrombosis, become more common. Abnormal placentation (placental development) is found in two-thirds of cases of miscarriage [5, 6]. Human chorionic gonadotropin (hCG) is the first hormonal message from the placenta to the mother. It is detectable in maternal blood two days after implantation [7]. hCG is a hormone comprising an α-subunit and a β-subunit which are held together by non-covalent hydrophobic and ionic interactions. The molecular weight of hCG is approximately 36,000. It is an unusual molecule in that 25-41% of the molecular weight is derived from the sugar side-chains [8]. As miscarriages are sometimes irreversible except threatened miscarriage, prevention is probably the only way to intervene in this problem. One possible approach is to develop biochemical marker that has high accuracy to predict or diagnose the occurrence of abortion [9, 10].

Material and Method
The present study was conducted in the Department of Biochemistry, in association with the Department of Obsetetric and Gynaecology, S.M.S. Medical College and Attached Hospitals, Jaipur, India. A total of 178 asymptomatic pregnant women with a gestation of 6 to 16 weeks attending routine antenatal booking visit, between June 2017 to November 2018 recruited as study participants. After taking written informed consent, a single blood sample was taken for the measurement of serum HCG. Emergency admissions or Cases of suspected miscarriage were excluded. The protocol was approved by the institutional Ethics Committee. All pregnancies were dated according to an ultrasound scan performed in the antenatal clinic.

Participants are followed upto 20 weeks or miscarriage was diagnosed by ultrasound scanning or self-reported. Measurement of serum HCG was performed using the Siemens Immulite 2000 and results were expressed as mIU/ml.

Statistics

Sample size aimed to recruit sufficient cases to determine the association of serum HCG with miscarriage. Data were analyzed with the SPSS software version 23.0 trial version for Windows (SPSS Inc., Chicago, IL, USA). Student's t-test was used for variables with normal distribution, and the values were presented as mean ± standard deviation. Significance level for tests were determined as 95% CI (P< 0.05).

Result

Women with Miscarriage have no significant difference in gestational age between the women with miscarriage and women without miscarriage (miscarriage Mean GA: 68.69±21.65 days v/s without miscarriage mean GA71.96±18.74 days; P<0.559) (miscarriage Mean GA: 9.82±3.07weeks v/s without miscarriage mean GA: 10.27±2.67weeks; P<0.568). Overall mean maternal age was 24.90±3.70years. There was no significant difference in maternal age, weight, height, Body Mass Index (BMI), Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) among the group. hCG comparative assay performance presented in table 1 hCG was lower in women with miscarriage (48725.31± 21933.20) when compared with unaffected pregnancy (97137.527±53745.46) (P<0.002). Table 2 and Figure 1 showed that ultrasonography confirmed fetal viability in 13 pregnancies who later miscarried. We investigated in more detail their length of time after hcg measurements, when patients were diagnosed with miscarriage. Lowest levels were observed in patients who miscarried within 10 days after the blood measurement of hCG (hCG in mIU/ml: [<10days (N=3) 44016.67±28495.53, 10-20days (N=8) 45903.25±21413.01, >20days (N=2) 67076.50±11636.86]. HCG levels were higher in women who miscarried after 20 days but significantly lower than the group that did not miscarry (mean± SD: 97137.53±53745.46). A non-significant poor positive correlation existed between the hCG level (miu/ml) and time to diagnosis of miscarriage (days) (r= 0.156; p value 0.314) by using Pearson's correlation coefficient.

Table 1: Comparative Analysis of the HCG among the Groups

Group	Women with Miscarriage (N=13)	Women without miscarriage(N=165)	P Value
	Mean±SD	Mean±SD	
Hcg (mIU/ml)	48725.31±21933.20	97137.53±53745.46	0.002

Table 1 shows hCG concentration in women with miscarriage and women without miscarriage (48725.31±21933.20 v/s 97137.53±53745.46). In women with miscarriage hCG concentration was found significantly lower (p value 0.002).

Table 2: Serum hCG level with time to diagnosis of miscarriage

	Women with No Miscarriage (N=165)	Women with Miscarriage in <10 Days (N=3)	Women with Miscarriage in 10 to 20 Days (N=8)	Women with Miscarriage in >20 Days (N=2)
	Mean±SD	Mean±SD	Mean±SD	Mean±SD
HCG (mIU/ml)	97137.527±53745.46	44016.67±28495.53	45903.25±21413.01	67076.50±11636.86

Mean serum hCG in Women without miscarriage (N=165) was 97137.527higher as compared to Women with Miscarriage in ≥20 Days 67076.50followed by Women with Miscarriage in 10 to 20 Days 45903.25 than Women with Miscarriage in <10 Days i.e level was significantly lower in early Miscarriage.

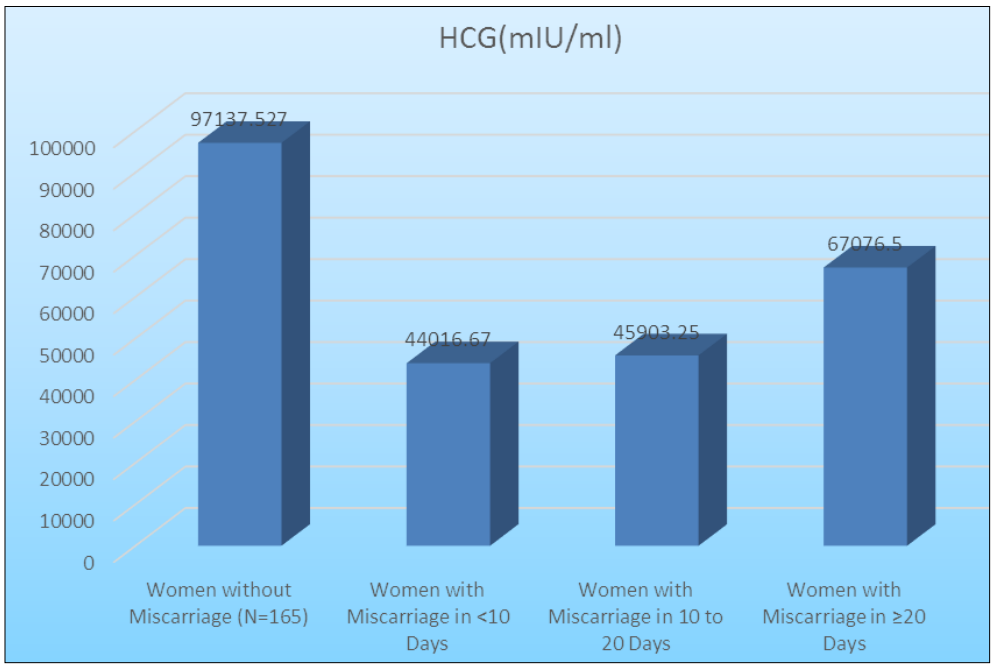

Fig 1: Association of serum hCG (mIU/ml) with time to diagnosis of miscarriage (days)

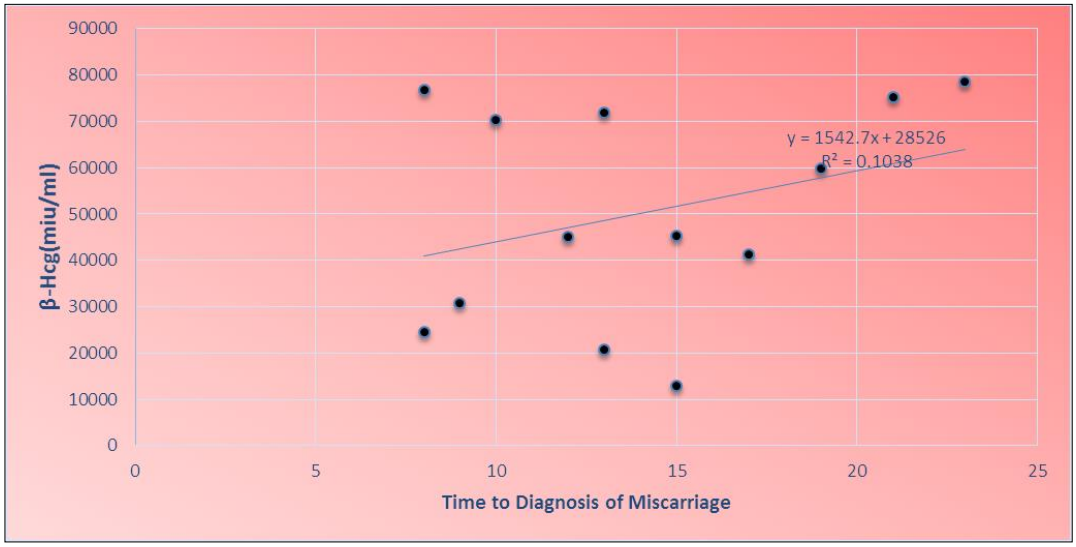

Fig 2: Correlation of HCG (mIU/ml) with time to diagnosis of miscarriage (days)

Discussion

Women affected by miscarriage not only suffer devastating emotional consequences [11] but are also at increased risk of developing serious antenatal morbidities such as preeclampsia and preterm delivery during subsequent pregnancies [12-14]. Therefore it is important to developed simple and safe test to identify pregnancies at high risk of miscarriage, because this could improve the diagnostic accuracy and potentially improve obstetric outcomes. The present study was undertaken to find out the association between hCG levels with miscarriage in asymptomatic pregnant women. A rising level of serum hCG measured during multiple hospital visits is currently used to assess fetal viability during early pregnancy [15]. However, this approach is valid only if performed before the eighth gestational week when serum hCG levels are still rising [16]. Furthermore, serum hCG is in general not used as a biomarker for pregnancy viability beyond the first trimester of pregnancy [17]. Our data indicate that serum hCG measurement at a gestation of 6 week or longer help in discrimination between viable and nonviable pregnancy. C. N. Jayasena, *et al* (2014) [10] found that hCG was lower only in women who experienced miscarriage when compared with unaffected pregnancy. If blood measurement was within 3 weeks prior to the diagnosis of miscarriage (hCG in international units per liter × 1000: 85.1 ± 39.3, no miscarriage; 17.2 ± 21.6, miscarriage < 7 d, P <.05, vs no miscarriage; 51.8 ± 55.6, miscarriage 7–21 d,P <.05, vs no miscarriage; 63.8 ± 37.0, miscarriage > 21 d, P = NS, vs no miscarriage. We also found that non-significant poor positive correlation existed between the hCG level (miu/ml) and time to diagnosis of miscarriage (days) (r= 0.156; p value 0.314)). In our study serum hCG levels significantly lower in women with miscarriage as compared to unaffected pregnancy (P<0.002).

Conclusion

In this study we concluded that low serum hCG level may be associated with risk of miscarriage in early asymptomatic pregnant women. However future studies are needed to validate these findings. Furthermore, it will be useful potential biomarkers of early pregnancy loss.

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