Predictive Value of Plasma Hematocrit Level in Early Diagnosis of Pre-Eclampsia

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ABSTRACT

Objective: To determine whether hematocrit level is associated with pre-eclampsia and assess its predictive value in diagnosing pre-eclampsia.

Study Design: Cross-sectional validation study.

Place and Duration of Study: Department of Obstetrics and Gynecology, CMH Quetta, from Jul 2019 to Jan 2020.

Methodology: A total of 561 pregnant women with a singleton pregnancy were included in the study. The diagnosis of pre-eclampsia was made as per operational definition. The samples were collected by non-probability consecutive sampling. Pregnant females with a parity of 0-4, gestational age > 16 weeks on last menstrual period (LMP) and singleton pregnancy on ultrasound were included in the study. In addition, data on plasma hematocrit findings and incidence of pre-eclampsia (positive/negative) were recorded.

Results: The age range in this study was from 18 to 40 years, with a mean age of 28.805 ± 2.41 years, mean parity of 1.258 ± 1.07 and mean gestational age was 11.352 ± 2.22 weeks. Plasma hematocrit findings predict 26 (4.6%) patients, and the incidence of pre-eclampsia was in 35 (6.2%) patients. Plasma hematocrit findings had shown a sensitivity of 60%, specificity 99%, diagnostic accuracy by 97%, PPV 80.7%, NPV 97.3%, (p<0.001) in diagnosis of preeclampsia.

Conclusion: Haematocrit can be valuable as a screening test for the timely diagnosis of pre-eclampsia in health centres. Women with a hematocrit above the cut-off of 38% must be scrutinized prudently for the signs of pre-eclampsia.

Keywords: Diagnostic accuracy, Pregnancy, Preeclampsia, Plasma hematocrit.

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INTRODUCTION

Hypertensive disorders of pregnancy are seen in roughly 10% of pregnant females and pre-eclampsia in around 3% of pregnancies in the USA.[1] Pre-eclampsia, bleeding and infection are the three foremost reasons of mortality in pregnant females, with pre-eclampsia being the commonest of the complications. In developing and developed countries, it remains a significant health peril.[2] WHO has declared it a global health problem.[3]

Gestational hypertension is noted after twenty weeks of gestation.[4] A diagnosis of pre-eclampsia can be made if the pregnant female has systolic blood pressure >140 mmHg or a diastolic blood pressure >90 mmHg after twenty weeks of gestation with proteinuria (>300 mg in 24-hour urine) or a protein/creatinine ratio of ≥0.3 in urine.[4] While a systolic BP of >160 mmHg or a diastolic BP of >110 mmHg is considered severe hypertension in pregnancy.[5] High BMI, low haemoglobin level, low K and high Na in diet are risk factors (modifiable) for these hypertensive disorders in pregnancy.[6,7]

Hemoconcentration is seen in people living at high altitudes. The basic phenomenon remains the same as seen in pre-eclampsia. However, in these pregnant females, blood volume does not rise at the same ratio as in pregnant females with normal BP, thus resulting in a relatively greater Hb level. As a result, numerous studies have evaluated haematocrit levels in predicting pre-eclampsia.[8] This measurement is characteristically taken in ANC clinics to formulate a predictive model for this clinical condition. It is attained by merging the results of this test with any risk factor detected in the history and examination of the patient, like high BMI and BP.

This relationship between the hematocrit levels provides grounds for further evaluation and may be valuable as a screening test for prompt diagnosis of pre-eclampsia in our local population. Many biochemical, biophysical and clinical tests are present to diagnose women with high risk for pre-eclampsia. However, these tests have a little predictive value or are expensive and even invasive. Considering that such a study has not yet been conducted in Pakistan, this study may benefit our pregnant population as different

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studies from the west cannot be applied in our setup due to different genetics. However, in our local data, different reports showing accelerated rates of hypertension prevalence in Pakistani adolescents have been documented by a meta-analysis by Shah *et al*.[9]

METHODOLOGY

This cross-sectional validation study was performed among pregnant females at the Department of Obstetrics and Gynaecology, CMH Quetta, from July 2019 to January 2020. Due approval was taken from the hospital ethical review committee (IRB/009). The calculated sample size was 561 pregnant females. The sample size was assessed using the sensitivity and specificity calculator, having a confidence interval of 95%, precision of sensitivity of 10% and specificity of 10%.[10] The study sample was collected by non-probability consecutive sampling.

Inclusion Criteria: Pregnant females aged 18-40 years with a parity of 0-4, gestational age >16 weeks on last menstrual period (LMP) and singleton pregnancy on ultrasound were included in the study.

Exclusion Criteria: Pregnant females with a history of diabetes, hypertension, previous pre-eclampsia on medical record and hyperuricemia (serum uric acid level > 6 mg/dl) were excluded from the study.

The parameters of age, parity and gestational age were documented. Informed consent was taken from patients, certifying privacy and the fact that there was no risk to the patient while participating in this study.

The diagnosis of pre-eclampsia was made as per the operational definition of a pregnant female with hypertension after twenty weeks of gestation with proteinuria (>300 mg in 24-hour urine) or a protein/creatinine ratio of ≥0.3 in urine.[4] Data of plasma hematocrit findings and pre-eclampsia (positive/negative) were recorded on especially designed proforma by the researcher herself.

Statistical Package for Social Sciences (SPSS) version 22.0 was used for the data analysis. Mean ± SD was presented for quantitative variables like age, parity and gestational age, while frequency and percentage for age groups. Sensitivity, specificity, positive predictive value (PPV), Negative predictive value (NPV), and diagnostic accuracy for plasma hematocrit against pre-eclampsia incidence were calculated using the 2X2 model. Effect modifiers like age, parity and gestational age were controlled by stratification. Post-stratification diagnostic accuracy was measured. The accuracy of plasma hematocrit was compared through a 2 x 2 table to calculate sensitivity, specificity, PPV, NPV and diagnostic accuracy.

RESULTS

The pregnant females included in this study were 18 to 40 years old. The mean age was 28.805 ± 2.41 years, the mean parity was 1.258 ± 1.07, and the mean gestational age was 11.352 ± 2.22 weeks. The age group 18 to 30 years included 424 (75.6%), females, while the group 31 to 40 years had 137 (24.4%) females.

Among the 561 pregnant females, plasma hematocrit was raised in 26(4.6%) patients, while the incidence of pre-eclampsia was noted in 35 (6.2%) patients, as shown in Table-I.

Table-I: Overall results of raised plasma hematocrit findings and preeclampsia for diagnosis of preeclampsia.

Status	Raised Plasma Hematocrit Findings	Pre-Eclampsia
Positive	26 (4.6%)	35 (6.2%)
Negative	535 (95.4%)	526 (93.8%)

The features of true positive, false positive, true negative and false negative association of raised plasma hematocrit findings with pre-eclampsia (p<0.001) have been highlighted in Table-II.

Table-II: Comparison of raised plasma hematocrit findings versus pre-eclampsia.

Raised Plasma Hematocrit Findings	Pre-eclampsia (Gold Standard)		*p*-value
	Positive	Negative	
Positive	21 (TP)	5 (FP)	<0.001
Negative	14 (FN)	521 (TN)	

In addition, the plasma hematocrit findings showed a sensitivity of 60%, specificity of 99%, diagnostic accuracy of 97%, PPV of 80.7% and NPV of 97.3% in the diagnosis of pre-eclampsia, which has been elaborated in Table-III.

DISCUSSION

The pathogenesis of pre-eclampsia is still not clear. The process may be silent initially before hypertension is noticed and the diagnosis of preeclampsia is made.[11] Some evidence proposes that plasma volume in pre-eclampsia is lesser than normal, which ensues in high haemoglobin concentration, causing decreased placenta circulation that plays a pathogenic role in the development of pre-eclampsia.[12] Various studies have reported that many biochemical laboratory tests can assess the physiological changes occurring during pregnancy. It is critical to distinguish between normal physiological changes and pathological changes.[13]

Knowledge of these physiolo-gical changes and pregnancy-related disorders resul-ting in laboratory tests' aberrations is crucial when dealing with pregnant females.[14]

Table-III: Sensitivity, specificity, diagnostic accuracy, ppv and npv of plasma hematocrit findings.

Parameter	Calculation	% Age
Sensitivity	$\frac{\text{True Positive}}{\text{True Positive + False Negative}} \times 100$ $\frac{21}{21 + 14} \times 100$	60%
Specificity	$\frac{\text{True Negative}}{\text{True Negative + False Positive}} \times 100$ $\frac{521}{521 + 5} \times 100$	99%
Diagnostic Accuracy	$\frac{\text{True Positive + True Negative}}{\text{True Positive + True Negative + False Positive + False Negative}} \times 100$ $\frac{21 + 521}{21 + 521 + 5 + 14} \times 100$	96.6%
PPV	$\frac{\text{True Positive}}{\text{True Positive + False Positive}} \times 100$ $\frac{21}{21 + 5} \times 100$	80.7%
NPV	$\frac{\text{True Negative}}{\text{True Negative + False Negative}} \times 100$ $\frac{521}{521 + 14} \times 100$	97.3%

Golboni *et al,* reported that plasma hematocrit has a sensitivity of 58.6% and specificity of 88.9%; PPV of 33.7%, and NPV of 95.7% in early diagnosis of pre-eclampsia.[10] Mello *et al,* also evaluated the biochemical patterns in the early diagnosis of pre-eclampsia and found a sensitivity and specificity of the hematocrit test of 63% and 90%, respectively, while a PPV of 36% and NPV of 92%.[15] Their results are in accordance with ours. In Mello's research, after eight weeks of gestation, the haematocrit was assessed four weekly, and the results of the second and third trimesters were compared. Mello's methods were unlike ours because we checked the haematocrit only at 24–28 weeks of gestation. Nevertheless, our results exhibited that it may be conceivable to get a similar predictive value by determining haematocrit only once.

Goudarzi *et al,* reported from a study from Iran that a statistically significant relationship was seen between the haematocrit value in the first and third trimester and the occurrence of pre-eclampsia.[16] Dai *et al,* assessed the values of haemoglobin, hematocrit, albumin and the difference between hematocrit and albumin in diagnosing pre-eclampsia and eclampsia. They concluded that this diagnosis could be made with a value of hematocrit–albumin of >12.65 with a sensitivity of > 57 % and a specificity of > 98.9%.[17]

In a similar study on Chinese women, Wang *et al,* documented that the haemoglobin levels in the first trimester can predict the risk of gestational diabetes mellitus, pre-eclampsia and preterm birth. They found that when the haemoglobin is >15 g/dL, the risk of pre-eclampsia increases significantly, especially in females with a pre-pregnancy body mass index of <24 kg/m2.[18] Likewise, Mehrabian and Hosseini reported on 973 pregnancies that gestational diabetes mellitus and pre-eclampsia was considerably higher in women who had early pregnancy haemoglobin of >12.5 g/dL than those with values <12.5 g/dL.[19]

In another study, Çakmak *et al,* reported the relationship between the level of haemoglobin with pregnancy outcomes in a Turkish population.[20] They concluded that low and high Hb levels were associated with untoward pregnancy outcomes with pregnancy-induced hypertension common in the higher-level group and more preterm births and NICU admission in both higher and lower haemoglobin level groups.[20] Indeed, routine screening of haemoglobin in the first trimester seems mandatory for the well-being of the mother and the child. Basak *et al,* evaluated the relationship of hematocrit level with pre-eclampsia in a Bangladeshi population. They found higher hematocrit in pre-eclamptic patients as compared to the normal pregnant females, which was statistically significant, indicating a strong association.[21]

However, a single diagnostic marker still cannot accurately predict subsequent pre-eclampsia. A detailed history, biophysical examination, and biochemical markers can achieve the best detection rate. Poon *et al,* initiated the assessment of a few serum parameters and maternal factors to attain an acceptable predictive power of early pre-eclampsia. The detection rate of pre-eclampsia before 34 weeks of pregnancy was 93.1% in the first trimester by algorithms from maternal risk factors, mean arterial BP and pulsatility index of the uterine arteries, while the detection rate after 37 weeks of pregnancy with an appropriate algorithm was 44.9%.[22] In a prospective observational study of 175 pregnant women, Sung *et al,* examined the association between serum placental growth factor (PlGF) and pregnancy-associated plasma protein-A (PAPP-A) with pre-eclampsia small-for-gestational-age infants. They found both as valuable markers in the first trimester for detecting small-for-gestational-age (SGA)

infants and hypertensive disorders of pregnancy.[23] Akolekar *et al,* established the detection of pre-eclampsia in the first trimester by combining various markers (PIGF, PAPP-A, PP13, inhibin A, activin A, sEndoglin, PTX3, P-selectin, blood pressure, Doppler sonography, and history) is improved considerably. The detection rate reached 91% for early-onset pre-eclampsia, 79.4% for intermediate-onset pre-eclampsia (34–37th weeks of gestation), and 60% for late-onset pre-eclampsia.[24] However, the relation between costs and benefits of these markers needs to be further explored, especially in our setup.

The importance of detecting pre-eclampsia is imperative from the baby's health point of view and the long-term health issues of pre-eclamptic pregnant women who have a more considerable lifetime risk for suffering from cardiac and blood vessel diseases. Integration of pre-eclampsia risk calculation into first-trimester perinatal care seems vital. Indeed, pregnancy is not just a short period in a female's life but an essential time giving insight into her health status. It seems to be the start of taking care of a family but also for better self-care.

CONCLUSION

Haematocrit is an established routine screening test for anaemia at the 24–28 weeks of gestation. However, it is also a vital screening test for early diagnosis of pre-eclampsia in these females. Therefore, pregnant females with a hematocrit above the cut-off of 38% should be supervised prudently for the signs of pre-eclampsia and its prompt detection.

Conflict of Interest: None.

Authors' Contribution

SS: Conception, design, final approval, HA: Collection of data, data analysis, interpretation, SMA: Data analysis, interpretation, BM: Drafting of article.

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