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# Study the association of human chorionic gonadotrophin in prediction of preeclampsia and its severity

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## Abstract

The objective of this study is to evaluate the potential clinical use of maternal serum free human chorionic gonadotrophine (β-hCG) in prediction of preeclampsia and its severity. Two hundred and ten blood samples were collected from patients. Twenty seven patients were developed PE. These patients were followed for up to five months (first reading at 16-20 week, second reading at 21-28 week and third reading at 29-40 week). Patients suffered from any other disease were not included in the current study. The control group consisted of one hundred and eighty subjects. They were pregnant women without preeclampsia and other complications. These patients also were followed for up to five months (first reading at 16-20 week, second reading at 21-28 week and third reading at 29-40 week). Three patients were escaped. Compared with the control, The elevation of serum β-hCG was statistically significant, P value (<0.001) in women who were developed preeclampsia (mild and sever preeclampsia) later on throughout their pregnancy at 16-20, 21-28, and at 29-40 weeks of gestation, and there is further significant increment in the level of serum β-hCG in women who develop sever preeclampsia when compared with women who develop mild preeclampsia throughout their pregnancy, p value (<0.001). We are concluded that serum β-hCG is significantly associated with preeclampsia and they can be used as a markers for prediction of preeclampsia early in pregnancy and for evaluation of its severity.

**Keywords**: Preeclampsia; β-hCG; Pregnancy

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## Introduction

Preeclampsia is a common obstetric problem, diagnosed in women how develops hypertension (blood pressure ≥140/90 mmHg) and proteinuria (≥300 mg/24 h urine collection) after the 20th week of pregnancy in a previously normotensive women [1-2].

It remains a leading cause of morbidity and mortality for both mothers and fetuses in as it affect 5-8% of pregnancies, the development of mild hypertension or preeclampsia at or near term is associated with minimal maternal and neonatal morbidities. In contrast, the onset of severe gestational hypertension and/or severe preeclampsia before 35 weeks' gestation is associated with significant maternal and perinatal complications [3], and was described as a preeclampsia pregnancyrelated disease as early as 3000 years ago by the ancient Egyptians [4], it has been considered a " disease of theories

"[5] as the main etiology of preeclampsia is still unknown, it is now believed to result from a combination of genetic, immunologic, and environmental factors that may leads to failure of normal trophoblastic invasion and remodeling of uterine spiral arteries [6].

Since trophoblast abnormalities believed to play a central role in the pathophysiological processes that lead to preeclampsia and may precede its clinical manifestations [7], Several studies have measured different markers placental biomarker that correlate with pathophysiological changes seen with defective early trophoblastic invasion and thereby to evaluate their risk [4], elevated level of human chorionic gonadotrophin (hCG), which a hormone secreted by the placental tissues/trophoblast cells to maintain the decidual spiral arteries and vascular supply of the pregnancy, has been associated with development of preeclampsia [8].

For the high prevalence of pre-eclampsia and its associated mortality and morbidities, early identification of women at high risk for developing this disorder is of great importance for both patients and providers and possibly prompt physicians to employ increased clinical surveillance, in our study we try to assess the level of human chorionic

gonadotrophin (hCG), from women who develops preeclampsia compared to normal pregnant controls.

**Method**

*Study objectives*

The objective of this study is to evaluate the potential clinical use of maternal serum free human chorionic gonadotrophine (β-hCG) in prediction of preeclampsia and its severity.

*Overall study design*

A randomized control prospective study using toss a coin as randomization technique was carried out in AL-Zahra'a Teaching Hospital in AL-Najaf City, from first of January 2014 to the first of January 2015. Pregnant women were selected at that time for study participation after their written consent.

*Participant, recruitment and randomization*

Two hundred and twenty three pregnant women were participated in this study , thirteen women out of the study from the this group, eight women had abortion , two women didn't continue with our study because of social causes and three women had preterm labour and they were non preeclamptic, so we had a total of two hundred and ten women in this study ,their age was from 21 to 34 years old, followed them up through their pregnancy 16-20 weeks of gestation in the same women at 29-40 weeks of gestation in the third visit, with each visit, informative history was taken from the participants, examination (general and obstetric examination ) was done, BMI calculated for each patient [9], then measuring of blood pressure and ultrasound was done. Laboratory investigations included; blood group and Rh, complete blood picture, general urine examination, blood urea and serum creatinine, serum ALT and AST, random blood sugar and serum β-hCG were done with each visit.

Out of these two hundred and ten pregnant women twenty seven had preeclampsia after 20 weeks of gestation. Eighteen were classified as mild PE and nine were classified as severe PE all of them started as mild PE after 20 wks then developed severe PE, patient were considered pre-eclamptic when systolic & diastolic blood pressure were ≥140 /90 mmHg two consecutive reading 4-6 hours apart (The first & fifth korotekoff sounds were used in the determination of systolic & diastolic blood pressure), BP was measured in one arm while women sit and after a 5-minute rest. Both on two occasions at least 4-6 hours apart,

the first visit, the same women at 21-28 and ≥1+ albumin(30 mg/dl) on dipstick weeks of gestation in the second visit,

by qualitative estimation a random mid-stream clean-catch urine sample (this is usually correlates with a urinalysis report of 300mg or more of protein in a timed 24-hour urine collection. In our study, we use the dipstick for urine albumin.

Severe preeclampsia was considered having blood pressure≥160/110 mmHg and proteinuria at least 3+on dip stick (this is usually correlates with a urinalysis report of 5 g of protein in a timed 24-hour urine collection, the remaining one hundred and eighty three were non preeclamptic normal pregnancy.

*Inclusion criteria*

Pregnant ladies with singleton pregnancy, and their gestational ages ranging from 16-20 weeks of gestation to be followed up later on at 21-28 wks and 29-40 wks. *The exclusion criteria include*

Pregnant women with multiple pregnancies, all medical diseases, and obstetrical problems were excluded from the study.

None of the participant were smoker, no maternal deaths had occurred and all participating women provided written informed consent prior to enrolment and the collection of blood samples after taking approval from ethical committee.

*Serum samples*

Five ml of peripheral venous blood (from the ante cubital vein or from the dorsum of the hand ) is drawn using a standard venipuncture techniques from each woman in the study 3 times at 1620 weeks in the first time, 21-28weeks in the second time, 29-40weeks of gestation in the third time, the blood sample used for investigations like blood group and Rh, complete blood picture, blood urea and serum creatinine, serum ALT and AST, random blood sugar and β-hCG.

VIDAS hCG (hCG): is an automated quantitative test for use on the VIDAS family instrument, for the quantitative measurement of human Chorionic Gonadotropin in human serum or plasma using Enzyme Linked Fluorescent Assay( ELFA) technique.

*Reference group*

A two hundred and twenty three pregnant women were selected for study participation after their written consent, all of them received a detailed explanation of their treatment, follow up by frequent examination, they were advised to contact by telephone in case they need any further explanation, close follow up for them done throughout their pregnancy starting from first visit till delivery and women how diagnosed as having preeclampsia require close evaluation of maternal and fetal conditions for the duration of pregnancy, and those with severe disease were managed in-hospital. The methods of assessment of our result done by the researchers each visit and the study was performed in accordance to Helsinki declaration and ethical approval was obtained from Kufa University in Al- Najaf city.

*Data handling*

Statistical analysis was done by using SPSS version 20 in which we use mean, standard deviation, and one way ANOVA (analysis of variance) for comparison between different measurement (numerical) data. We set P value <0.05 as significant.

**Results**

We compare these data between normal women (non preeclamptic) and women who develops preeclampsia later on, which is further divided into mild and sever preeclampsia.

| demographic Characteristics | Normal(N) 183 women | Mild PE(M) 18 women | Sever PE(S) 9 women | P-value | | |
|---|---|---|---|---|---|---|
| | mean±SD | mean±SD | mean±SD | N vs M | N vs S | M vs S |
| Age/Years | 27.24±6.157 | 29.16±5.249 | 28.88±5.819 | 0.202 | 0.429 | 0.911 |
| Parity | 2.24±1.2 | 2.16±2.1 | 2.22±2.2 | 0.839 | 0.971 | 0.926 |

**Table 1.**

The demographic characteristics of study group women. There was no statistically significant difference in the age and parity among the study group women.

| Parameters | Normal(N) | Mild PE(M) | Sever PE(S) | P-value | | |
|---|---|---|---|---|---|---|
| | mean±SD | mean±SD | mean±SD | N vs M | N vs S | M S |
| Systolic BP mmHg | 116.9±7.18 | 116.05±7.41 | 117.2±4.73 | 0.627 | 0.899 | 0. |
| Diastolic BP mmHg | 70.25±4.80 | 75.11±5.84 | 75.55±5.89 | <0.001 | 0.002 | 0. |
| Proteinuria | 0 | 0 | 0 | 1 | 1 | 1 |
| BMI Kg/M^2 | 25.27±3.75 | 24.38±2.76 | 24.00±2.39 | 0.324 | 0.305 | 0. |
| B.Urea mg/dl | 28.94±5.76 | 29.77±3.28 | 35.44±5.24 | 0.547 | 0.001 | 0. |
| S.creatinine mg/dl | 0.52±0.137 | 0.60±0.141 | 0.61±0.078 | 0.027 | 0.065 | 0. |
| RBS g/dl | 90.71±8.31 | 91.27±7.25 | 89.67±7.79 | 0.782 | 0.709 | 0. |
| S.GOT U/L | 18.91±10.54 | 19.23±9.77 | 26.16±10.34 | 0.900 | 0.044 | 0. |
| S.GPT U/L | 18.57±6.68 | 22.57±8.30 | 28.31±8.33 | 0.020 | <0.001 | 0. |
| Hb g/dl | 11.09±1.30 | 11.35±0.71 | 12.25±1.54 | 0.414 | 0.008 | 0. |
| Platelet 10^3/UL | 205.02±56.60 | 201.11±35.63 | 197.77±61.48 | 0.775 | 0.702 | |

**Table 2.**

Comparison between different parameters during the period of 16-20 week gestation at the first visit.

There was no statistically significant difference in the Systolic BP, Platelets count and, there was statistically significant difference in the mean diastolic BP between normal versus mild PE and normal versus sever PE. There was statistically significant difference in blood urea between normal versus sever PE and mild versus sever PE and in serum creatinine between normal versus mild PE. There was statistically significant difference in serum S.GOT between normal versus sever PE. While there was statistically significant difference in serum S.GPT between normal versus mild PE, normal versus sever PE and mild versus sever PE. Regarding Hb level there was statistically significant difference in Hb level between normal versus sever PE.

| | | | | |
|---|---|---|---|---|
| **B-HCG** | **11170±1475** | **32060±1775** | **49850±2433** | **<0.001** |

**Table 3.**

Level of B-HCG at the first visit.

Serum β-HCG in nonpreeclamptic women, mildPE, severe PE at 16-20wks gestation(first visit) was, 11170±1475, 32060±1775, 49850±2433 respectively, there was statistically significant difference among normal versus mild PE, normal versus sever PE and mild versus sever PE, this serum level of β-HCG in those women before developing PE but after 20 wks they develop PE.

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| parameters | Normal(N) | Mild PE(M) | Sever PE(S) | P-value | | |
|---|---|---|---|---|---|---|
| | Mean±SD | Mean±SD | Mean±SD | N vs M | Nvs S | M vs S |
| Systolic BP mmHg | 112.76±7.409 | 148.61±3.957 | 150.22±4.79 | <0.001 | <0.001 | 0.579 |
| Diastolic BP mmHg | 69.51±7.74 | 96.55±4.03 | 104.77±4.52 | <0.001 | <0.001 | 0.007 |
| Proteinurea | 0 | 1 | 1 | <0.001 | <0.001 | 1 |
| BMI Kg/M^2 | 28.2±2.92 | 28.7±2.67 | 28.5±2.83 | 0.493 | 0.743 | 0.888 |
| B.urea mg/dl | 30.3±3.62 | 27.5±2.97 | 34.0±6.00 | 0.002 | 0.004 | <0.001 |
| S.creatinine mg/dl | 0.54±0.119 | 0.54±0.119 | 0.78±0.078 | 0.003 | <0.001 | 0.002 |
| RBS g/dl | 88.62±7.26 | 90.11±7.48 | 91.44±6.72 | 0.410 | 0.257 | 0.653 |
| S.GOT U/L | 19.9±10.11 | 20.4±9.50 | 27.2±10.32 | 0.833 | 0.036 | 0.103 |
| S.GPT U/L | 18.9±6.12 | 22.9±8.13 | 28.3±7.76 | 0.014 | <0.001 | 0.037 |
| Hb g/dl | 10.9±1.27 | 11.3±0.79 | 11.9±1.24 | 0.205 | 0.031 | 0.298 |
| Platelets 10^3/UL | 218.0±62.16 | 202.3±39.80 | 200.6±60.28 | 0.298 | 0.403 | 0.945 |

**Table 4.**

Comparison between different parameters during the period of 21-28 week of pregnancy at the second visit.

There was no statistically significant difference in the BMI and the Platelets counts. But here was statically significant difference in the mean systolic BP between normal versus mild PE, normal PE versus severe PE and mean diastolic BP between normal versus mild PE, normal versus severe and mild versus severe PE. There was statically significant difference if we compare Blood urea and serum creatinine between normal versus mild PE, normal versus severe PE mild versus severe PE.

There was statically significant difference if we compare S.GOT between normal versus severe PE and mild versus severe PE. In addition there was statically significant difference if we compare S.GPT between normal versus mild PE, normal versus severe PE and mild versus severe PE. Lastly regarding Hb level there was statically significant difference between normal versus severe PE.

| parameters | Normal(N) | Mild PE(M) | Sever PE(S) | P-value | | |
|---|---|---|---|---|---|---|
| | Mean±SD | Mean±SD | Mean±SD | N vs M | Nvs S | M vs S |
| B-HCG mIU/L | 10820±1570 | 35930±1680 | 55170±2970 | <0.001 | <0.001 | <0.001 |

**Table 5.**

Level of B-HCG at the second visit

Serum B-HCG at 21-28-wks gestation (second visit) in non-preeclamptic women, mild PE, severe PE was10820 ±1570, 35930±1680, 55170±2970 respectively, there was statistically significant difference if we compare the serum B-HCG between normal versus mild PE and normal versus severe PE.

| Parameters | Normal(N) | Mild PE(M) | Sever PE(S) | P-value | | |
|---|---|---|---|---|---|---|
| | Mean±SD | Mean±SD | Mean±SD | N vs M | Nvs S | M vs S |
| Systolic BP mmHg | 114.4±6.22 | 151.5±3.43 | 174.8±10.30 | <0.001 | <0.001 | <0.001 |
| Diastolic BP mmHg | 72.8±6.90 | 99.7±3.39 | 118.7±5.33 | <0.001 | <0.001 | <0.001 |
| Proteinurea | 0 | 2±1 | 3±1 | <0.001 | <0.001 | <0.001 |
| BMI Kg/M^2 | 31.26±2.54 | 32.33±2.37 | 33.11±3.01 | 0.093 | 0.036 | 0.456 |
| B.urea mg/dl | 29.78±3.919 | 28.33±2.910 | 33.55±5.294 | 0.135 | 0.005 | 0.001 |
| S.creatinine mg/dl | 0.57±0.108 | 0.59±0.125 | 0.83±0.086 | 0.589 | <0.001 | <0.001 |
| RBS g/dl | 88.50±6.43 | 90.94±7.66 | 89.77±3.92 | 0.129 | 0.566 | 0.659 |
| S.GOT U/L | 18.53±9.01 | 19.40±7.68 | 82.60±157.34 | 0.913 | <0.001 | <0.001 |
| S.GPT U/L | 20.18±6.76 | 23.83±8.64 | 94.26±190.16 | 0.698 | <0.001 | <0.001 |
| Hb g/dl | 11.1±1.20 | 11.9±0.74 | 12.3±1.28 | 0.003 | 0.002 | 0.431 |
| Platelet 10^3/UL | 218.33±62.10 | 195.72±20.85 | 174.77±38.51 | 0.123 | 0.032 | 0.386 |

**Table 6.**

Comparison between different parameters during the period of 29-40 week of pregnancy at third visit.

There was statically significant difference if we compare mean systolic BP, Diastolic BP, Proteinurea, BMI,

B.urea, S.creatinine, RBS, S.GOT, S.GPT, Hb, and Platelet between normal versus mild PE, normal versus severe PE and mild versus severe PE.

| parameters | Normal(N) | Mild PE(M) | Sever PE(S) | P-value | | |
|---|---|---|---|---|---|---|
| | Mean±SD | Mean±SD | Mean±SD | N vs M | Nvs S | M vs S |
| BHCGmIU/L | 10200±1190 | 52800±2530 | 67400±3620 | <0.001 | <0.001 | <0.001 |

**Table 7.**

Level of B-HCG at the third visit.

Serum B-HCG at 29-40wks gestation (third visit) in non-preeclamptic women, mild PE, severe PE was 10200±1190, 52800±2530, 67400±3620 respectively, there was statically significant difference if we compare the serum BHCG between normal versus mild PE and normal versus severe PE.

| Variable | 16-20 weeks(P1) | 21-28 weeks(P2) | 29-40 weeks(P3) | P- value | | |
|---|---|---|---|---|---|---|
| | Mean±SD | Mean±SD | Mean±SD | P1 vs P2 | P1 vs P3 | P2 vs P3 |
| B-HCG In mild PE | 32060±1770 | 35930±1680 | 52840±2530 | <0.001 | <0.001 | <0.001 |
| B-HCG In sever PE | 49850±2433 | 55170±2970 | 67480±3620 | <0.001 | <0.001 | <0.001 |

**Table 8.**

Level of β-HCG among those with mild and sever PE with gestational age.

There was statically significant increase in the level of serum β-HCG in women with mild and sever PE with increase in the gestational age.

## Discussion

Screening pregnant women with an effective diagnostic marker for PE could reduce unnecessary suffering and major health care costs, our hope is that by learning more about the nature of early and late preeclampsia, we may be able to make better predictive models that address the different natures of these disease states and identify high-risk women for

prospective clinical trials, while concurrently working for better preventive strategies [10].

In the present study the serum β- hCG level was found to be significantly increased in preeclampsia group than in the control group (Table no. 3, 5, and 7) with further increase in the β- hCG level in sever PE when compared to mild one, and this increase was prior to the clinical diagnosis of preeclampsia at the gestational age of 16-20 wks (Table no. 3), This early increase in β-hCG at this early gestational age in patients who will have preeclampsia , may make β-hCG play one of the important roles in the pathogenesis of preeclampsia, and may make it a successful cheap predictor for preeclampsia. The strict relationship between severe preeclampsia and elevated serum β-hCG levels indicating that there may be an abnormal placental secretary function in patients with severe preeclampsia lead to this higher level of

PE, and this findings makes β-hCG a useful predictor for severity of preeclampsia. In addition to that the increment in the β- hCG level in mild and sever PE were parallel to the increment of gestational age as shown in tables 8. This results of continuing elevation of serum β-hCG with continuing of pregnancy with PE may be associated with the progression of the disease and its severity.

The present finding is agreed with study done by Choudhury,et al .who took 50 preeclamptic and 50 control women at 26-36 wks gestation and reported that the serum level of maternal-hCG was markedly raised in preeclampsia in comparison to controlled and parallel with the severity of preeclampsia [11]. And it also consistent with finding of Olsen RN, et al. who conducted a retrospective study of 7767 subjects undergoing second-trimester aneuploidy screening ,value of β-hCG of 459 cases of preeclampsia were elevated >2MoM [12]. Other study done by Davidson E J ,et al .,who ,conducted retrospectives case-control study of 15-20 week serum samples of 39 women who subsequently developed pre-eclampsia and 155 women who remain normotensive throughout pregnancy, demonstrated that

hCG levels were significantly elevated in women who later developed pre-eclampsia (24% increase compared with controls), and demonstrated that analyses of second trimester serum hCG may yet prove to be helpful predictor of women at risk of pre-eclampsia [13]. Other study done by Remzi G, et al., on thirteen pregnant women with severe preeclampsia were matched with twenty-one normotensive pregnant women with singleton pregnancies in the third trimester ,serum β-hCG levels were found to be significantly higher in severe preeclampsia ,compared with controls [14].

Kharfi A, et al measured serum levels of β-hCG in twenty preeclamptic and twenty normotensive term pregnant women (control), using an enzymatic immunoassay, and found that higher levels of serum β-hCG were observed in patients with preeclampsia in comparison to control [15].

Lorzadeh N, et al., in a cross-sectional study and 139 women with singleton pregnancies in the third trimester were studied, 71 pregnancies were uncomplicated, 68 pregnancies were complicated by preeclampsia ,human chorionic gonadotropin was measured in maternal peripheral blood, maternal βhCG serum levels were significantly higher in preeclamptic than normotensive mothers (P<0.001) [16]. On the other hand, a study was done by

Pouta AM, et al., reported that serum β- hCG is not helpful in predicting preeclampsia, which is a populationbased cohort study included 637 nulliparous women, measurement of βhCG was made from maternal serum collected at 15-19 weeks gestations, the sensitivity and specifity of elevated βhCG were 20% and 84%, respectively, for that serum β- hCG is considered not helpful in predicting preeclampsia [17].

**In conclusion,** Serumβ- hCG level was significantly higher from 16 wks of gestation in women who develop PE later in their pregnancy so it may be used for prediction of PE and as there is a significant increase in β-hCG in women who develop severe PE later on in their pregnancy than those who develop mild

PE so β-hCG level in patients with PE may be used in the detection of the severity of the disease.

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**Competing interests**

Authors declare that we have no competing interests.

**Authors Contributions** All authors wrote, read and approved the final manuscript.

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