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ORIGINAL ARTICLE

A Prospective Study to Determine the Predictive Ability of HDP-Gestosis Score for the Development of Pre-eclampsia

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Abstract

Background HDP-gestosis score is a risk scoring system (score 1–3) for the development of pre-eclampsia. When a pregnant woman's total score is equal to or greater than 3, she is labelled as "at risk for pre-eclampsia" and is managed accordingly.

Objectives To determine the sensitivity, specificity, Positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy of HDP-gestosis score for predicting pre-eclampsia.

Methods This prospective study included 473 pregnant women who presented at the department of Obstetrics and Gynaecology, from June 2020 to December 2021. After 20 weeks of pregnancy, the patients were assessed for the development of pre-eclampsia. Details of age, gravida, obstetric history, menstrual cycle regularity, polycystic ovarian disease history, duration of marriage, parity, past medical and surgical intervention, previous/present medication, and family history were taken. Gestosis score was calculated and classified into mild (score of 1), moderate (score of 2) and high risk (score of ≥ 3) for the development of Pre-eclampsia (PE). Sensitivity, Specificity, PPV, NPV and diagnostic accuracy of HDP-gestosis score for predicting the development of PE were determined.

Results The mean age, gestational age, and BMI of the women were 28.4 ± 6.8 years, 11.5 ± 2.04 weeks, and 24.5 ± 3.7 kg/$m^{2,}$ respectively. The gestosis score was 2 in 43.13% of the participants, 1 in 42.28%, and ≥ 3 in 14.59% of the women. PE developed in 15.01% ($n = 71$) participants. The Sensitivity, Specificity, PPV, NPV, and Diagnostic accuracy of HDP-gestosis score for predicting PE were 83.1%, 97.51%, 85.51%, 97.03% and 95.35%, respectively.

Conclusion Gestosis score is a novel early marker for prediction of the development of PE allowing for a prompt management for the patients, thereby curbing the adverse consequences.

Keywords Gestosis · Pre-eclampsia · Diagnosis · Prediction

Introduction

Pre-eclampsia (PE) is one of the commonest complications of pregnancy, affecting 4.6% pregnancies worldwide [1] and 1.8–16.7% pregnancies in the developing countries [2]. It is identified by systolic blood pressure (SBP) and diastolic blood pressure (DBP) greater than 140 mm Hg and 90 mm Hg, respectively, after 20 completed weeks of pregnancy. As reported in an Indian study, the overall pooled prevalence of PE in India was 11% [3].

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PE is the major cause of maternal (that include abruptio placentae, disseminated intravascular coagulation, pulmonary oedema, acute renal failure, heart rhythm disturbances, and effects on other organs like liver, brain and lungs) as well as perinatal (fetal growth retardation, preterm deliveries and fetal deaths) complications worldwide [4].

The grave nature of the condition continues to baffle us to use certain predictive markers in the early part of the pregnancy which may help us to identify the women who may develop PE—so that appropriate preventive measures are begun for the prevention and management.

A plethora of maternal risk factors have been established to be positively linked with the development of PE, which include higher age, parity, comorbidities, family history, previous personal history, ethnicity, investigative markers like thyroid profile, uterine artery Doppler velocimetry, PAPP-A levels, placental IGF levels and certain systemic conditions [5, 6]. As these factors are described by individual researchers, taking all of them into account and devising a scoring system for PE prediction were the need of the hour, especially for countries with limited resources and lack of biomarker testing facility.

A simple risk model named HDP-gestosis score has been devised by Dr Gorakh Mandrupkar with further modifications by committee including "Dr. Sanjay Gupte, Dr. Suchitra Pandit, Dr. Alpesh Gandhi and Dr. Girija Wagh" for effective screening and prediction of Pre-eclampsia [7]. This score considers all of the pregnant woman's present and emerging risk factors. Each clinical risk factor is given a score of 1, 2, or 3 based on its severity in the development of pre-eclampsia. A total score is obtained from detailed history and examination of the woman. When a pregnant woman's total score is equal to or greater than 3, she is labelled as "at risk for pre-eclampsia" and is managed accordingly [7].

Till date, to our knowledge, no study has been conducted in the practical setting to determine the diagnostic accuracy and sensitivity of prediction of Pre-eclampsia for HDP-gestosis score. So this study was conducted wherein HDP-gestosis score was applied and the pregnant women were followed-up to confirm and note the predictive ability for the development of PE.

Methods

A prospective study was done wherein 473 patients who presented in the department of Obstetrics and Gynaecology, ASCOMS, Jammu, over a duration of 18 months from June 2020 to December 2021, were enrolled. The inclusion criteria were: Age more than 18 years, and booked deliveries with first antenatal visit during the initial 11 weeks of pregnancy. Pregnant patients with COVID-19 disease, malignancy, liver diseases, intake of alcohol, substance abuse and smoking were excluded.

The sample size calculation was based on a study by Mishra et al. [8] where individual parameters used in the gestosis score were analysed for the relative risk in increasing pre-eclampsia. It was noted that mean arterial pressure (MAP) > 85, Dyslipidemia, Hypothyroidism, family history of HDP, Chronic hypertension, Thrombophilia, autoimmune disease were significant risk factors of Pre-eclampsia with odds ratio of 22.03, 5.02, 4.82, 3.37, 7.58, 2.07 and 4.40, respectively, in the HDP-gestosis score [8]. With these figures as reference, the minimum required sample size was 315 patients under 80% power and 5% significance. Considering the attrition rate and loss to follow-up, a 50% higher sample size was taken with total patients enrolled being 473.

A written consent was signed by all enrolled patients. Institutional ethical clearance was obtained for the study.

A detailed demographic history about age, gravida, obstetric history, menstrual cycle regularity, polycystic ovarian disease history, duration of marriage, parity, past medical and surgical intervention and previous/present medication were taken, followed by a routine clinical obstetric examination as per hospital protocol. Weight and height was measured based on which body mass index was calculated. Venous blood sample (5 ml) was collected in the antenatal visit (at 11–18 weeks of gestation) for assessing complete blood counts, thyroid profile, blood sugar levels, blood grouping and autoantibodies which included anti-TPO, antinuclear antibody (ANA), Rheumatoid factor, anti-dsDNA, SS-A and SS-B antibodies for specific diagnosis of the autoimmune disorders..

Taking all these factors into account, gestosis score was calculated by using the app (https://m.apkpure.com/hdp-gestosis-score/hdp.gestosis.score) [9] and classified into mild (score of 1), moderate (score of 2) and high risk (score of equal to or more than 3) for the development of PE. All the parameters mentioned in the gestosis score were assessed from the history and investigations, and a total score was entered in the master chart for every patient. The various parameters and HDP-Gestosis score are shown in Table 1.

Standards and Criteria

The standards and criteria used in the study for classifying the diseases of the patients were [10–19].

Hypertensive Disease of Pregnancy

Hypertensive disorders during pregnancy (HDP) include 4 categories: "(1) pre-eclampsia/eclampsia; (2) gestational hypertension (GH); (3) chronic hypertension; and (4) pre-eclampsia/eclampsia variants superimposed on chronic hypertension".

Table 1 HDP-Gestosis score

Risk factor	Score
Age > 35 years	1
Age < 19 years	1
Maternal anaemia	1
Obesity (BMI > 30)	1
Primigravida	1
Short duration of sperm exposure (cohabitation)	1
Woman born as small for gestational age	1
Family history of cardiovascular disease	1
Polycystic ovary syndrome	1
Inter pregnancy interval more than 7 years	1
Conceived with Assisted Reproductive (IVF/ ICSI) Treatment	1
MAP > 85 mm of Hg	1
Chronic vascular disease (Dyslipidemia)	1
Excessive weight gain during pregnancy	1
Maternal hypothyroidism	2
Family history of preeclampsia	2
Gestational diabetes mellitus	2
Obesity (BMI > 35 kg/m^2)	2
Multifetal pregnancy	2
Hypertensive disease during previous pregnancy	2
Pregestational diabetes mellitus	3
Chronic hypertension	3
Mental disorders	3
Inherited/Acquired Thrombophilia	3
Maternal chronic kidney disease	3
Autoimmune disease (SLE/APLAS/RA)	3
Pregnancy with Assisted Reproductive (OD or Surrogacy)	3
Treatment for hypertensive disease of pregnancy	3

Classification for risk of development of PE: Mild risk (score of 1), Moderate risk (score of 2) and High risk (score of equal to or more than 3) for the development of PE. The app used is (https://m.apkpure.com/hdp-gestosis-score/hdp.gestosis.score)

Pre-eclampsia

Pre-eclampsia was defined as de novo blood pressure (BP) elevations (Systolic blood pressure of 140 mm Hg or more or diastolic blood pressure of 90 mm Hg or more on two occasions at least four hours apart) after 20 weeks of gestation coupled with proteinuria (300 mg or more per 24 h urine collection or Protein/creatinine ratio of 0.3 mg/dL or more or Dipstick reading of 2 +). Eclampsia is defined as PE with seizures.

Gestational Hypertension

De-novo hypertension that develops at > 20 weeks in absence of features of Pre-eclampsia.

Chronic Hypertension

Elevated BP before 20 weeks of gestation or persisting beyond 12 weeks postpartum.

Chronic Hypertension with Superimposed Pre-eclampsia

Increased BP and new-onset proteinuria or other end-organ dysfunction in addition to preexisting hypertension.

Thyroid Profile

A laboratory normal range of 0.1–3 mIU/L for TSH, 0.9–1.7 ng/dL for fT4 and 0–35 IU/mL for anti-TPO was used to classify thyroid disease. An increase in the TSH levels or fall in the fT4 levels with presence of symptoms was classified as hypothyroidism, and a fall in the TSH levels or rise in the fT4 levels with presence of symptoms (such as fatigue, weight gain/loss, reduced exercise capacity, constipation hair loss, dry skin, and bradycardia/tachycardia) was classified as hyperthyroidism.

PCOS

The guidelines from the Endocrine Society using the Rotterdam criteria for diagnosis were applied which mandate the presence of two of the following three findings—hyperandrogenism, ovulatory dysfunction, and polycystic ovaries.

MAP

$MAP = DBP + 0.33 \times PP$ (SBP-DBP) where PP is the pulse pressure, SBP is systolic blood pressure and DBP is diastolic blood pressure.

Gestational Diabetes Mellitus (GDM)

The diagnosis of GDM was confirmed in the presence of "at least one abnormal value (≥ 92, 180 and 153 mg/dl for fasting, 1-h and 2-h plasma glucose concentration, respectively), following 75-g oral glucose tolerance test (OGTT)".

Excessive Weight Gain During Pregnancy

A weight gain during the 2nd and 3rd trimester (in kgs) > 18 (among women with BMI < 18.5 kg/m^2), > 16 (among women with BMI 18.5–24.9 kg/m^2), > 11.5 (among women with BMI 25–29.9 kg/m^2) and > 9 (among women with BMI > = 30 kg/m^2) was considered excess weight gain.

SLE/APLA/RA/thrombophilia

The American College of Rheumatology has 11 classification criteria for lupus. If a patient meets at least four criteria, lupus can be diagnosed. The criteria include malar or discoid rash; photosensitivity; oral ulcers; arthritis; serositis; abnormal antinuclear antibody (ANA) titers; and renal, neurologic, hematologic, or immunologic disorders.

The participants were tested for the presence of circulating autoantibodies, including ANA. The ANA test was considered positive at a titer ≥ 1:80. Rheumatic diseases were classified according to widely used criteria for undifferentiated connective tissue disease (UCTD), RA, SLE, anti-phospholipid syndrome (APS), Sjögren's syndrome, systemic sclerosis, polymyositis/dermatomyositis and mixed connective tissue disease.

Thrombophilia was diagnosed if there was idiopathic or recurrent venous thromboembolism; a first episode of venous thromboembolism at a "young" age (e.g., < 40 years); a family history of venous thromboembolism; venous thrombosis in an unusual vascular territory; and neonatal purpura fulminans or warfarin-induced skin necrosis.

Management of PE

The treatment for PE was started if BP remained higher than 140–90 mm Hg. It comprised of labetalol as a first-line therapy at dose of 100 mg BD up to maximum dose of 2400 mg. Nifedipine (preferably extended release) at dose of 10–30 mg OD was prescribed as a second line drug [20].

Outcome Measures

The final outcomes were proportion of women having "at high risk" gestosis score and those developing PE during the pregnancy.

The final data were entered in Microsoft EXCEL spreadsheet and analysed by "SPSS (Statistical Package for The Social Sciences) version 21.0". A p-value < 0.05 was considered statistically significant.

Statistical Analysis

The data presentation was done in the form of frequency numbers or percentages with mean (SD) and median values. Fisher's Exact test or Chi-Square test was used for determining the association between variables. Sensitivity (Sn), Specificity (Sp), Positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy of HDP-gestosis score for predicting the development of PE was determined. $p < 0.05$ was considered statistically significant.

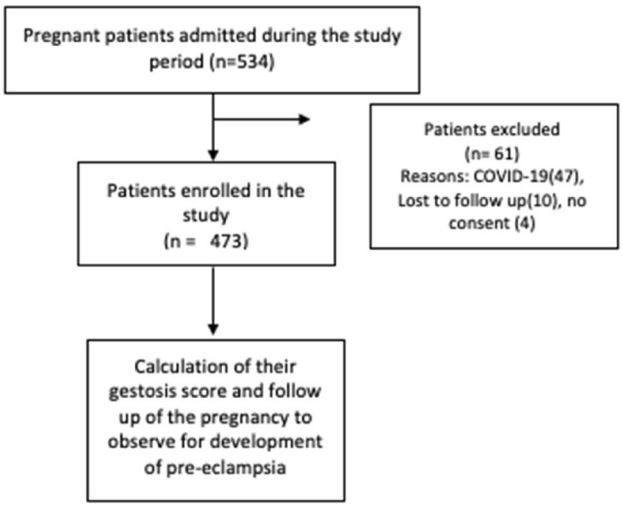

Fig. 1 Study flow

Table 2 Baseline demographic variables

Demographic characteristics	Mean ± SD/n(%)
Age(years)	28.4 ± 6.8
Gestational age(weeks)	11.5 ± 2.04
Gravida	
Primi	308 (65.12%)
Multi	165 (34.88%)
Body mass index(kg/m^2)	24.5 ± 3.7
Systolic blood pressure(mmHg)	117.4 ± 10.2
Diastolic blood pressure(mmHg)	78.7 ± 5.8

Results

Of the 534 pregnant patients admitted and screened, 473 were finally included in the study. The study flow is shown in Fig. 1.

The mean age, gestational age, and BMI of the enrolled women were 28.4 ± 6.8 years, 11.5 ± 2.04 weeks, and 24.5 ± 3.7 kg/m^{2,} respectively. The mean SBP and DBP were 117.4 ± 10.2 and 78.7 ± 5.8 mm Hg, respectively. 65.12% of the women were primigravida, and 34.88% were multigravida (Table 2).

The gestosis score was 2 in 204 (43.13%) of the participants, 1 in 200 (42.28%), and ≥ 3 (at risk) in 69 (14.59%) of the women (Fig. 2). During the follow-up, PE developed in 15.01% ($n = 71$) participants (Fig. 3).

Among the 71 women developing PE, 59 were correctly predicted by HDP-gestosis score > = 3, while among the remaining 12 cases of PE, eight patients had HDP-gestosis score of 2 and four patients had HDP-gestosis score of 1.

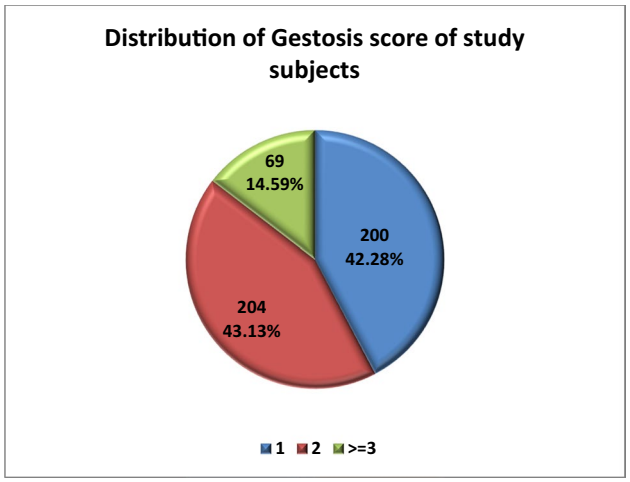

Fig. 2 Distribution of Gestosis score of study subjects

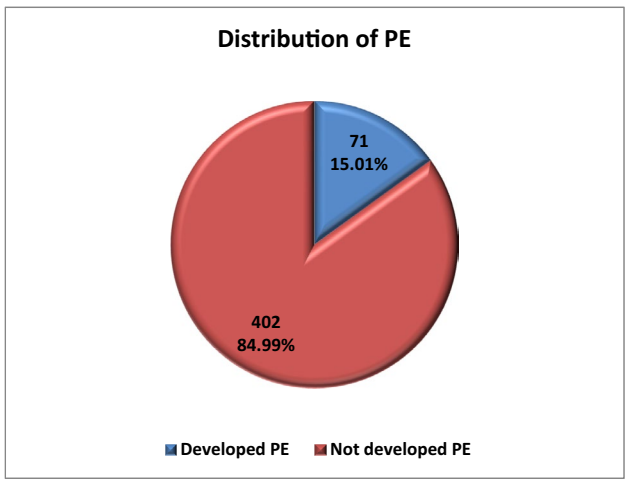

Fig. 3 Distribution of PE

For the HDP-gestosis score of > = 3, true positives were 59, false positives were 10 and false negatives were 12. Based on it, the Sensitivity, Specificity, PPV, NPV and Diagnostic accuracy of HDP-gestosis score (> = 3) for predicting PE were 83.1%, 97.51%, 85.51%, 97.03% and 95.35%, respectively. Taking the HDP-gestosis score cutoff of 2 or more (moderate), the Sensitivity, Specificity, PPV and NPV were 94%, 49%, 25% and 98%, respectively (Table 3).

Discussion

In our study, the prevalence of PE was 15.01%. Recently, Mou et al [2] found that the overall prevalence rate of PE was 14.4%. In a recent study, the lower rate of prevalence of PE was reported in Sweden and China (3.98% and 4.02%, respectively) [1]. Mayrink et al. [21] found that PE was present in 7.5% participants. Similarly, Mishra et al. [8] also reported incidence of HDP to be 15.4% among Indian women. Overall, PE ranges from 3 to 16% and is more common in the developing countries.

The study holds importance in raising the awareness of the prevalence of PE and how a simple scoring system may be able to predict the development of PE—thereby providing an opportunity of adequate management of the patients to curb adverse outcomes associated with PE.

We found that HDP-gestosis score > = 3 carried a sensitivity of 83.1% for predicting pre-eclampsia. This remains of use since for screening such high values may hold importance from the point of view of management. Though HDP-gestosis score > = 2 carried a higher sensitivity of 94%, but the specificity fell short to 49% in comparison to HDP-gestosis score > = 3 which showed a specificity of 97.51% for predicting PE- thereby indicating that HDP-gestosis score > = 3 very accurately rules out the development of PE. Since there is a trade-off between sensitivity and specificity for an ideal screening test, HDP-gestosis score (> = 3) seems to be a better predictor for PE. However notwithstanding, preventive measures and regular monitoring may be done for the moderate risk (HDP-gestosis score = 2).

Moreover, this is the first study to practically provide a validity data for the application of gestosis score. Previously, one study by Mishra et al. [8] analysed the odds ratio for individual factor of gestosis score wherein factors significantly associated with PE included MAP > 85 mmHg [adjusted odds ratio (AOR): 22.03; 95% confidence interval (CI) 10.06–48.22], age > 35 years (AOR: 5.21, 95% CI

Table 3 Sensitivity, specificity, positive predictive value and negative predictive value of Gestosis score > = 3 for predicting PE

Variables	Sensitivity (95% CI)	Specificity (95% CI)	AUC (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Diagnostic accuracy (%)
Gestosis score > = 3	83.1% (72.34–90.95%)	97.51% (95.47–98.80%)	0.9 (0.87– 0.93)	85.51% (74.96–92.83%)	97.03% (94.87–98.46%)	95.35
Gestosis score > = 2	94.37% (86.20–98.44%)	48.76% (43.77–53.76%)	0.72 (0.67–0.76)	24.54% (19.56–30.09%)	98% (94.96–99.45%)	55.60

2.75–9.85), maternal hypothyroidism (AOR: 4.82; 95% CI 2.54–9.37), primi (AOR: 4.54, 95% CI 2.50–8.25) and age < 19 years (AOR: 4.04; 95% CI 2.05–8.18).

The literature search shows that one such screening scoring system is already validated in the international community which inculcate mean arterial pressure (MAP), uterine artery PI (UTPI) and serum PLGF (or PAPP-A when PLGF is not available) [22]. It also has an app https://fetalmedicine.org/research/assess/preeclampsia/first-trimester. Gestosis score differs from this in avoiding the USG or biomarkers and making the scoring easy at the grassroot level by inculcating the maternal history and baseline tests.

As per the gestosis score, three categories of scoring factors exist. Studies have individually found risk association with these factors [23–40], thereby justifying the inclusion of these factors in gestosis score.

Mechanisms underlying the increasing of odds for development of PE in association with these factors remain diverse such as arterial stiffening, compliance of uterine vessels and endothelial dysfunction, placental functioning, placental maladaptation, depletion of maternal nutrients, maternal inflammatory response, increased lipid oxidation products or decrease in the levels of antioxidants, antipaternal immune response, and genetic or epigenetic influences [27–35].

The study holds strength in validating a scoring system that can be routinely applied in the obstetric practice. The study results must be interpreted under limitations of being a single centre study with no association of fetomaternal outcomes with gestosis score.

Conclusion

In conclusion, gestosis score (> = 3) carried sensitivity, specificity, PPV, and NPV of 83.1%, 97.51%, 85.51%, and 97.03%, respectively, for predicting the development of PE. Overall, it seems to be a novel early marker with diagnostic accuracy of 95.35% for prediction of the development of PE allowing for a prompt management for the patients, thereby allowing to curb the adverse consequences.

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Declarations

Conflict of interest The authors report no conflicts of interest.

Ethical Statement The research complies with the guidelines for human studies and was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. The study was approved by the institute's ethical committee on human research of ASCOMS, Jammu (IEC/RP & T/2021/459), dated 26.06.2021.

Informed Consent Written informed consent was obtained from patients.

Human and Animals Rights None.

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