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Original Research Article

Association of serum beta-hCG and urine albumin-creatinine ratio with hypertensive disorders during pregnancy

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ABSTRACT

Background: Preeclampsia with or without severe symptoms, chronic hypertension with or without superimposed pre-eclampsia/eclampsia, gestational hypertension, HELLP syndrome, or eclampsia all pose a significant risk of morbidity for both the mother and the unborn child. The aim of this study was to investigate if the albumin-to-creatinine ratio in urine spots and the serum beta-hCG level correlate with the hypertensive illness of pregnancy.
Method: The current inquiry was conducted during the months of October 2020 and August 2022 at the obstetrics and gynaecology department of Subharti medical college in Meerut, Uttar Pradesh. The study was not open to women who were more than 20 weeks pregnant, had gestational diabetes mellitus, had more than one pregnancy, had chronic hypertension, chronic renal disease, chronic liver disease, cardiac disease, systemic lupus erythematosus, or haematological illnesses. We measured the levels of serum beta hCG and the urine albumin-creatinine ratio, and we compared them between the groups.
Results: After ensuring that each participant had given their informed permission, the trial comprised a total of 200 patients. In the hypertensive group of the participants in the study, 31% were between the ages of 21 and 35, and 29% were less than 20 years old. With increased beta hCG and UACR, there was a higher incidence of hypertensive retinopathy, acute renal failure, DIC, and PPH among the patients, as well as the poorest fetal outcomes. ($p<0.05$)
Conclusions: The presence of a substantial relationship between hypertensive diseases and raised levels of beta-hCG during pregnancy, as well as a greater ratio of urine albumin to creatinine. There is a considerable increase in the incidence of fetal growth retardation, preterm, and mortality occurring within the uterus among mothers who have higher levels of beta-hCG and urine ACR.

Keywords: Hypertension, Pregnancy, Urine albumin-creatinine ratio, Beta- hCG

INTRODUCTION

Preeclampsia with or without severe symptoms, chronic hypertension with or without superimposed pre-eclampsia/eclampsia, gestational hypertension, HELLP syndrome, or eclampsia all pose a significant risk of morbidity for both the mother and the unborn child. Although rates of morbidity and death have dropped as a consequence of better prenatal care, which includes close monitoring to spot pre-eclampsia warning signs and quick delivery to reduce or eliminate negative effects, these issues persist. Although pregnancy-related hypertension alone is a cause for worry, pre-eclampsia and eclampsia represent more serious dangers concern.[1-3] One of the major causes of maternal and perinatal morbidity and mortality, hypertensive disorders of pregnancy are thought to complicate between 5 and 10 percent of pregnancies globally. In wealthy countries, hypertension disorders are thought to be the cause of 16% of maternal deaths. Between 8 and 10% of expectant mothers in India suffer from pre-eclampsia. Preeclampsia complicates four to five percent of all pregnancies.[4-6] The 5-7% of all pregnancies

are impacted by hypertension diseases, with PE accounting for around half of them and GHTN for the other half. Chronic hypertension complicates pregnancies in 1-2% of cases, whether it has PE or not.[7] The PE syndrome, which can appear on its own or in addition to persistent hypertension, affects three to five percent of pregnancies. One of the main causes of maternal and fetal morbidity and mortality is this syndrome.[8] Between 2 and 7% of women who have never given birth are affected by PE.[9] According to studies, it accounts for 10 to 15 percent of all fatalities worldwide and can raise perinatal mortality by five times.[10,11]

The human chorionic gonadotropin, often known as hCG, is a hormone that is produced from the syncytiotrophoblastic cells that are found in the placenta. The levels of hCG in a pregnant woman's blood can be measured to help differentiate between a healthy pregnancy, a pathological pregnancy, and an abortion. The measurement of hCG can also be valuable in the diagnosis of a variety of tumors, such as choriocarcinoma and extra-uterine malignancies. It reaches its highest level in the maternal serum between weeks 8 and 10, after which it begins to gradually decline until it reaches a plateau between weeks 18 and 20 of gestation. Alpha and beta are the two subunits that are found in the glycoprotein that makes up the hormone. During pregnancy, the unbound subunits of the hormone as well as the intact hormone can be found in the urine and serum of the pregnant woman in a variety of different forms. The liver is responsible for the majority of the hCG's breakdown, with the urine accounting for the elimination of around 20%. The kidney is responsible for the digestion of the beta subunit, which results in the production of a core fragment that may be identified using urine hCG tests.[12,13] The collection of urine over a period of 24 hours is the gold standard for determining the quantity of urine albumin excretion; nevertheless, this method is laborious and causes a delay in diagnosis of at least 24 hours. As a simple alternative, the spot urine albumin to creatinine ratio has been promoted as a result. There is a correlation between the ratio of protein to creatinine in a single urine sample and the amount of protein that is excreted in 24 hours. Urinary creatinine is excreted at a reasonably steady rate, which enables it to be used as an internal reference when there is a stable glomerular filtration rate. The international organization for the study of hypertension in pregnancy (ISSHP) has recognized the spot urine protein to creatinine ratio as a technique for the diagnosis of substantial proteinuria (defined as more than 300 mg in 24 hours). If the ratio of protein to creatinine is less than 0.2, substantial proteinuria cannot be present.[14-16]

Objective

Therefore, the purpose of this study was to investigate whether or not a connection exists between maternal serum -hCG, the ratio of urine albumin to creatinine, and hypertensive disease of pregnancy.

METHOD

This prospective observational study was carried out between October 2020 and August 2022 at the department of obstetrics and gynecology at the Subharti medical college in Meerut, Uttar Pradesh. There was a total of 200 women who agreed to take part in the study. Of them, there were 100 women who had hypertension and 100 women who were considered to have normal blood pressure. Women who were pregnant for more than 20 weeks, had gestational diabetes mellitus, multiple pregnancies, or other medical conditions such as chronic hypertension, chronic renal disease, chronic liver disease, cardiac illness, systemic lupus erythematosus, or hematological abnormalities were not allowed to participate in the study. We determined the serum beta hCG levels as well as the urine albumin-creatinine ratio and compared them across the groups.

It was recorded that each participant's demographic information was documented. A comprehensive history was taken, which included noting the history of the present pregnancy, the history of obstetrics, the history of menstruation, both in the present and in the past, and the history of the patient's family. As part of the comprehensive physical examination, the patient's temperature, pulse rate, blood pressure when lying down, and breathing rate were all recorded. The existence of pallor, icterus, cyanosis, clubbing, lymphadenopathy, and edema were all noted, as well as the presence of lymphadenopathy. A comprehensive assessment was performed to rule out the possibility of any heart or respiratory conditions. An evaluation of the obstetrical status was performed and recorded. Investigations of a routine prenatal nature, such as blood group, VDRL, HBsAg, HCV, and HIV 1 and 2 testing, were carried out. USG obstetrics to ensure the health of the fetus. The investigations that were conducted related to hypertensive disorders of pregnancy included a complete blood count, platelet count, urine albumin test, liver function test, kidney function test, and lactate dehydrogenase levels. The results that were obtained from these tests were then documented on the cases group.

Under aseptic conditions, a sample of venous blood consisting of around 3 ml was obtained and placed in a test tube. After the sample had been collected for 2 hours, it was centrifuged at a speed of 3000 rpm for 5 minutes. After the separation of the serum, it is placed in a polythene tube that has a cork. The assay of beta-hCG was performed using the sera that showed no evidence of hemolysis. Utilizing the DIMENSION RXL equipment, determine the ratio of urine albumin to creatinine on the spot. Urine that has been recently taken from the middle of the stream is preferred for regular testing. Calculation Urine albumin/creatinine ratio (UACR): It is the ratio of the amount of albumin in the urine to the amount of creatinine in the urine, and it is stated as the amount of albumin excreted in milligrams per gram of creatinine in

the urine. UACR (mg/g)=albumin (mg/dl)/ creatinine (mg/dl)×1000.

Statistical analysis

After being input into an excel sheet, all of the data that was obtained was analyzed using SPSS v21, which was run on Windows 10. The demographic data and the variables of the research were summed up as the mean, the standard deviation, the frequency, and the percentage. Tables, figures, bar diagrams, and pie charts were used to depict the data once they had been summarized. The paired t test was used to investigate the difference in mean values of the continuous variables, and the Pearson correlation coefficient was utilized to investigate the degree to which the variables were associated with one another. The ROC was carried out so that an evaluation of the diagnostic accuracy of the approach could be made. It was determined to be statistically significant if the p value was less than 0.05.

RESULTS

In the current study, a total of two hundred patients agreed to take part in the research after receiving information and explanations. In the hypertensive group of the participants in the study, 31% were between the ages of 21 and 35, and 29% were less than 20 years old (Table 1). Hypertensive mothers were shown to have a lower educational standing when compared to normotensive mothers when it came to assessing their educational standing. Rural inhabitants do not have a noticeably greater prevalence of the hypertension compared to those who live in the urban regions (Table 1).

When compared with women who had normotensive blood pressure, hypertensive mothers have a much greater incidence of beta hCG. According to an analysis of the urine albumin creatinine ratio, hypertensive moms had a much higher UACR than normotensive mothers do. This finding was made after comparing the two groups of mothers' blood pressure. In comparison, only 10% of normotensive moms who were pregnant had a blood pressure reading of 30 or higher. In moms who have chronic hypertension, the incidence of beta-hCG is greater than in those who have pre-eclampsia, eclampsia, gestational hypertension, or chronic hypertension with superimposed pre-eclampsia. There is a greater frequency of the increased UACR among moms who have chronic hypertension with superimposed preeclampsia, eclampsia, and chronic hypertension. This condition is referred to as a "triple threat" (Table 2).

According to an analysis that correlated the amount of beta hCG with the problems, there was a greater incidence of hypertensive retinopathy, acute renal failure, DIC, and PPH among the patients whose beta hCG level was higher, in comparison to the patients whose beta hCG level was lower ($p<0.05$) individuals with a greater level of UACR had a higher incidence of problems such HELLP syndrome, acute renal failure, and PPH, according to an evaluation that correlated the UACR level with the consequences. This was in contrast to individuals with a lower level of UACR. ($p<0.05$) (Table 3).

Based on an analysis of the relationship between beta hCG and fetal outcome, it was discovered that there is a greater incidence of the fetal growth retardation, preterm, and intrauterine mortality among expecting mothers who had considerably higher levels of beta-hCG compared to those who had significantly lower levels. This was the case regardless of whether the beta-hCG levels were high or low ($p<0.05$). When the UACR was evaluated in relation to the fetal outcome, it was discovered that there is a higher incidence of the fetal growth retardation, preterm, and intrauterine mortality among expectant mothers who had higher UACR levels as opposed to lower levels. This was shown to be the case when compared to those who had lower UACR levels. ($p<0.05$) (Table 4).

Table 1: Comparison of demographic details of patients with hypertensive disorders.

Variables		Normotensive	Hypertensive	Chi-square (p value)
Age (Years)	<20	13	29	10.78 (0.12)
	21-25	27	31	
	26-30	28	16	
	> 30	32	24	
Religion	Hindu	47	29	6.89 (0.317)
	Muslim	38	50	
	Others	15	21	
Socio economic status	Upper	27	14	9.096 (0.10)
	Upper middle	21	16	
	Lower middle	15	22	
	Upper lower	22	11	
	Lower	15	37	
Education	Illiterate	21	38	8.72 (0.124)

Continued.

Variables		Normotensive	Hypertensive	Chi-square (p value)
	Primary	12	32	
	Secondary	38	17	
	Graduate/ post-graduate	29	13	
Residence	Urban	64	49	6.05 (0.146)
	Rural	36	51	
Parity	Nulli para	72	61	2.71 (0.09)
	Multi para	28	39	
Beta hCG	<30000-50000	78	20	69.81 (0.01)
	51000-80000	15	36	
	>81000	7	44	
Urine albumin creatinine ratio	<3	62	13	51.90 (0.01)
	3-30	28	57	
	>30	10	30	

Table 2: Comparison of hypertensive disorders with beta hCG and ACR.

Variables		Pre-eclampsia	Eclampsia	Gestational HTN	Chronic HTN with superimposed preeclampsia	Chronic HTN	Chi-square (p)
Beta hCG	<30000-50000	3	3	6	6	2	2.855 (0.94)
	51000-80000	4	11	7	11	11	
	>81000	3	8	9	8	16	
Urine albumin-creatinine ratio	<3	3	4	1	4	4	78.08 (0.01)
	3-30	3	5	17	9	10	
	>30	4	13	4	12	11	

Table 3: Comparison of maternal complications with beta-hCG and ACR.

Variables		HELLP	Hypertensive retinopathy	Acute renal failure	DIC	PPH	Chi-square (p)
Beta hCG levels	<30000-50000	3	3	5	3	5	17.39 (0.04)
	51000-80000	10	3	8	3	6	
	>81000	6	4	15	10	15	
Urine albumin-creatinine ratio	<3	7	1	1	1	4	19.37 (0.03)
	3-30	13	2	13	3	3	
	>30	20	1	9	5	11	

Table 4: Comparison of fetal complications with beta-hCG and ACR.

Variables		FGR	Prematurity	Intrauterine death	Chi-square (p)
Beta hCG levels	<30000-50000	5	6	3	3.45 (0.04)
	51000-80000	3	14	9	
	>81000	10	18	12	
Urine albumin-creatinine ratio	<3	4	6	4	15.201 (0.02)
	3 to 30	1	12	11	
	>30	8	13	15	

DISCUSSION

It may still be advantageous to be able to identify the women who are at risk so that they may be followed correctly, even if there is no medication that has been shown to prevent the condition. However, there is data that supports early screening of women who are at risk for hypertensive disorders may minimize maternal mortality and morbidity. There is no test that can definitively determine the diagnosis. There are several tests available, but none of them can reliably identify pre-eclampsia. Blood tests for vitamin D, C-reactive protein, and the

plasminogen activator inhibitor VEGF are a few examples.[17,18] One of the proposed reasons of pregnancy-related hypertension is insufficient trophoblastic invasion and placental vascular remodelling. One of the hypothesized causes is this. Numerous studies have suggested that high amounts of hCG production may be caused by decreasing oxygen levels in the placenta. An in vitro trophoblastic cell culture that was grown in an oxygen-depleted environment was used to illustrate it.[19,20] It is more crucial than ever to comprehend this situation and investigate the pathologic and secretory response of the placenta since it is believed that preeclampsia is a trophoblastic condition and that hCG is generated by the trophoblasts. This is because the key to treating this condition is understanding it. Numerous studies have found a favorable link between the levels of beta-hCG and the development of pre-eclampsia.

The aim of this study was to investigate if the albumin-to-creatinine ratio in urine spots and the serum beta-hCG level correlate with the hypertensive illness of pregnancy. The 31% of the study's hypertensive participants were between the ages of 21 and 35, and 29% were younger than 20. The urine albumin creatinine ratio (UACR) was examined, and it was shown that hypertension mothers had substantially higher UACRs than normotensive mothers do. After comparing the blood pressure of the two groups of moms, this conclusion was reached. Only 10% of pregnant normotensive mothers had blood pressure readings of 30 or higher, in contrast. The prevalence of beta-hCG is higher in mothers with chronic hypertension than it is in those with pre-eclampsia, eclampsia, gestational hypertension, or chronic hypertension with superimposed pre-eclampsia. A higher amount of circulating-hCG was associated, in Wang et al study, with a more severe instance of pregnancy-induced hypertension. Significant ($p=0.001$) independent contributions to severe pregnancy-induced hypertension were made by oxidative stress factors like thiobarbituric acid reactive substance and total antioxidant capacity as well as inflammatory factors like interleukin-6, tumor necrosis factor, and interferon. In individuals who experienced perinatal pregnancy-induced hypertension, it was demonstrated that there was a statistically significant correlation between circulating levels of hCG and inflammatory and oxidative stress markers.[21]

The degree of sensitivity, specificity, and positive predictive value were all determined to be 82%, 93.2%, and 74.3%, respectively, in the study carried out by Rathore et al. The study's findings indicate a link between elevated beta-hCG levels and the severity of the underlying illness, as well as a link between elevated beta-hCG levels and prenatal hypertension and preeclampsia among pregnant women in their second trimester.[22] UPCR had a sensitivity of 79.37 percent, a specificity of 46.67 percent, a positive predictive value (PPV) of 92.59 percent, a negative predictive value (NPV) of 21.21 percent, and an accuracy of 75.79 percent for sensitivity was 76.98%, specificity was 13.33%, PPV was 88.18%, NPV was 6.45%, and accuracy was 70.21% for predicting adverse maternal outcomes; for unfavorable foetal outcomes. The results show that UPCR is a straightforward laboratory technique that may be used as a complement to assist guide treatment decisions and may be able to predict abnormal fetomaternal outcomes in preeclampsia with excellent sensitivity and PPV.[23]

In the current study, an assessment of the beta hCG level with the complications found that there was a greater incidence of hypertensive retinopathy, acute renal failure, DIC, and PPH among the patients with higher beta hCG compared to patients with lower levels of beta hCG. This was the case regardless of whether the patients had higher or lower levels of beta hCG ($p<0.05$). Based on an analysis of the relationship between beta hCG and fetal outcome, it was discovered that there is a greater incidence of the fetal growth retardation, preterm, and intrauterine mortality among expecting mothers who had considerably higher levels of beta-hCG compared to those who had significantly lower levels. This was the case regardless of whether the beta-hCG levels were high or low ($p<0.05$). Individuals with a greater level of UACR had a higher incidence of problems such HELLP syndrome, acute renal failure, and PPH, according to an evaluation that correlated the UACR level with the consequences. This was in contrast to individuals with a lower level of UACR ($p<0.05$). When the UACR was compared to the fetal outcome, it was discovered that pregnant women who had higher UACR levels had a considerably greater incidence of fetal growth retardation, preterm, and mortality within the uterus than those who had lower levels. This was the case regardless of whether or not the UACR was elevated ($p<0.05$).

The beta-hCG blood levels were discovered to be a significant clinical diagnostic for predicting PE during the early stages of the second trimester. On the other hand, their predictive power was found to be restricted during the first trimester. However, further study on the predictive ability of hCG in populations that are bigger and more diverse is required needed.[24] Similar to present study Kumari et al documented. When compared with normotensive women, hypertensive disorders of pregnancy are associated with greater levels of serum beta-hCG. The levels are also greater in patients who have severe preeclampsia as opposed to patients who have non-severe preeclampsia, and they are higher in primigravida hypertension women as opposed to multigravida hypertensive women.In cases of early onset preeclampsia, it has also been noted that the levels of b-hCG in the serum are higher than normal. Therefore, determining the levels of b-hCG in the blood can potentially assist in the early identification of hypertensive disease of pregnancy, and it also has the potential to act as an indication of the degree to which the condition has progressed. Because of its low sensitivity and the difficulty in determining where the cut off value should be, the serum b-hCG test has limited application as a diagnostic tool.[25] Serum beta-hCG estimate in primigravida patients at the middle of the first

trimester (13-20 weeks) is an excellent predictor of PIH, and greater levels of beta-hCG are related with increased PIH severity. The conclusion of the study was that assessing a woman's levels of beta-hCG during the second trimester of pregnancy is helpful in clinical practice for identifying women who would develop PIH during the same pregnancy. Additionally, greater levels of -hCG have been linked to an increased risk of developing PIH. Due to the low number of participants in this study, more research on a larger scale is required, especially when taking into account the significance of b-hCG in the prediction of PIH.[26]

Patients diagnosed with PIH saw a significant increase in their blood levels of cholesterol, triglycerides, and very low-density lipoprotein in both the early and late stages of the disease. According to the findings of this research, beta-hCG levels in the blood and lipid profiles taken during the second trimester of pregnancy can assist in the identification of pregnant women who are at an increased risk of developing PIH, preeclampsia, or eclampsia.[27] Upadhyay et al demonstrated that the ratio of albumin to creatinine is an extremely accurate predictor of the presence of proteinuria and that it is suitable for use as a convenient alternative test. The diagnosis of severe proteinuria and the screening for preeclampsia might be made using a method that is easier and more expedient. This method would include determining the random protein to creatinine ratio rather than collecting urine for 24 hours.[28] In male-bearing pregnancies, the levels of hCG and testosterone in the blood of preeclamptic women were significantly higher than those of normotensive mothers ($p=0.001$ for both of these comparisons).[29] Devi et al found that urine albumin/creatinine ratio of severity of preeclampsia. Spot urine albumin/creatinine ratio correlates better than spot Urine albumin/creatinine ratio to 24-hour urinary protein excretion to the severity of disease and as predictor of severity of disease. and 24-hour urinary protein excretion ($p<0.001$). The optimal spot Urine albumin/creatinine ratio value was 202.82 mg/g (22.92 mg/mmol) for 0.3 gm/24 h of protein excretion (mild preeclampsia) with a sensitivity and specificity of >80% and >99.5% respectively for urine albumin/creatinine ratio, and 1381.24 mg/g (156.08 mg/mmol) for 2 gm/24 h of protein excretion (severe preeclampsia) with a sensitivity and specificity of >91% and >99.5% respectively. In present study, it was shown that urine albumin/creatinine ratio is significantly higher in patients with severe preeclampsia.[30]

Similarly, Mazhari et al found that pre-eclampsia affected 13.33% (12/90). Out of 40 patients with serum beta hCG levels greater than 35,000 mIU/ml, 25% (10/40) had hypertension disorders, whereas only 4% (2/50) developed hypertensive disorders in 50 cases with serum beta hCG levels less than 35,000 mIU/ml. When the two groups were compared, the $p=0.003$, which is statistically significant. The current study revealed that maternal serum beta hCG estimate in the mid-trimester (13-20 weeks) is a good predictor of the development of hypertensive problems during pregnancy.[31] Raised ACR levels were shown to be associated with illness severity as well as a poor fetomaternal outcome in our investigation.[32] Amin et al demonstrated that the random urine protein: creatine ratio is a more accurate means of assessing proteinuria in hypertensive pregnant women than the dipstick approach. Clinical laboratories, on the other hand, should standardise the reference values for their setting.[33] Study showed that measuring second trimester beta-hCG levels is useful in clinical practice to identify women who will develop PIH in the same pregnancy. Also, higher levels of beta-hCG are associated with increase severity of PIH. The sample size for this study being small, necessitate the need of further large scale studies considering the importance of B-hCG in PIH prediction.[34]

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