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Original Research Article

Study of prognostic significance of platelet count as a predictor of severity of preeclampsia

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ABSTRACT

Background: Pre-eclampsia is a pregnancy-specific syndrome, recognised from antiquity as a leading cause of maternal and perinatal mortality, and it accounts for almost 15% of pregnancy associated death. Hence, the current study was planned to assess the role of platelet count as a predictor of the severity of preeclampsia and its prognosis.
Methods: In this retrospective analytical study, a total of 100 pregnant women with preeclampsia were included and divided into two groups of non-severe and severe. Demographic data, socio-economic status, period of gestation and platelet count were recorded and compared.
Results: The average age of patients was 27.07±5.14 years, with no significant difference between patients based on preeclampsia severity. Most of the patients were multigravida females (69%). The distribution based on the socio-economic status was similar, with no significant difference ($p>0.05$). The average period of gestation was 36.01±3.41 weeks in the study. The average platelet count of patients with severe preeclampsia at the time of admission was seen to be lower compared to the non-severe patients. A ROC curve analysis was done to assess the ability of platelet count to differentiate severe PWE from non-severe PE. The area under the curve was high at 0.879. The LSCS rate was 54% in the study, followed by Pre-term birth seen in 48% of patients. There was no significant difference between the two groups in terms of maternal outcome parameter-based distribution. The proportion of patients with APGAR score <7 at 5 minutes was significantly higher in the non-severe PE group. It was seen that preeclamptic patients were associated with a significantly higher prevalence of pre-term birth and Ante partum haemorrhage (APH).
Conclusions: Platelet count is an accurate predictor of severe preeclampsia in pregnant females. The patients with low platelet counts were associated with significantly higher adverse pregnancy outcomes, as suggested by a significantly higher prevalence of pre-term birth, APH and rate of LSCS.

Keywords: Pre-eclampsia, Platelet count, Gravida, Antepartum haemorrhage, Cesarian section

INTRODUCTION

Preeclampsia is a pregnancy-specific syndrome, recognised from antiquity as a leading cause of maternal and perinatal mortality, and it accounts for almost 15% of pregnancy associated death. Hippocrates, the "father of western medicine," had observed the sudden and unexpected appearance of maternal grand-mal seizures, which occur when Pre-eclampsia progresses to eclampsia, the word being derived from the Greek for "lightning". It was believed for many centuries that preeclampsia was a seizure disorder unique to pregnancy, but during the last 200 years, this view of the disease has changed drastically. Several new findings have led to this change in opinion.[1] Various studies revealed that preeclampsia occurs because of endothelial dysfunction and vasospasm.

Endothelial dysfunction occurs due to oxidative stress and release of inflammatory mediators while vasospasm results from the imbalance of vasodilators (PGI2, NO) and vasoconstrictors (Angiotensin II, TXA2, Endothelin 1).[2-4] It occurs in 10% of first pregnancies and in 20-25% of women with a history of chronic hypertension.[5] WHO estimates the incidence of preeclampsia to be seven times higher in developing countries (2.8% of live births) than in developed countries (0.4%).[6] In India, the incidence of preeclampsia is reported to be 8-10% among pregnant women.[7]

According to ACOG-2013 task force, the diagnosis of preeclampsia has been made by the presence of hypertension and proteinuria after 20 weeks of gestation in a previously normotensive patient. Maternal and perinatal outcome in preeclampsia is usually dependent on gestational age at onset of preeclampsia as well as at time of delivery, the severity of the disease process, the presence of multifetal gestation, and the presence of pre-existing medical conditions such as pregestational diabetes, renal disease, or thrombophilia.

Perinatal mortality and morbidity, as well as the rates of abruptio placentae are substantially increased in women with severe preeclampsia.[8] To prevent maternal and foetal complication of preeclampsia, early prediction of preeclampsia is necessary. Out of all the haematological changes that occur in preeclampsia and eclampsia, thrombocytopenia is the most common haematological abnormality found, and it affects 7-10% of the cases.[9,10]

Though the previous studies show an association between platelet count and preeclampsia, severity of disease and platelet count in women having preeclampsia still requires further exploration. Hence, the current study was planned to assess the role of platelet count as a predictor of the severity of preeclampsia and its prognosis.

METHODS

This retrospective analytical study was carried out at the Department of Obstetrics and Gynaecology, Era's Lucknow Medical College & Hospital, Lucknow, after obtaining approval from the Institutional Ethical Committee and informed consent. During 2019-2022, a total of 100 patients were taken up into two groups by randomization. Group I: Non-severe. Group II: Severe.

One hundred women with preeclampsia were included in this study. However, pregnant women with hypertension before 20 weeks gestation and women with pre-existing: - renal disease, liver disorder, epilepsy, cardiac disease, and gestational thrombocytopenia were excluded. Their general and clinical data were included in the proforma. As per inclusion criteria data has been collected retrospectively in a pre-designed proforma from 1st January 2017 to 31st December 2019.

Platelet count has been noted at the time of admission for all patients from the case records. Repeat platelet count has been noted for patients who progressed from non-severe pre-eclampsia to severe pre-eclampsia. Changes in the value of platelet count has been associated with the severity of pre-eclampsia and its prognosis.

Statistical analysis

The data was compiled and analysed using MS Excel (R) office 365, GraphPad prism 8.4.2 and SPSS version 25.

Descriptive statistics were presented in the form of proportions/percentages for categorical variables and mean and standard deviation for continuous data variables Fisher Exact test/Chi square test was used for the comparison of proportions (Categorical variables). Continuous variables were analyzed using the Mann-Whitney test/student T-test (Independent group/Unpaired data) and Wilcoxon sign rank test/Paired T-test (for paired data) based on the normality of the data. A ROC analysis was performed to assess the diagnostic ability of platelet count in differentiating severe pre-eclampsia from the non-severe preeclampsia. Area under the curve was calculated and optimal cut off was reached using the sensitivity and specificity parameters using a contingency table.

Diagnostic accuracy of the optimal cut-off, along with specificity, sensitivity, negative predictive value, and positive predictive value, were assessed using standard definitions. P value of <0.05 was considered significant.

RESULTS

The average age of patients was 27.07±5.14 years. A total of 39 patients were less than 25 years, and 61 patients were more than 25 years. Therefore, the maximum number of patients were more than 25 years of age. Maximum number of patients had a BMI of 18.5–24.9 kg/m^2. Most of the patients were multigravida females (69%). The distribution of primigravida and multigravida patients was similar, with no significant difference statistically ($p=0.3787$). The distribution based on the socio-economic status was similar with no significant difference ($p>0.05$) (Table 1). The average period of gestation was 36.01±3.41 weeks in the study.

The average platelet count of patients with severe preeclampsia at the time of admission was seen to be lower compared to the non-severe patients. The average platelet count for the non-severe group was 1.62 lakhs, while that for the severe group was 1.24 Lakhs at the time of admission. A comparison of the platelet counts of severe PE patients at progression with the platelet count at the time of admission for the non-severe group showed that the platelet count for the severe PE group was significantly lower ($p<0.0001$). The mean difference between these two levels was 70410 per cu mm (Table 2, Figure 1).

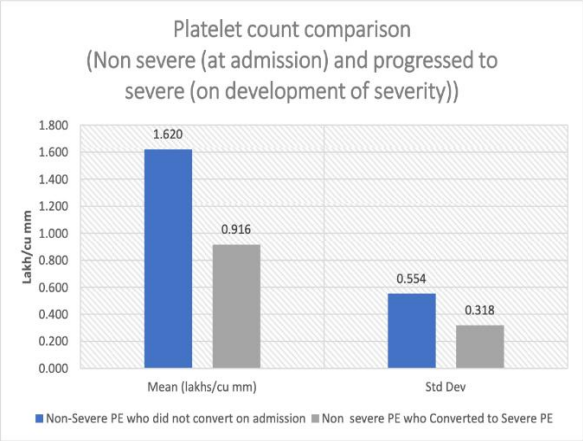

Figure 1: Distribution based on platelet count in non-severe preeclampsia vs who progressed to severe preeclampsia.

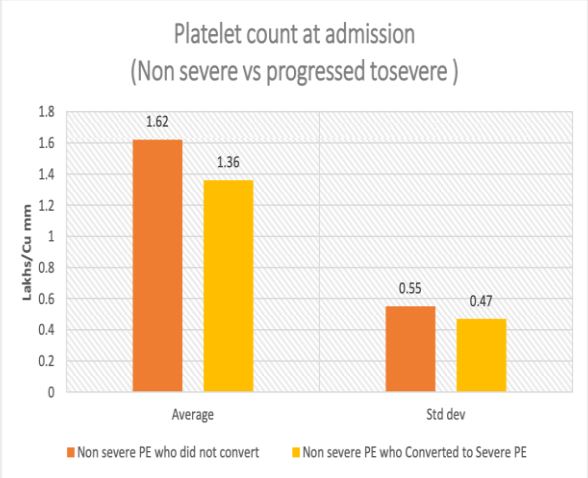

Figure 2: Platelet count on admission- non-severe PE versus converted severe PE.

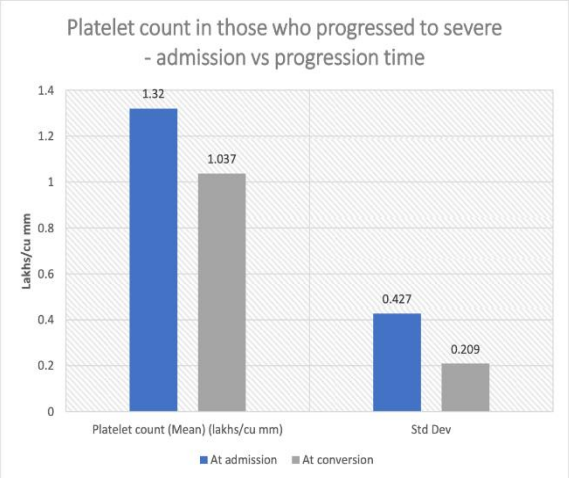

Figure 3: Platelet count based on change in the mean platelet count in cases who progressed.

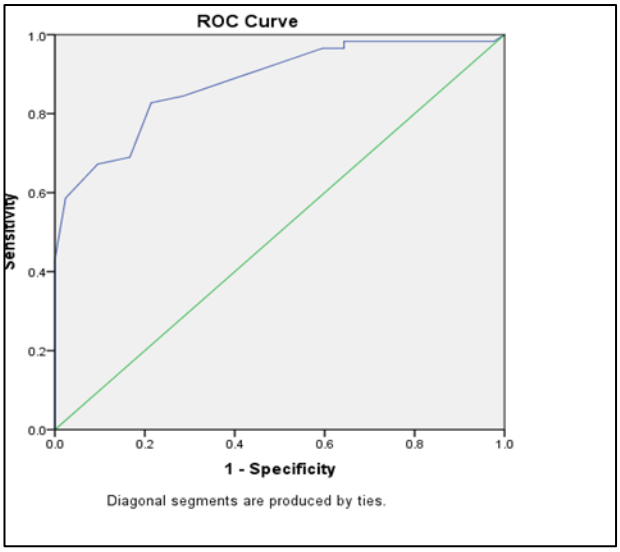

Figure 4: ROC Curve for platelet count–with severe PE as the outcome to differentiate non severe from severe pre-eclampsia.

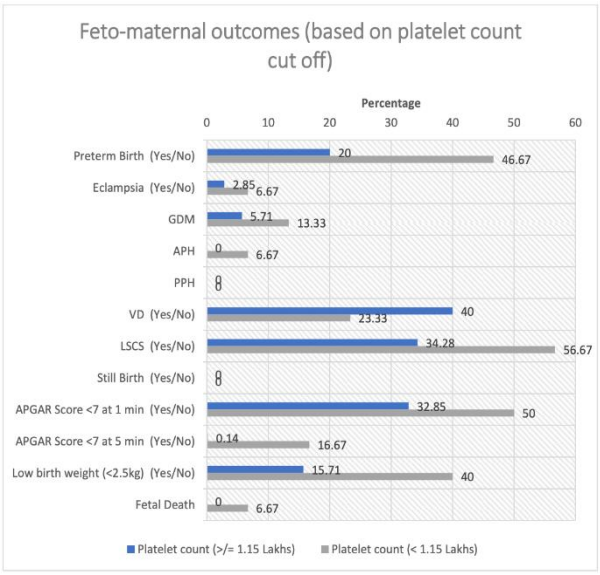

Figure 5: Feto-maternal outcomes and platelet count-based assessment.

Since there were 2 stillbirths, and one baby died in immediate neonatal period, analysis for neonatal nursery admission is done in 107 babies. There was a total of 39 babies of 107 (36.4%) who required nursery admission for observation either due to respiratory complications, metabolic complications or sepsis. The abnormal waveforms of umbilical artery and middle cerebral artery were also compared with neonatal nursery admission (Figure 1). It was seen that the platelet count for non-severe PE patients at time of admission was statistically significant (p=0.0196) (Figure 2).

The mean platelet count difference between the two groups was 37400 per cu mm. It was observed that the patients

who were severe at the time of admission had a much lower platelet count compared to those who progressed from non-severe to severe (p=0.0015). A correlation of the total severe PE with the platelet count showed that as the severity worsened from non-severe to severe, the platelet count was seen to decrease (r=-0.65). The results for the correlation were significant statistically (Table 3). It was seen that platelet count at admission was 1.32 lakhs while that at the time of progression was 1.037 lakhs. The mean fall seen at the time of progression to severe was 28,300 per cu mm. This fall in platelet count had a CI 95% of 12400 to 44200 per cumm (Figure 3).

It was seen that a higher proportion of patients with non-severe PE who progressed to severe as the platelet count worsened from >1.5 lakhs (24.25% converted) to less than 1 lakhs (60% progressed). It was also seen that proportion of patients who progressed had a lower mean platelet count on average (Table 4).

Table 1: Distribution based on age category, Socioeconomic Status, Gravida and preeclampsia severity.

		Non-severe PE	%	Severe PE	%	Total	%	P value
Age category	25 years or less	26	44.83	13	30.95	39	39	
	More than 25 years	32	55.17	29	69.05	61	61	0.1623
Socio economic status	Lower	14	24.14	7	16.67	21	21	0.3678
	Lower middle	27	46.55	17	40.48	44	44	0.5482
	Upper lower	7	12.07	9	21.43	16	16	0.2099
	Upper middle	10	17.24	9	21.43	19	19	0.5999
Gravida	Primi	20	34.48	11	26.19	31	31	0.3787
	Multi	38	65.52	31	73.81	69	69	
	Total	58	100.00	42	100.00	100	100	

Table 2: Distribution based on period of gestation and platelet count (at time of admission).

		Non-Severe PE	Severe PE	Total	P value
	Number of patients	58	42	100	
Period of gestation	Period of gestation (Mean)	36.22±3.42	35.71±3.42	36.01±3.41	0.4635
Platelet count (in lakhs) on admission	Platelet count (Mean) (lakhs/cu mm)	1.620±0.554	1.246±0.460		0.0006*

*Statistically significant

Table 3: Severe preeclampsia and platelet count correlation.

Severe preeclampsia	Platelet count
Spearman r	-0.65
95% confidence interval	-0.75 to -0.52
P value	<0.0001*

*Statistically significant

Table 4: Pre-eclampsia and platelet count severity.

Preeclampsia severity	Number	Platelet count (mean)	Std Dev
Non severe PE+ non severe who progressed to severe PE	95	1.5029	0.5287
Greater than 1.5	33	2.0758	0.4352
No	25 (75.75%)	2.1240	0.4255
Yes	8 (24.25%)	1.9250	0.4590
1 to 1.5 Lakhs	57	1.2386	0.2016
No	31(54.38%)	1.2742	0.1949
Yes	26 (45.61%)	1.1962	0.2049
Less than 1 lakh	5	0.7360	0.2151
No	2 (40%)	0.6700	0.3818
Yes	3 (60%)	0.7800	0.1114

Continued.

Preeclampsia severity	Number	Platelet count (mean)	Std Dev
On admission Severe PE	5	0.6960	0.2257
Less than 1 lakh	5	0.6960	0.2257
No	5	0.6960	0.2257
Grand Total	100	1.4626	0.5465

Table 5: Optimal cut-off of 1.15 lakhs-based analysis.

Platelet count cut off 1.15 Lakhs/cu mm	Severe PE	Non-severe PE	Grand total
<1.15 Lakhs per cu mm	33 (78.57%)	10 (17.24%)	43
1.15 and above	9 (21.43%)	48 (82.76%)	57
Grand Total	42	58	100

A ROC curve analysis was done to assess the ability of platelet count to differentiate severe from non-severe PE. It was seen that platelet count was an excellent measure for the differentiation of severe PE from non-severe cases. The area under the curve was high at 0.879. A contingency table analysis using the same cut-off was done (Table 5). The results were significant statistically ($p<0.0001$) (Figure 4). The LSCS rate was 54% in the study followed by Pre-term birth seen in 48% patients. The proportion of patients with APGAR score <7 at 5 minutes was significantly higher in the non-severe PE group compared to the severe group (32.76% vs 14.29%, $p=0.0362$). It was seen that preeclamptic patients with platelet counts less than 1.15 lakhs at admission were associated with a significantly higher prevalence of pre-term birth and APH. Both cases of foetal death were seen in these patients with admission platelet count of less than 1.15 Lakhs per cu mm (Figure 5).

DISCUSSION

Preeclampsia is one of the major health problems causing maternal morbidity and mortality, complicating 3–8% of pregnancies. It is a complex, multisystem disorder of unknown aetiology. According to the international society for the study of hypertension in pregnancy (ISSHP), PE is defined as de novo hypertension, occurring after 20 weeks of pregnancy, together with proteinuria.[11] The average age of the patients was 27.07±5.14 years, with most of the patients in the age group of 21-25 years (36%) followed by 26-30 years (33%). The proportion of patients more than 25 years of age was higher in the severe preeclampsia group of patients (69.05% vs 55.17%, $p=0.1623$).

Most of these patients in the study were housewives from lower-middle SES families showed that the females in both groups were in the age group (20–35 years).[12] The mean age of the patients with preeclampsia was 26 years, with most in the age group 26–29 years. The mean period of gestation at the time of the collection of samples in the preeclampsia group was 24 weeks, with the highest duration being 32 weeks and 48% of the patients belonging to the group 23–25 weeks. The mean age of patients in our study was slightly higher as observed by Dhakreet et al at 24.45±4.23 years and Prakash et al who reported mean age of 24.75±3.360 years respectively.[13,14]

Benjamin et al in their Nigerian study on the platelet function parameters and adverse maternal and neonatal outcomes in severe pre-eclampsia patients showed that the odds of developing eclampsia were low at higher mean platelet count and platelet crit levels above 161.36 73.74 109/l ($p<0.02$, AOR=0.27, 95% CI (0.08–0.88)) and 0.13 0.05% ($p<0.001$, AOR=0.22, 95% CI (0.08–0.58)), respectively. Eclampsia was strongly associated with p LCR (platelet-large cell ratio) above 23.15 4.92% ($p<0.004$, AOR=11.00, 95%CI (1.48–89.02)). Abruptio placentae had low odds at lower levels of mean platelet crit. Pre-term birth was significantly lower at mean platelet crit levels above 0.14 0.05%; admission into neonatal intensive care unit was strongly associated with a mean PLC ratio above 22.73 5.91%. The average platelet count for the non-severe group was 1.62 lakhs, while that for the severe group was 1.24 Lakhs at the time of admission.

The mean platelet count difference between the two groups was 37400 per cu mm. However, the average platelet count for the severe group at the time of severity assessment was 99640 per cumm. The mean difference between these two levels was 62360 per cumm. The difference aggravated further at the time of progression since the average platelet count for the severe group of progressed patients at the time of progression was 91590 per cu mm. The mean difference between these two levels was higher at 70410 per cumm.

Ruchika et al, showed that platelet count decreases while MPV and PDW increase as pregnancy advances, and these changes are more pronounced in preeclampsia than normotensive pregnancy.[13] They showed that out of 50 preeclampsia patients, 24 (48%) were of severe type, out of which 54% had platelet count <1.5 lac, 83% had PDW as 15-16 fl, and 54% had MPV in the range of 10-11 fl. In the pre-eclampsia group, 16 (32%) patients had thrombocytopenia (platelet count between 50-1.5 lac), whereas in normal pregnant patients, none of the patients had lower platelet count.

Amit et al, showed that the mean platelet count was significantly lower ($p<0.05$) in mild and severe preeclampsia than that in the normal pregnancy. Decreased platelet count in severe preeclampsia was significant compared to that in mild preeclampsia. They concluded that the frequency of thrombocytopenia was found to be directly related to the severity of disease, so platelet count can be used as a simple and cost-effective tool to monitor the progression of preeclampsia, thereby preventing complications to develop during the gestational period. Amita et al also showed similar findings where they concluded that the platelet count was a reliable indicator for diagnosing preeclampsia and predicting the severity of disease.[17]

Han et al showed that decreased platelet counts were seen as the disease progressed, but normal counts were also observed in the initial stages. They, however showed that they did not observe a significant difference between normal and mild preeclampsia and severe preeclampsia patients and suggested that decreased platelet count may be due to the gestation itself rather than the preeclampsia. Thus, the platelet count, though an important parameter in preeclampsia, cannot be used as a definitive marker for the same.[18]

Vijaya et al, concluded that estimation of platelet indices could be considered an early, simple, and rapid procedure in the assessment of the severity of preeclampsia and eclampsia, which can be used as a prognostic marker.[19] Similarly, Freitas et al showed that lower Platelet count and PCT were observed in severe preeclampsia comparing to normal pregnant ($p=0.031$ and 0.035, respectively) and to non-pregnant women ($p<0.001$ and 0.004, respectively).[20] We also observed that as the severity worsened from non-severe to severe, the platelet count was seen to decrease ($r=-0.65$).

The results for the correlation were also significant statistically. Based on ROC curve analysis, It was seen that platelet count was an excellent measure for the differentiation of severe preeclampsia from non-severe cases. The area under the curve was high at 0.879. The trends were significant statistically ($p<0.0001$). We observed that optimal platelet count cut-off was 1.15 lakhs for differentiating severe preeclampsia from non-severe preeclampsia. The sensitivity and specificity at this cut-off were 78.57% and 82.76%. The PPV and NPV were 76.74% and 84.21%.

Feven et al showed that all platelet indices showed significant increment with the severity of preeclampsia. Platelet count was negatively correlated with platelet indices.[21] There was a positive correlation among platelet indices. ROC analysis revealed that MPV had the largest area under the ROC curve (0.85; 95% CI (0.79, 0.89)) with cut off value >9.45 fl, the sensitivity of 83.5%, specificity of 86.4%, positive predictive value of 77.6% and negative predictive value of 90.3%. Patient with mild preeclampsia had an average age of 25.20±3.5 years and patients with severe preeclampsia had an average age of 25.64±5.26 years.

Their analysis also showed that platelet could differentiate normotensive pregnant women from preeclamptic pregnant women at a cut-off value <233×109/l (compared to 1.15 Lakhs in our study) with sensitivity of 70.9% and specificity of 83.9%. The area under the curve for platelet count was 0.77 (0.879 in our study). Their analysis was for differentiating preeclamptic from normotensive patients, while in our study, the platelet count was used as a marker to differentiate severe preeclampsia from the non-severe pre-eclampsia.

Shiva et al, in their study on pre-eclampsia cases where there was no thrombocytopenia, showed that even in the absence of thrombocytopenia, mean platelet volume (MPV) and PLT distribution width were significantly higher in severe preeclampsia group ($p<0.001$) and were also positively correlating with mean arterial pressure ($r=0.38$ and 0.20, respectively).[22] These results are relatively closer to the study by Alkholya et al, Freitas et al, in their analysis using the ROC curve, showed that the parameters have regular diagnostic significance, except for PCT, which was not considered as good for preeclampsia identification purpose.[11,20] The area under the curve analysis showed that platelet count and PDW had the highest AUC levels at 0.73 and 0.77.

Some of the limitations of our study were that there was no comparison with the normotensive control group, the study was a retrospective analysis, factors which could be assessed in a prospective study along with long-term follow-up were not done in this study, and other platelet indices like Platelet crit, MPV and PDW were not assessed. The objective findings of our study need to be validated by larger studies for generalized applicability.

CONCLUSION

Platelet count is an accurate predictor of severe preeclampsia in pregnant females. High Platelet count was associated with high AUC and it was seen that the platelet counts for the severe disease patients were significantly lower compared to the non-severe group when compared at the time of admission or progression to severity. The patients with low platelet counts were associated with significantly higher adverse pregnancy outcomes, as suggested by significantly higher prevalence of pre-term birth, APH and rate of LSCS.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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