



Prediction of Placenta Previa from Serial Reading of Serum Human Chorionic Gonadotropin Late in the First Half of Pregnancy

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Abstract

Background Abnormally sited placenta is considered a major life-threatening condition for pregnant woman, and many debate about the way of early diagnosis and management to decrease the mortality and morbidity.

Aim of Study To evaluate the role of beta-human chorionic gonadotrophin (B-HCG) level in the first half of pregnancy as a marker for prediction of placenta previa.

Study Design This is a prospective study done in Al-Yarmouk Teaching Hospital from first of January 2020 till first of January 2021.

Material and Methods A total of 57 patients have been recruited. For all participated women in this study were sampled between 14 and 18 weeks of gestational age for serum human chorionic gonadotropins measured in international units. Patients who developed placenta previa were diagnosed on the basis of development of vaginal bleeding either late in the second trimester or early in the second trimester. After developing vaginal bleeding, all patients were sent for routine ultrasound scan to confirm the presence of placenta previa.

Result After recruiting a total of 57 women among which 14 patients were found to have placenta previa, ANOVA test shows a statistically significant difference between women with normal placenta and women with placenta previa P value < 0.001 . Receiver operator characteristics curve was constructed to evaluate the optimum cutoff value for serum HCG between normal women and women with placenta previa sampled at 14–18 weeks of gestation. The optimum cutoff value is mean serum HCG $> 105,380$ IU in 14 weeks of gestation, and the sensitivity and specificity were calculated as 100% and 72.2%, respectively.

Conclusion B-HCG level in first half of pregnancy can be used as a predictor marker for placenta previa.

Keywords Placenta previa · Human chorionic gonadotropin · Antepartum bleeding

Introduction

Placenta previa is one of the serious causes of maternal mortality and maternal health complications due to its association with both antepartum and postpartum hemorrhage which may be a massive one. Placenta previa is defined as placenta developed in the lower uterine segment on or

near the internal os of the cervix, and according to that, it is classified into major placenta previa when the placenta covering the internal os totally or part of it and minor when it implanted in the lower segment away from the os. The incidence of placenta previa at term is about 0.5% [1, 2].

It is unknown why some placentas implant in the lower uterine segment and not in the usual upper uterine segment. Some explanation about the pathogenesis appears that any uterine scarring may play an important role in this issue. More than 90% of these placentae which were identified early in pregnancy will move away from the cervix as the pregnancy proceeds and this called placental migration. The idea that the placenta move from lower to upper segment of uterus not accepted by many authorities but the theory of trophotropism which mean that the placenta grows toward a better vascularized fundus its seem more accepted. The

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apparent movement of the placenta may also be due to the development of the lower uterine segment [3].

The traditional simple method for the diagnosis of placenta previa in addition to the clinical presentation of painless vaginal bleeding was the ultrasound (UIs) which can be either transvaginal, transabdominal or translabial. Transvaginal UIs is much more accurate than transabdominal UIs, and it is safe. Sixty percent of women who undergo transabdominal sonography (TAS) may have another classification of placental site when TVS is done for them. Posterior placenta is poorly visualized by TVS. Many factors play a role in the accuracy of UIs like the presenting part that may interfere with the visualization of the lower segment, and whether bladder is filled or not, obesity also interferes with accuracy. Magnetic resonance imaging (MRI) can diagnose placental site accurately and better than TAS. But with no other benefit over TVS for placental site detection, MRI is not readily available in most units [4].

Human chorionic gonadotropin (HCG) is a glycoprotein that consists of 36,000 Dalton molecular weight composed of 2 noncovalently bound subunits. The alpha subunit (92-amino acids) which is similar to the structure of luteinizing hormone, follicle-stimulating hormone and thyrotropin. New research revealed an important role of HCG in the implantation process. Makrigiannakis et al. showed that HCG is important molecules during implantation process. HCG metabolically affects the decidua and leads to endometrial receptivity [5].

Patients and Methods

Setting

The study was a prospective study conducted in Al-Yarmouk Teaching Hospital—Department of Gynecology and Obstetrics. Between January 2020 and late 2021, a total of 57 patients have been recruited. For all the patients' serum, HCG serum has been measured between 14 and 18 weeks. This study was approved by the Institutional Review Board of the local hospital (Al-Yarmouk Teaching Hospital), in accordance with the Declaration of Helsinki 2013; in addition, participated women received appropriate management by the researchers.

Methods

The inclusion criteria included women who were chosen between 20 and 30 years age. All the women who have participated in the study were pregnant with singleton pregnancy that remained free of any complication till the end of pregnancy apart from placenta previa. For all participated

women in this study were sampled between 14 and 18 weeks of gestational age for serum human chorionic gonadotropins measured in international units. Patients who developed placenta previa were diagnosed on the basis of development of vaginal bleeding either late in the second trimester or early in the second trimester. After developing vaginal bleeding, all patients were sent for routine ultrasound scan to confirm the presence of placenta previa. All women who have developed other high-risk pregnancy complications during routine follow-up like preeclampsia and diabetes were excluded from the study. At the end of this study, a total of 57 women were recruited with complete data, and out of them, 14 patients were pregnant with placenta previa complication. It should be mentioned that patients with placenta previa were screened individually apart from the rest patients in order to verify the primary assumption of this study.

Statistical analysis

Continuous data were expressed as mean and standard deviation. The normality of data distribution was checked by Shapiro–Wilk test. Required sample size was checked for type I error equivalent to 95% and type II error for 80%. Analysis of variance test was used to show the high statistical difference in the mean serum HCG between women with placenta previa and control women sampled at 14–18 weeks of gestation. Receiver operator characteristic curve was used to calculate the cutoff serum level of mean HCG between normal women and women with placenta previa. P values less than 0.05 were considered as significant.

Results

After recruiting a total of 57 women, among which 14 patients were found to have placenta previa, the basic characteristics of their demographic criteria are given in Table 1.

In Table 2, ANOVA test was done for serum HCG difference between 43 pregnant women with normal pregnancy and 14 women with placenta previa. As it is shown in Table 2, the *F* ratio is 96.155 with *P* value < 0.001

Table 1 Basic characteristics of the whole study group with regard to the demographic criteria

Characteristics	Mean ± standard deviation
Age	32.5439 ± 5.6032
Gravida	4.1404 ± 1.8750
Parity	2.8596 ± 1.6949
Serum HCG 14–18 weeks	89,951 ± 74,038.6035

Table 2 ANOVA test showing a statistically significant difference between women with normal placenta and women with placenta previa

ANOVA			
Source of variation	Sum of squares	DF	Mean square
Between groups (influence factor)	195,277,934,241.22	1	195,277,934,241.22
Within groups (other fluctuations)	111,698,094,668.77	55	2,030,874,448.52
Total	306,976,028,910.00	56	

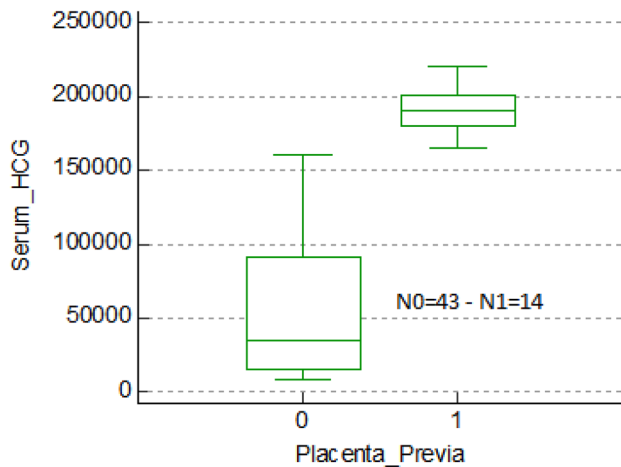


Fig. 1 Box-whisker plot showing the relation between the mean of serum HCG between normal and that of women with placenta previa

<i>F</i> ratio	96.155
Significance level	$P < 0.001$

Figure 1 shows a highly statistically significant difference in the mean serum HCG between normal women and women with placenta previa, and the mean level was below 100000 IU in normal placenta and 200000 IU in placenta previa.

Finally receiver operator characteristics curve was constructed to evaluate the optimum cutoff value for serum HCG between normal women and women with placenta previa sampled at 14–18 weeks of gestation. The optimum cutoff value is mean serum HCG > 105,380 iu in 14 weeks of gestation. The sensitivity and specificity were calculated as 100% and 72.2%, respectively, as shown in Fig. 2.

Discussion

Placental trophoblastic tissue is the main source of HCG in normal pregnancy and is responsible for the persistence of corpus luteum of pregnancy which supports the pregnancy through its hormonal secretion in early first trimester. When

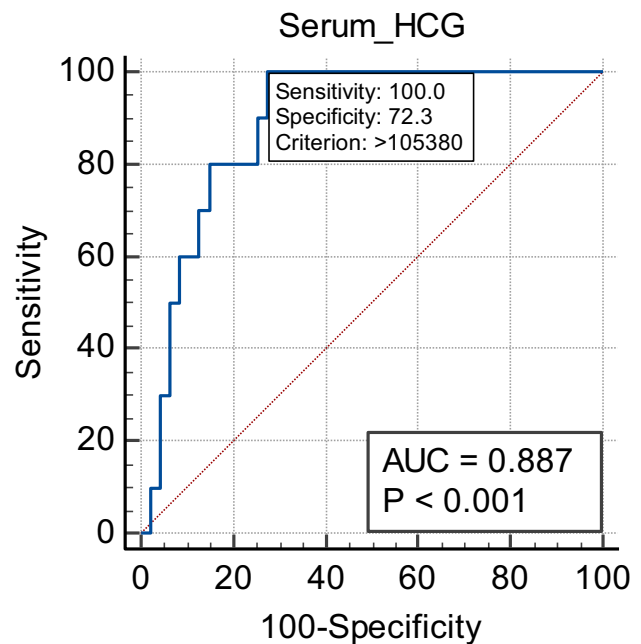


Fig. 2 Receiver operating characteristic curve (ROC) showing the cutoff value of HCG level between normal women and women with placenta previa

the level of HCG was lower than normal, this may predict a complication in the pregnancy: miscarriage, extrauterine pregnancy and fetal demise [6]. HCG level may differ markedly among individuals and from one to next pregnancy in the same person. However, HCG levels had an ideal range within a normal pregnancy. Many studies try to correlate between B-HCG and abnormal placentation, especially placenta accreta; Brett D Einerson et al. evaluated the role of hyperglycosylated human chorionic gonadotropin (HCG-H) and morbid adherent placenta in the last two trimesters of pregnancy. After studying 60 patients, half as a case of accreta and 30 as control, it was concluded that the levels of hyperglycosylated HCG were lesser in patients with accreta than in controls [7].

Maad Mahdi Shalal et al study predict accreta by using hyperglycosylated human chorionic gonadotropin in this study 90 case tird of them as control and two-third as studying group with placenta accreta diagnosis all patient was in

third trimester and it is revealed that the level of hyperglycosylated HCG was higher in case of placenta accreta than in placenta previa and normally situated placenta [8].

So both of the above studies revealed that there was a relationship between the level of HCG and placental spectrum syndrome and relay the result toward the level of invasion of trophoblastic tissue. In our recent study, we search for the relation between placenta previa and HCG, the site the size of placenta, vascularity at the level of implantation may play role in the hormonal changes and vice versa according to the result.

Boulis et al. studied the relationship between B-HCG and other analyte and placenta previa and compared it between two groups, placenta previa group and control, and they concluded that there were no differences between groups with respect to first-trimester free β -HCG and second-trimester free β -HCG [9].

The result of the recent study showed that there was a highly statistically significant difference in the mean serum HCG between normal women and women with placenta previa P value < 0.001 and the optimum cutoff value is mean serum HCG $> 105,380$ IU in 14 weeks of gestation. The sensitivity and specificity were calculated as 100% and 72.2%, respectively.

The action of trophoblast cells is affected by the extracellular matrix, endometrial materials, trophoblast products, maternal hormones and utero-placental perfusion, which controls the accessibility of oxygen and nutrients. All these and many other factors detect the trophoblast cell differentiation pathways, endocrine function and secretion of hormones into the maternal blood vessels which may be the cause this significant difference [10].

The exact cause of placenta praevia is not clear till now, but it is hypothesized to be related to abnormal vascularization of the endometrium caused by scarring or fibrosis from previous trauma, surgery or infection.

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Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval This study was approved by the Institutional Review Board of the local hospital (Al-Yarmouk Teaching Hospital), in accordance with the Declaration of Helsinki 2013; in addition, participated women received appropriate management by the researchers.

Informed Consent Written informed consent was obtained from each woman before participating in the study.

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