Scientific Research Publishing

Open Journal of Obstetrics and Gynecology, 2023, 13, 153-165
https://www.scirp.org/journal/ojog
ISSN Online: 2160-8806
ISSN Print: 2160-8792

Factors Predicting Transformation of Non-Severe Pre-Eclampsia into Pre-Eclampsia with Severe Features

Mohammed Mahmoud Samy[1*], Ahmed Nagy Abdul-Rahman Younis[2], Karim Mohammed Labib[1]

[1]Departmenrt of Obstetrics and Gynecology, Faculty of Medicine Ain Shams University, Cairo, Egypt
[2]Ain Shams University, Cairo, Egypt
Email: *mohammedsamy8132@gmail.com

How to cite this paper: Samy, M.M., Younis, A.N.A.-R. and Labib, K.M. (2023) Factors Predicting Transformation of Non-Severe Pre-Eclampsia into Pre-Eclampsia with Severe Features. *Open Journal of Obstetrics and Gynecology*, **13**, 153-165.
https://doi.org/10.4236/ojog.2023.132017

Received: January 2, 2023
Accepted: February 10, 2023
Published: February 13, 2023

Abstract

Background: Pre-eclampsia (PE), a complex, multisystem, pregnancy-associated hypertensive disorder, typically developing after the 20th week of gestation, that complicates 2% - 8% of pregnancies, is a leading cause of neonatal and maternal mortality and morbidity. **Aim of the Work:** To identify different factors predicting transformation of non-severe pre-eclampsia in to pre-eclampsia with severe features. **Patients and Methods:** This prospective cohort study was conducted at tertiary care hospital at Ain Shams University hospitals from June 2021 till January 2022 and performed on total of 100 patients who diagnosed as non-severe pre-eclampsia after exclusion of severity features. **Results:** The current study revealed that transformation to severe pre-eclampsia occurred in 33% of the studied cases. Body mass index (BMI), past and family histories of preeclampsia statistically were significantly higher in cases transformed into preeclampsia with severe features. Admission blood pressure, albumin dipstick, Oligohydramnios and IUGR statistically were significantly higher in cases with transformation from non-severe pre-eclampsia into pre-eclampsia with severe features. Platelet count statistically was significantly lower in cases with transformation from non-severe pre-eclampsia into pre-eclampsia with severe features **Conclusion:** Our study results identified the most important clinical risk factors for transformation to severe features of pre-eclampsia from non-severe features and provided new information on the level of risk associated with specific combinations of risk factors (BMI ≥ 35.4, admission systolic blood pressure, admission diastolic blood pressure, albumin dipstick 4+ and platelets count) with low significant diagnostic performance in predicting transformation from non-severe pre-eclampsia into pre-eclampsia with severe features.

Keywords

Pre-Eclampsia, Blood Pressure, Body Mass Index, Platelet Count

1. Introduction

Eclampsia was known as a disease of convulsions in late gestation that resolves by childbirth. With the advanced noninvasive blood pressure measurement, it was observed that those women had hypertension and proteinuria was defined as "pre-eclampsia" that now it is of high morbidity for both the mother and the fetus [1].

Nowadays, hypertensive disorders during pregnancy can exceed 10% in some population. Pre-eclampsia and eclampsia are the second or third cause of maternal morbidity and mortality [2].

WHO between 2003 and 2009 ranked hypertensive disorders as a cause of maternal mortality in the second grade, occurring in 14% of the cases [3].

The 20th week of gestation is a period of interest as it is the landmark in classification of hypertensive disorders because it is the time of the second wave of trophoblast invasion. Thus, hypertensive disorders were classified as two groups. The first one before 20 weeks of gestation and includes essential chronic or secondary hypertension. The second group which appears at or after 20 weeks of gestation includes gestational hypertension and pre-eclampsia [4].

In 2019, *the American College of Obstetricians and Gynecologists* (*ACOG*) [5] replaced the term "severe pre-eclampsia" with the term "preeclampsia with severe features" which means systolic blood pressure (SBP) ≥ 160 mmHg or diastolic blood pressure (DBP) ≥ 110 mmHg on at least 2 occasions, at least 4 hours apart after 20 weeks of gestation in a previously normotensive patient (with or without proteinuria) and the new onset of 1 or more of the following features: Symptoms including Epigastric pain, hypochondrial pain, Cerebral or visual symptoms (e.g., new-onset and persistent headaches not accounted for by alternative diagnoses and not responding to usual doses of analgesics, blurred vision, flashing lights or sparks, scotomata), Signs that included pulmonary edema and/or generalized edema and Laboratory findings in form of:

- Proteinuria ≥ 0.3 gm in a 24-hour urine specimen or protein/creatinine ratio ≥ 0.3 (mg/mg) (30 mg/mmol) in a random urine specimen or dipstick ≥ 2+ if a quantitative measurement is unavailable.
- Platelet count < 100,000/μL.
- Serum creatinine > 1.1 mg/d L (97.2 μmol/L) or doubling of the creatinine concentration in the absence of other renal disease.
- Liver transaminases at least twice the upper limit of the normal concentrations for the local laboratory [5].

So, non-severe pre-eclampsia means that systolic BP from 130 to less than 160 mmHg, diastolic BP from 80 to less than 110 mmHg and Proteinuria ≥ 0.3 gm in a

24-hour urine specimen or protein/creatinine ratio ≥ 0.3 (mg/mg) (30 mg/mmol) in a random urine specimen or dipstick ≥ 2+ if a quantitative measurement is unavailable without presence of the above-mentioned severity features [5].

In a woman with chronic hypertension, criteria for superimposed preeclampsia are new onset of proteinuria, significant end-organ dysfunction, or both after 20 weeks of gestation. For women with chronic hypertension who have proteinuria in early pregnancy, superimposed preeclampsia is defined by worsening or resistant hypertension (especially acutely) in the last half of pregnancy or development of signs or symptoms of severity [5].

Shed light on transformation of non-severe preeclampsia to PET with severe features according to different factors [age, parity, previous history of PET, BMI, Initial BP at diagnosis, quantitative albumin in urine, initial lab (PLT count, kidney function, liver enzymes) and fetal condition] will add more predictive values for PET with severe features as an advanced step in the management as selection of well equipped hospitals for admission and treatment, ICU&NICU availability, and well-trained medical staff.

The aim of study is identifying different factors predicting transformation of non-severe pre-eclampsia in to pre-eclampsia with severe features.

2. Patients and Methods

After ethical committee approval and informed consent from the patients, this prospective cohort study was conducted at tertiary care hospital at Ain Shams University hospitals from June 2021 till January 2022 and performed on total of 100 patients who diagnosed as non-severe pre-eclampsia after exclusion of severity features, with the following inclusion criteria: gestational age above 20 weeks of gestation, cases diagnosed as non-severe pre-eclampsia (SBP 130:159, DBP 80:109 & albuminuria) after exclusion of severity features which include: systolic blood pressure ≥ 160 mmHg or diastolic blood pressure ≥ 110 mmHg, symptoms of central nervous system dysfunction of new onset such as scotomata, cortical blindness, retinal vasospasm, and severe headache, hepatic abnormality (severe persistent right upper quadrant or epigastric pain or serum transaminase concentration ≥ 2 times the upper limit of the normal range, or both.), thrombocytopenia: <100,000 platelets/μL, pulmonary oedema & abruptioplacenta.

While women with vesicular mole, any cause of albuminuria rather than PE such as (chronic kidney disease, type 1 Diabetes mellitus), any liver disease, any autoimmune disease that affects blood vessels or platelet count such as (Immune thrombocytopenia, thrombocytopenic purpera, systemic Lupus Erythromatosis and rheumatoid arthritis).

2.1. Study Procedure

***The next steps were applied for all patients under the study*:**

1) ***History taking*:** A full history was taken with confirmation on (age, parity, gestational age, past history of pre-eclampsia, family history of pre-eclampsia,

preexisting auto immune disease, chronic liver disease, chronic kidney disease, diabetes mellitus, hematological disease, right hypochondrial pain, epigastric pain and headache).

2) ***General examination*****:** The patient was examined to give full comment about a. (BMI, blood pressure in 2 different occasions at least 4 hours apart) b. Chest and heart examination. **Abdominal examination:** a) Gestational age b) Fetal weight, amount of liquor, fetal lie and presentation, fetal heart sounds c) Uterine contractions and scar of previous surgeries.

3) ***Laboratory investigations*****:** (Urine analysis, complete blood picture, Liver function tests, Kidney function tests and 24 hour urinary protein).

4) ***Radiological investigations*****:** obstetric ultrasound for assessment of fetal growth pattern and liquor volume, placenta location.

Admission and follow up of each patient under the study till delivery either for full term or for transformation in to pre-eclampsia with severe features as follows: Hospitalization, measuring blood pressure twice daily, labs (CBC, AST, ALT, Creatinine, 24 hour urinary protein) and fetal imaging twice weekly. The mother about symptoms and signs (persistant headache, blurring of vision, epigastric pain, vaginal bleeding) indicating an increase in the severity of the disease and the need to inform a member of the medical staff immediately.

2.2. Ethical Considerations

The study was approved from the Ethical Committee of the Department of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University. Informed written consents will be taken from all women before recruitment in the study, and after extensive explanation and clear discussion of risks and benefits.

2.3. Sample Size

Using pass 11 program for sample size calculation, setting margin of error at 10% and confidence level at 95%, Sample size of 80 pregnant women with non-severe pre-eclampsia was needed to detect an expected 30% transformation rate from non-severe pre-eclampsia into pre-eclampsia with severe features.

2.4. Statistical Analysis

The collected data was coded, tabulated, and statistically analyzed using IBM SPSS statistics (Statistical Package for Social Sciences) software version 22.0, IBM Corp., Chicago, USA, 2013 and Microsoft Office Excel 2007.

Descriptive statistics were done for quantitative data as minimum & maximum of the range as well as mean ± SD (standard deviation) for quantitative normally distributed data, while it was done for qualitative data as number and percentage.

Inferential analyses were done for quantitative variables using Shapiro-Wilk test for normality testing, independent t-test in cases of two independent groups with normally distributed data. In qualitative data, inferential analyses for inde-

pendent variables were done using Chi square test for differences between proportions and Fisher's Exact test for variables with small expected numbers. The level of significance was taken at p-value < 0.050 is significant, otherwise is non-significant.

3. Results

Tables 1-3 show that: Transformation from non-severe pre-eclampsia into pre-eclampsia with severe features occurred in about one third of the studied cases.

Table 1. Baseline demographic characteristics of the studied cases.

Characteristics		Mean ± SD	Range
Age (years)		32.0 ± 5.9	19.0 - 42.0
BMI (kg/m^2)		33.6 ± 6.4	22.1 - 44.7
Gestational age of diagnosis of non severe preeclampsia (in weeks)		30.2 ± 2.8	24.0 - 35.0
		N	%
Parity	Nulli para	38	38.0
	Multi para	62	62.0
Past history of PET		34	34.0
Family history of PET		18	18.0

Total = 100.

Table 2. Baseline clinical characteristics of the studied cases.

Characteristics		Mean ± SD	Range
Admission SBP (mmHg)		135.8 ± 7.2	120.0 - 155.0
Admission DBP (mmHg)		84.4 ± 8.0	60.0 - 105.0
Platelets (×10^3/mL)		204.9 ± 72.2	107.0 - 416.0
AST (U/L)		42.3 ± 27.3	5 - 70
ALT (U/L)		46.0 ± 29.8	5 - 80
Creatinine (mg/dL)		0.8 ± 0.1	0.5 - 1.1
		N	%
Albumin dipstick	2+	53	53.0
	3+	37	37.0
	4+	10	10.0
24-hour albumin (gm)		2.0 ± 1.2	0.4 - 5.0
Oligohydramnios		18	18.0
IUGR		23	23.0

Total = 100.

Table 4 shows that: BMI, past and family histories of pre-eclampsia statistically were significantly higher in cases with transformation from non-severe pre-eclampsia into pre-eclampsia with severe features.

Table 5 shows that: Admission blood pressure, albumin dipstick, Oligohydramnios and IUGR statistically were significantly higher in cases with transformation from non-severe pre-eclampsia into pre-eclampsia with severe features. Platelet count statistically was significantly lower in cases with transformation from non-severe pre-eclampsia into pre-eclampsia with severe features.

Table 6 shows that: Only BMI, Gestational age at diagnosis, admission SBP, admission DBP and platelet count statistically had low significant diagnostic performance in predicting transformation of non severe pre-eclampsia into pre-eclampsia with severe features. Other parameters had no predictive value.

Table 7 shows that: BMI ≥ 35.4 kg/m^2 had highest sensitivity and negative predictive value, albumin dipstick 4+ had highest Specificity and positive predictive value, while Platelet count ≥ 163.0 × 10^3/mL had highest diagnostic accuracy and Youden's index.

Table 8 and Figure 1 & Figure 2 show that: number of baseline risks statistically had significant moderate diagnostic performance in predicting transformation from non-severe pre-eclampsia into pre-eclampsia with severe features.

Table 9 shows that: number of baseline risks ≥ 2 had high sensitivity and positive predictive values and low other characteristics, while ≥ 6 had high specificity and negative predictive values. Number of baseline risks ≥ 2 had higher Youden's

Table 3. Transformation of non severe preeclampsia to preeclampsia with severe features.

Findings	N	%
Transformed into PET with severe features	33	33.0
Delivery ≥ 37 wks of gestation without transformation	67	67.0

Total = 100.

Table 4. Comparison according to transformation from non-severe pre-eclampsia into pre-eclampsia with severe features regarding baseline demographic characteristics.

Characteristics		Transformation from non-severe pre-eclampsia into pre-eclampsia with severe features		p-value
		Positive (N = 33)	Negative (N = 67)	
Age (years)		32.0 ± 6.1	32.1 ± 5.9	^0.944
BMI (kg/m^2)		36.0 ± 6.8	32.4 ± 5.8	^0.007*
Parity	Nulli	15 (45.5%)	23 (34.3%)	#0.281
	Multi	18 (54.5%)	44 (65.7%)	
Past history of PET		16 (48.5%)	18 (26.9%)	#0.032*
Family history of PET		10 (30.3%)	8 (11.9%)	#0.025*

^Independent t-test. #Chi square test. *Significant.

Table 5. Comparison according to transformation from non-severe pre-eclampsia into pre-eclampsia with severe features regarding baseline clinical characteristics.

Characteristics		Transformation from non-severe pre-eclampsia into pre-eclampsia with severe features		p-value
		Positive (N = 33)	Negative (N = 67)	
Admission SBP (mmHg)		138.9 ± 8.8	134.3 ± 5.8	^0.008*
Admission DBP (mmHg)		88.0 ± 7.7	82.6 ± 7.7	^0.001*
Platelets ($\times 10^3$/mL)		181.3 ± 65.1	216.5 ± 73.1	^0.021*
AST (U/L)		44.2 ± 23.8	41.3 ± 29.0	^0.620
ALT (U/L)		46.2 ± 31.3	45.9 ± 29.3	^0.957
Creatinine (mg/dL)		0.8 ± 0.2	0.8 ± 0.1	^0.226
24-hour albumin (gm)		2.2 ± 1.5	1.9 ± 1.1	^0.266
Albumin dipstick	2+	16 (48.5%)	37 (55.2%)	#0.003*
	3+	9 (27.3%)	28 (41.8%)	
	4+	8 (24.2%)	2 (3.0%)	
Oligohydramnios		10 (30.3%)	8 (11.9%)	#0.025*
IUGR		12 (36.4%)	11 (16.4%)	#0.026*

^Independent t-test. #Chi square test. *Significant.

Table 6. Diagnostic performance of different baseline characteristics in predicting transformation from non-severe pre-eclampsia into pre-eclampsia with severe features.

Factors	AUC	SE	p-value	95% CI	Cut point
Age	0.497	0.063	0.965	0.374 - 0.620	NA
BMI	0.669	0.062	0.006*	0.548 - 0.790	≥35.4
Gestational age at diagnosis of non severe PET	0.683	0.054	0.003*	0.577 - 0.789	≤30.0
Admission SBP	0.642	0.061	0.021*	0.522 - 0.763	≥138.0
Admission DBP	0.688	0.055	0.002*	0.579 - 0.796	≥87.0
Platelets	0.668	0.060	0.006*	0.550 - 0.786	≥163.0
AST	0.555	0.060	0.371	0.437 - 0.673	NA
ALT	0.480	0.065	0.744	0.353 - 0.607	NA
Creatinine	0.564	0.066	0.303	0.434 - 0.693	NA
24-hour albumin	0.534	0.067	0.580	0.404 - 0.665	NA

NA: Not applicable. AUC: Area under curve, SE: Standard error, CI: Confidence interval, *significant.

Index than ≥ 6.

4. Discussion

Pre-eclampsia (PE), a complex, multisystem, pregnancy-associated hypertensive

disorder, typically developing after the 20th week of gestation, that complicates 2% - 8% of pregnancies, is a leading cause of neonatal and maternal mortality and morbidity [6].

Table 7. Diagnostic characteristics of baseline characteristics cut points in predicting transformation from non-severe pre-eclampsia into pre-eclampsia with severe features.

	BMI ≥ 35.4	GA at diagnosis ≤ 30 weeks	Past history	Family history	Albumin dipstick 4+
Sensitivity	66.7%	84.8%	48.5%	30.3%	24.2%
Specificity	67.2%	41.8%	73.1%	88.1%	97.0%
DA	67.0%	56.0%	65.0%	69.0%	73.0%
YI	33.8%	26.6%	21.6%	18.4%	21.3%
PPV	50.0%	41.8%	47.1%	55.6%	80.0%
NPV	80.4%	84.8%	74.2%	72.0%	72.2%
LR+	2.03	1.46	1.80	2.54	8.12
LR−	0.50	0.36	0.70	0.79	0.78
DOR	4.09	4.02	2.56	3.21	10.40
	Oligohydramnios	**IUGR**	**Admission SBP ≥ 138.0**	**Admission DBP ≥ 87.0**	**Platelets ≥ 163.0**
Sensitivity	30.3%	36.4%	39.4%	39.4%	54.5%
Specificity	88.1%	83.6%	85.1%	85.1%	80.6%
DA	69.0%	68.0%	70.0%	70.0%	72.0%
YI	18.4%	19.9%	24.5%	24.5%	35.1%
PPV	55.6%	52.2%	56.5%	56.5%	58.1%
NPV	72.0%	72.7%	74.0%	74.0%	78.3%
LR+	2.54	2.21	2.64	2.64	2.81
LR−	0.79	0.76	0.71	0.71	0.56
DOR	3.21	2.91	3.71	3.71	4.98

CI: Confidence interval. DA: Diagnostic accuracy. YI: Youden's Index. PPV: Positive Predictive value. NPV: Negative Predictive value. LR+: Positive likelihood ratio. LR−: Negative likelihood ratio. DOR: Diagnostic odds ratio.

Table 8. Diagnostic performance of number of baseline risks in predicting transformation from non-severe pre-eclampsia into pre-eclampsia with severe features.

Factors	AUC	SE	p-value	95% CI	Cut point
Number of risks	0.823	0.044	<0.001*	0.737 - 0.909	≥2, ≥6

NA: Not applicable. AUC: Area under curve, SE: Standard error, CI: Confidence interval, *significant.

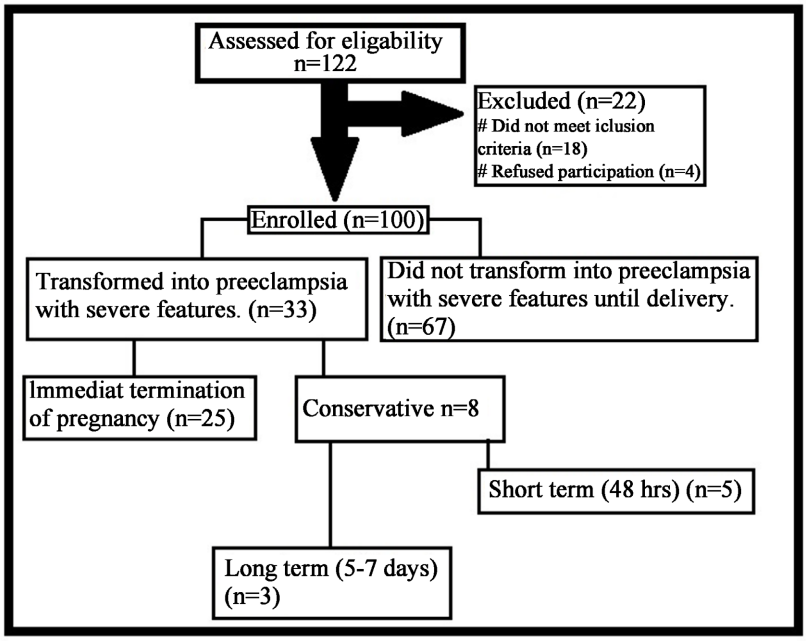

Figure 1. Flow diagram of the studied cases.

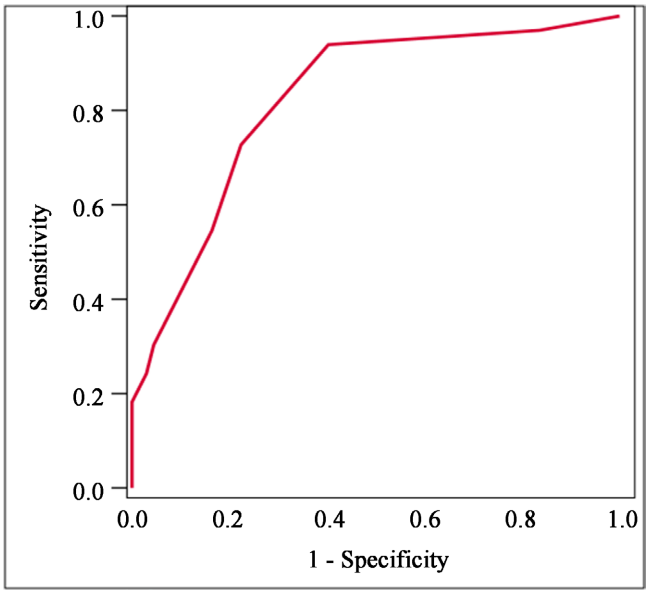

Figure 2. ROC curve for number of baseline risks in predicting transformation from non-severe pre-eclampsia into pre-eclampsia with severe features.

Table 9. Diagnostic characteristics of number of baseline risks cut points in predicting transformation from non-severe pre-eclampsia into pre-eclampsia with severe features.

Characters	Number ≥ 2		Number ≥ 6	
	Value	95% CI	Value	95% CI
Sensitivity	93.9%	79.8% - 99.3%	30.3%	15.6% - 48.7%
Specificity	59.7%	47.0% - 71.5%	95.5%	87.5% - 99.1%
DA	71.0%	61.1% - 79.6%	74.0%	64.3% - 82.3%

Continued

Youden's index	53.6%	39.4% - 67.9%	25.8%	9.4% - 42.3%
PPV	53.4%	39.9% - 66.7%	76.9%	46.2% - 95.0%
NPV	95.2%	83.8% - 99.4%	73.6%	63.0% - 82.4%
LR+	2.33	1.72 - 3.16	6.77	2.00 - 22.95
LR−	0.10	0.03 - 0.39	0.73	0.58 - 0.92
DOR	22.96	5.07 - 104.05	9.28	2.34 - 36.70

CI: Confidence interval. DA: Diagnostic accuracy. PPV: Positive Predictive value. NPV: Negative Predictive value. LR+: Positive likelihood ratio. LR−: Negative likelihood ratio. DOR: Diagnostic odds ratio.

Recent guidelines from the National Institute for Health and Clinical Excellence (NICE) also recommend routine screening for specific risk factors for pre-eclampsia (nulliparity, older age, high body mass index (BMI), family history of pre-eclampsia, underlying renal disease or chronic hypertension, multiple pregnancy, more than 10 years between pregnancies, and a personal history of pre-eclampsia) [7].

The expected rate of pre-eclampsia when any one of these risk factors is present ranges from 3% to more than 30%, and many women have several risk factors. The absolute risk for an individual will be determined by the presence or absence of these and other predisposing or protective factors not incorporated in the NICE guidelines [8].

Since prediction of pre-eclampsia represents major conflict and often associated with an increased risk of both short- and long-term complications for both the mother and the neonate, a predictive model for preeclampsia based on clinical risk factors for women and to identify a subgroup at increased risk was highlighted as a main point of interest, in order to start low dose aspirin early in pregnancy at 12 weeks according to guidelines [6].

This Prospective Cohort study was conducted at tertiary care hospital at Ain Shams University hospitals from June 2021 till January 2022 and performed on total of 100 patients who diagnosed as non-severe pre-eclampsia after exclusion of severity features.

This study was approved by ethical committee before start of the recruitment and registered on clinical.trial.gov and has the following ID: NCT05152550.

During this study, 122 patients were assessed for eligibility and 100 patients were included in the study. Of all eligible patients, 18 patients were excluded from the study based on the inclusion criteria and 4 patients refused to participate in of the study.

Ultimately, the analysis was based on the data of 100 patients diagnosed with non-severe pre-eclampsia after exclusion of severity features.

To the best of our knowledge, data regarding clinical factors for prediction of transformation of mild features to severe features of pre-eclampsia are very limited and conflicting. Thus, the present study was conducted and aimed to

identify different factors predicting transformation of non-severe pre-eclampsia in to pre-eclampsia with severe features.

Most of the previous literature used combinations of biomarkers with clinical factors in diagnostic performance in predicting pre-eclampsia, while our study used clinical factors only for prediction of transformation of non-severe PE into PE with severe features.

The current study revealed that transformation into pre-eclampsia with severe features occurred in 33% of the studied cases and BMI, past and family histories of preeclampsia statistically were significantly higher in cases with severe PE transformation (p-values = 0.007, 0.032, 0.025) respectively.

These findings are in agreement with previous studies. *North et al.* (2011) conducted a prospective multi-center cohort study that enrolled 3572 women with a singleton pregnancy from a large international study to develop multivariable predictive models for pre-eclampsia (based on clinical risk factors present in early pregnancy alone or in combination with ultrasound estimates of uteroplacental perfusion and fetal measurements at 19 - 21 weeks' gestation) and determine their performance to predict pre-eclampsia as a baseline for future external validation [7].

North et al. (2011) revealed that there was statistically significant correlation between increased BMI (≥30) with development of severe preeclampsia ($p < 0.001$) [7].

In contrast to our results, *North et al.* (2011) revealed that younger maternal age (mean 28.1 (SD 5.8) and lower socioeconomic index are significant risk factors for development of severe preeclampsia ($p < 0.001$) [7].

Poon et al. (2010) conducted a prospective study that included 9149 singleton pregnancies to develop prediction algorithms for hypertensive disorders based on multivariate analysis of factors from the maternal history and compare the estimated performance of such algorithms in the prediction of early preeclampsia (PE), late-PE and gestational hypertension [9].

Poon et al. (2010) reported that increased maternal age and BMI are associated with increased risk for late-Pre-eclampsia and Gestational Hypertension and the risk for late-PE and GH increases by 4% for every year over the age of 32 years and by 10% for every 1 kgm_2 above 24 kgm_2 for BMI [9].

Our study results revealed that admission blood pressure, albumin dipstick, Oligohydramnios and IUGR statistically were significantly higher in cases with transformation of non severe pre-eclampsia into pre-eclampsia with severe features. Platelets statistically were significantly lower in cases with transformation of non severe pre-eclampsia into pre-eclampsia with severe features (*p-value* < 0.05).

In concordance with our results, *North et al.* (2011) revealed that there was statistically significant correlation between development of severe preeclampsia and SGA, low birth weight, higher blood pressure and 24 hour urinary protein excretion of 0.78 g [7].

Our study results revealed that only admission gestational age, BMI, admission SBP, admission DBP and platelets statistically had low significant diagnostic

performance in predicting transformation of non severe pre-eclampsia into pre-eclampsia with severe features and the reported performance of clinical risk factors to predict pre-eclampsia is modest, with an AUC (area under the curve) in the order of 0.642 to 0.669.

Consequently, BMI ≥ 35.4 kg/m^2 had highest sensitivity and negative predictive value, albumin dipstick 4+ had highest Specificity and positive predictive value, while Platelets < 163.0 × 10^3/mL had highest diagnostic accuracy and Youden's index and Number of baseline risks ≥ 2 had high sensitivity and positive predictive values and low other characteristics, while ≥ 6 had high specificity and negative predictive values. Number of baseline risks ≥ 2 had higher Youden's Index than ≥ 6.

North et al. (2011) revealed that the algorithm that included well recognized clinical risk factors of (blood pressure, BMI, and a family history of pre-eclampsia) along with less established factors, such as maternal low birth weight, and the woman's father having coronary artery disease, had moderate predictive performance—the area under the receiver operating characteristics curve (AUC) was 0.76—and detected 37% and 61% of women who developed pre-eclampsia with a false positive rate of 10% and 25%, respectively [7].

Myers et al. (2013) conducted a Prospective multicentre cohort study that included 3529 women to assess the performance of clinical risk factors, uterine artery Doppler and angiogenic markers to predict preterm pre-eclampsia in women [10].

Neither the addition of biomarkers of soluble endoglin (sEng) nor soluble fms-like tyrosine kinase-1 (sFlt-1) to clinical risk factors alone or in combination with PlGF further improved prediction of preterm pre-eclampsia. Also, neither uterine artery Doppler at 20 weeks, nor uterine artery Doppler with 20-week endoglin added to the predictive performance of the combination of 15-week clinical risk factors and PlGF levels [10].

The strength points of this study:

The strength points of this study are that it is prospective study design and having no patients lost to follow-up during the study. It is the first study in Ain Shams Maternity Hospital to predict the transformation of non-severe PET to PET with severe features.

The limitations of the study:

The limitations of the study are worthy of mention including relatively smaller sample size relative to the previous studies, not being a multicentric study and this represents a significant risk of publication bias. Another limitation is the lack of follow-up of biomarkers and Doppler studies which may improve the identification of women at increased risk of developing severe features of preeclampsia, and the diagnostic performance as a clinical screening test. Presence of pandemic COVID-19 limits the recruitment of pregnant women.

5. Conclusions

As evident from the current study, our study results identified the most impor-

tant clinical risk factors for transformation to severe features of pre-eclampsia from non-severe features and provided new information on the level of risk associated with specific combinations of risk factors (BMI ≥ 35.4, admission SBP, admission DBP, albumin dipstick 4+ and platelet count) with low significant diagnostic performance in predicting transformation from non-severe pre-eclampsia into pre-eclampsia with severe features.

Number of baseline risks ≥ 2 had high sensitivity and positive predictive values and low other characteristics, while ≥ 6 had high specificity and negative predictive values.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Chesley, L. (2015) Chesley's Hypertensive Disorders in Pregnancy. 4th Edition, Elsevier.

[2] Moussa, H.N., Arian, S.E. and Sibai, B.M. (2014) Management of Hypertensive Disorders in Pregnancy. *Women's Health Journal*, **10**, 385-404. https://doi.org/10.2217/WHE.14.32

[3] Say, L., Chou, D. and Gemmill, A (2014) Global Causes of Maternal Death: A WHO Systematic Analysis. *The Lancet Global Health*, **2**, e323-e333. https://doi.org/10.1016/S2214-109X(14)70227-X

[4] Bokslag, A., van Weissenbruch, M., Mol, B.W. and de Groot, C.J.M. (2016) Preeclampsia: Short and Long-Term Consequences for Mother and Neonate. *Early Human Development*, **102**, 47-50. https://doi.org/10.1016/j.earlhumdev.2016.09.007

[5] American College of Obstetricians and Gynecologists (ACOG) (2019) ACOG Practice Bulletin No. 203: Chronic Hypertension in Pregnancy. *Obstetrics and Gynecology*, **133**, e26-e50. https://doi.org/10.1097/AOG.0000000000003020

[6] Giannakou, K. (2021) Prediction of Pre-Eclampsia. *Obstetric Medicine*, **14**, 220-224. https://doi.org/10.1177/1753495X20984015

[7] North, R.A., McCowan, L.M. and Dekker, G.A. (2011) Clinical Risk Prediction for Pre-Eclampsia in Nulliparous Women: Development of Model in International Prospective Cohort. *BMJ*, **342**, d1875. https://doi.org/10.1136/bmj.d1875

[8] Snydal, S. (2014) Major Changes in Diagnosis and Management of Preeclampsia. *Journal of Midwifery & Women's Health*, **59**, 596-605. https://doi.org/10.1111/jmwh.12260

[9] Poon, L.C., Kametas, N.A., Chelemen, T., Leal, A. and Nicolaides, K.H. (2010) Maternal Risk Factors for Hypertensive Disorders in Pregnancy: Amultivariate Approach. *Journal of Human Hypertension*, **104**, 104-110. https://doi.org/10.1038/jhh.2009.45

[10] Myers, J.E., Kenny, L.C., McCowan, L.M., Chan, E.H., Dekker, G.A., Poston, L., Simpson, N.A., North, R.A. and SCOPE Consortium (2013) Angiogenic Factors Combined with Clinical Risk Factors to Predict Preterm Pre-Eclampsia in Nulliparous Women: A Predictive Test Accuracy Study. *BJOG*, **120**, 1215-1223. https://doi.org/10.1111/1471-0528.12195