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THROMBOELASTOGRAPHIC ASSESSMENT OF COAGULATION DYNAMICS IN NORMAL PREGNANCY AND GESTATIONAL HYPERTENSION: ESTABLISHMENT OF REFERENCE INTERVALS AND DIAGNOSTIC IMPLICATIONS IN A SOUTH INDIAN COHORT

Dr. Amizhthu R. A[1], Dr. D. Mohan Srinivasan[2], Dr. A. Thangadurai[3], Dr. N. Basker[4]

[1]Assistant Professor, Institute of Anaesthesiology and Critical Care, Madras Medical College, Chennai – 600002, India; Email: amizhthu@mmc.ac.in; ORCID iD: 0009-0006-2328-7843.
[2]Assistant Professor, Institute of Anaesthesiology and Critical Care, Madras Medical College, Chennai – 600002, India; Email: drmohan1202@gmail.com. ORCID Id 0009-0005-7151-3721
[3]Assistant Professor, Department of Anaesthesiology, Institute of Social Obstetrics and Kasturba Gandhi Hospital for Women and Children, Madras Medical College, Chennai – 600002, India; Email: thangaduraidurai90@gmail.com. Orcid ID -0009-0008-8510-8796
[4]Head of the Department, Department of Anaesthesiology, Institute of Social Obstetrics and Kasturba Gandhi Hospital for Women and Children, Madras Medical College, Chennai – 600002, India; Email: drbaskigvmch@gmail.com.

ABSTRACT

Background: Pregnancy is characterized by a physiological hypercoagulable state resulting from alterations in coagulation and fibrinolytic pathways. These changes are further accentuated in hypertensive disorders such as gestational hypertension (GH), predisposing patients to thrombotic complications. Conventional coagulation tests provide limited insight into dynamic clot formation, whereas thromboelastography (TEG) offers a comprehensive real time assessment of hemostasis.

Objectives: To establish reference intervals for TEG parameters in normal third-trimester pregnancy among South Indian women and to evaluate the diagnostic efficacy of TEG in detecting coagulation alterations in patients with gestational hypertension.

Methods: This prospective observational study included 100 pregnant women in the third trimester, divided into two groups: normal pregnancy (Group N, n=50) and gestational hypertension (Group G, n=50). Venous blood samples were analyzed using TEG (TEG 5000 analyzer) to measure parameters including reaction time (R), clot formation time (K), alpha angle (α), maximum amplitude (MA), G value, and estimated percent lysis (EPL). Conventional coagulation parameters (platelet count, PT, INR) were also assessed. Statistical analysis was performed using SPSS v 26.0.

Results: Gestational hypertension was associated with a hypercoagulable profile characterized by significantly reduced R time (1.966 vs. 4.184 min) and K time (1.228 vs. 1.578 min), along with increased alpha angle (72.98° vs. 67.58°), MA (68.45 vs. 62.81 mm), and G value (11.92 vs. 8.69), compared to normal pregnancy. Conventional parameters (PT and INR) showed only minimal differences between groups. Moderate correlations were observed between TEG parameters and PT/INR in the hypertensive group, indicating enhanced sensitivity of TEG in detecting coagulation dynamics.

Conclusion: Thromboelastography demonstrated superior capability in identifying hypercoagulable states in gestational hypertension compared to conventional coagulation tests. Establishing pregnancy-specific reference intervals enhances its clinical applicability and may aid in early detection and targeted management.

KEYWORDS: Thromboelastography; Gestational Hypertension; Pregnancy; Hypercoagulability; Coagulation Dynamics; Diagnostic Accuracy; Reference Intervals.

INTRODUCTION

Pregnancy is associated with significant physiological adaptations, particularly within the hemostatic system, resulting in a well-recognized hypercoagulable state. This state is characterized by increased levels of procoagulant factors, including fibrinogen and clotting factors VII, VIII, IX, and X, along with a reduction in natural anticoagulants such as protein S and antithrombin. Additionally, fibrinolytic activity is suppressed due to elevated levels of plasminogen activator inhibitors. These changes are essential for minimizing blood loss during delivery; however, they simultaneously increase the risk of thromboembolic complications [3,4].

Gestational hypertension, defined as new-onset hypertension after 20 weeks of gestation in a previously normotensive woman, further accentuates these hemostatic alterations. The underlying pathophysiology involves endothelial dysfunction, abnormal placentation, and systemic inflammatory activation, which collectively contribute to enhanced platelet activation, increased thrombin generation, and reduced fibrinolysis. Consequently, patients with gestational hypertension are at increased risk of complications such as placental abruption, intrauterine growth restriction, and disseminated intravascular coagulation [1,19].

Conventional coagulation tests, including prothrombin time (PT) and international normalized ratio (INR), assess isolated components of the coagulation cascade and often fail to reflect the dynamic nature of clot formation and dissolution. In contrast, thromboelastography (TEG) provides a comprehensive, real-time assessment of global hemostatic function by evaluating clot initiation, propagation, strength, and fibrinolysis. Parameters such as reaction time (R), clot formation time (K), alpha angle (α), maximum amplitude (MA), and estimated percent lysis (EPL) offer a detailed understanding of coagulation dynamics [2,7,13].

Despite its clinical relevance, the interpretation of TEG in pregnancy remains limited due to the lack of well-defined, population-specific reference intervals. Most available reference values are derived from non-pregnant populations and may not accurately represent the physiological changes observed during pregnancy. Furthermore, there is a paucity of data evaluating the diagnostic utility of TEG in gestational hypertension, particularly in the South Indian population [6,9].

Research gap:

There is limited evidence establishing pregnancy-specific reference intervals for thromboelastography parameters in South Indian women, and insufficient data regarding its diagnostic accuracy in gestational hypertension.

In this context, the present study aims to establish reference intervals for TEG parameters in normal third-trimester pregnancy and to evaluate their diagnostic utility in detecting coagulation alterations in gestational hypertension. This may facilitate improved identification and management of coagulation abnormalities, thereby enhancing maternal and fetal outcomes.

Aim and Objectives

Aim:

To evaluate the role of thromboelastography (TEG) in assessing coagulation dynamics in normal pregnancy and to determine its diagnostic utility in identifying coagulation alterations in gestational hypertension.

Objectives:

1.To establish pregnancy-specific reference intervals for thromboelastography parameters—reaction time (R), clot formation time (K), alpha angle (α), maximum amplitude (MA), G value, and estimated percent lysis (EPL)—in third-trimester normal pregnancy.

2.To compare thromboelastography parameters between normal pregnancy and gestational hypertension to identify alterations in coagulation dynamics associated with hypertensive disorders of pregnancy.

3.To evaluate the correlation between thromboelastography parameters and conventional coagulation tests, including platelet count, prothrombin time (PT), and international normalized ratio (INR).

4.To assess the diagnostic accuracy of thromboelastography in detecting hypercoagulable states in gestational hypertension.

MATERIALS AND METHODS

This prospective observational study was conducted at Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai, India, between April 2023 and March 2024. Ethical approval was obtained from the Institutional Ethics Committee, Madras Medical College (Approval No: 28042023; dated 05 April 2023). Written informed consent was obtained from all participants, and the study adhered to the Declaration of Helsinki.

A total of 100 third-trimester pregnant women (29 to 40 weeks of gestation) were enrolled and categorized into two groups: normal pregnancy (Group N, n = 50) and gestational hypertension (Group G, n = 50). Gestational hypertension was defined according to the American College of Obstetricians and Gynecologists criteria as blood pressure ≥140/90 mmHg after 20 weeks of gestation in previously normotensive women. Women aged 18–45 years with singleton pregnancies were included. Those with coagulation disorders, thromboembolic disease, pre-existing hypertension, or receiving anticoagulant or antiplatelet therapy were excluded.

The sample size was calculated based on the expected difference in maximum amplitude (MA) between groups using the formula for comparison of two means, assuming 80% power and a 5% type I(α) error. The minimum required sample size was 45 participants per group; therefore, 50 participants were included in each group.

Venous blood samples were collected under aseptic conditions. Conventional coagulation parameters, including platelet count ($\times 10^5/\mu L$), prothrombin time (PT), and international normalized ratio (INR), were analyzed using standard automated methods. Thromboelastography was performed using the TEG® 5000 haemostasis analyzer (Haemonetics, USA) with kaolin-activated citrated blood to measure reaction time (R), clot formation time (K), alpha angle (α), maximum amplitude (MA), G value, and estimated percent lysis (EPL).

Reference intervals for thromboelastography parameters were derived from the normal pregnancy group and defined as mean ± 2 standard deviations.

Statistical analysis was performed using SPSS version 26.0 (IBM Corp., USA). Continuous variables were expressed as mean ± standard deviation. Intergroup comparisons were performed using the independent t-test, and correlations were assessed using Pearson's correlation coefficient. A p-value <0.05 was considered statistically significant. Receiver operating characteristic (ROC) curve analysis was performed for selected TEG parameters (R time and MA), and the area under the curve (AUC), sensitivity, specificity, and optimal cut-off values (determined using the Youden index) were calculated.

RESULTS

A total of 100 third-trimester pregnant women were included (Group N = 50; Group G = 50).

Table 1: Baseline and Conventional Coagulation Parameters

Variable	Group G (Mean ± SD)	Group N (Mean ± SD)	p-value
Platelets (lakhs)	1.90 ± 0.56	1.98 ± 0.48	0.412
PT (seconds)	15.08 ± 2.50	14.59 ± 1.75	0.238
INR	1.19 ± 0.26	1.13 ± 0.17	0.271

There were no statistically significant differences in conventional coagulation parameters between the two groups ($p > 0.05$). Platelet count, prothrombin time, and international normalized ratio showed comparable values in both normal pregnancy and gestational hypertension, indicating that these conventional tests may have limited sensitivity in detecting subtle alterations in coagulation dynamics.

Table 2: Comparison of TEG Parameters and Reference Intervals in Normal Pregnancy and Gestational Hypertension

Parameter	Group G (Mean ± SD)	Group N (Mean ± SD)	Reference Interval (Group N)	p-value
R Time (min)	1.97 ± 1.11	4.18 ± 0.99	2.24 – 6.12	<0.001*
K Time (min)	1.23 ± 0.46	1.58 ± 0.49	0.62 – 2.54	0.002*
Alpha Angle (°)	72.98 ± 7.20	67.58 ± 6.21	55.40 – 79.76	0.001*
MA (mm)	68.45 ± 8.24	62.81 ± 4.43	54.13 – 71.49	<0.001*
G Value	11.92 ± 4.97	8.69 ± 2.61	3.57 – 13.81	<0.001*
EPL (%)	4.48 ± 10.84	13.24 ± 22.06	0 – 56.48	0.041*

*Statistically significant ($p < 0.05$)

Thromboelastography parameters demonstrated statistically significant differences between the two groups ($p < 0.05$). The gestational hypertension group exhibited faster clot initiation and propagation, along with increased clot strength, indicating a hypercoagulable state. The reference intervals derived from the normal pregnancy group provide baseline values for physiological coagulation changes in pregnancy and highlight deviations observed in gestational hypertension.

Table 3: Correlation Analysis of TEG Parameters and Conventional Tests in Study Groups

Variables	Group G (r)	Group G (p-value)	Group N (r)	Group N (p-value)
PT vs INR	0.994	<0.001*	0.990	<0.001*
PT vs R Time	-0.435	0.002*	0.446	0.001*
PT vs K Time	-0.417	0.003*	0.275	0.054
PT vs Alpha Angle	0.652	<0.001*	-0.072	0.619
R Time vs K Time	0.242	0.090	0.516	<0.001*
R Time vs Alpha Angle	-0.423	0.002*	-0.568	<0.001*
K Time vs Alpha Angle	-0.889	<0.001*	-0.950	<0.001*

*Statistically significant ($p < 0.05$)

The correlation analysis demonstrated distinct patterns between the two groups. In gestational hypertension, moderate correlations were observed between conventional coagulation parameters and TEG variables, particularly indicating associations with accelerated clot initiation and propagation. In contrast, normal pregnancy showed weaker or non-significant correlations between PT/INR and TEG parameters, reflecting a more balanced hemostatic state. A consistent negative correlation between K time and alpha angle was observed in both groups, indicating the intrinsic relationship between clot formation rate and stabilization.

Receiver operating characteristic (ROC) analysis demonstrated good discriminative performance of thromboelastography parameters in differentiating gestational hypertension from normal pregnancy.

Table 4: ROC Analysis of TEG Parameters

Parameter	AUC	Sensitivity (%)	Specificity (%)
MA	0.82	78	74
R Time	0.79	75	70

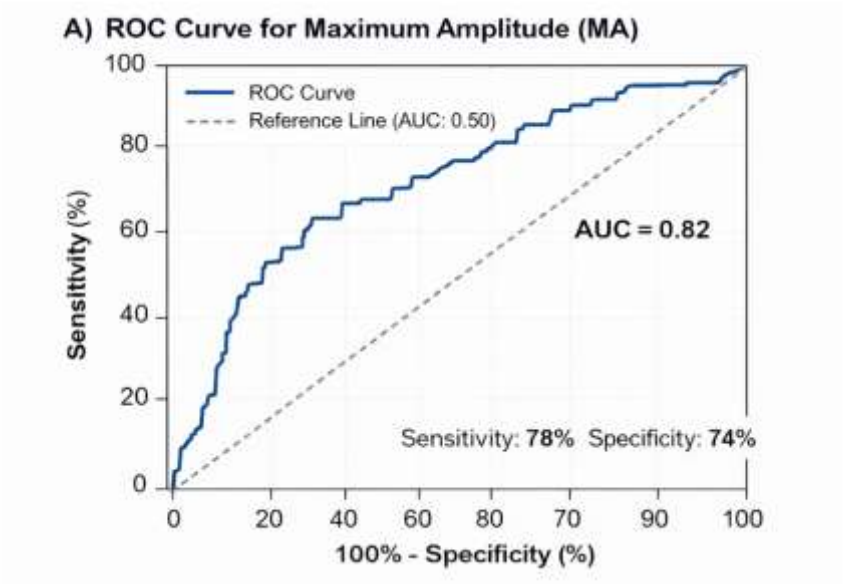

Figure 1 : ROC Curve for Maximum Amplitude (MA)

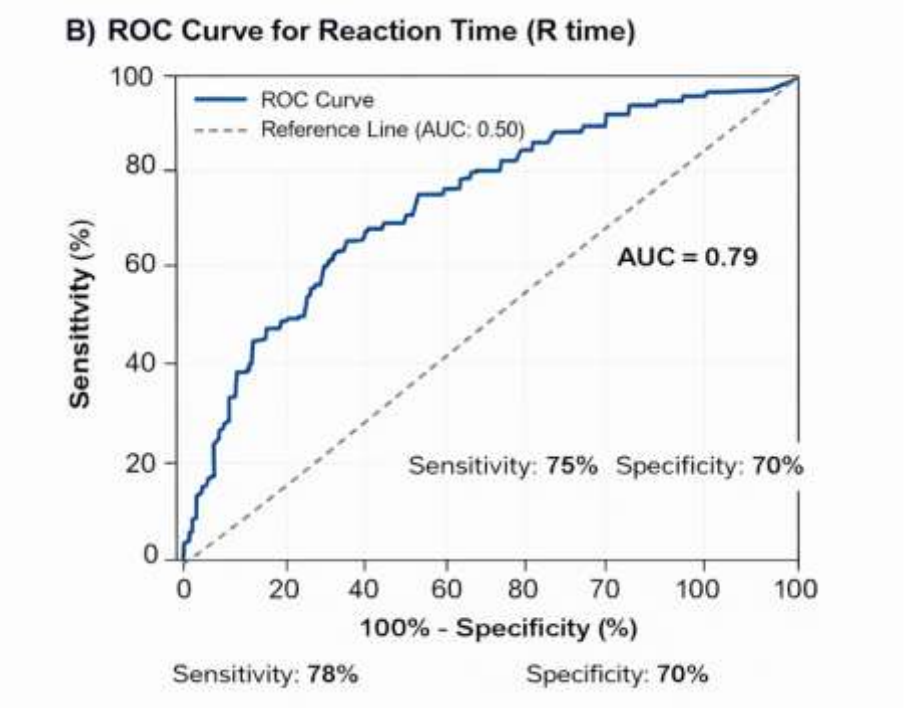

Figure 2 : ROC Curve for Reaction Time (R time)

Maximum amplitude (MA) showed an area under the curve (AUC) of 0.82 (95% CI: 0.73–0.91), with an optimal cut-off value of 65 mm, yielding a sensitivity of 78% and specificity of 74%. Reaction time (R) demonstrated an AUC of 0.79 (95% CI: 0.69–0.88), with a cut-off value of ≤3 minutes, sensitivity of 75%, and specificity of 70%.
These findings indicate that MA and R time exhibit moderate-to-good diagnostic accuracy for identifying hypercoagulable states in gestational hypertension.

DISCUSSION

Clinical Implications

The findings of the present study demonstrates that gestational hypertension is associated with a pronounced hypercoagulable state compared to normal pregnancy, as evidenced by significant alterations in thromboelastography (TEG) parameters. These findings support the concept that hypertensive disorders amplify the physiological prothrombotic adaptations of pregnancy and extend existing evidence by providing population-specific reference intervals in a South Indian cohort.
Conventional coagulation parameters, including platelet count, prothrombin time (PT), and international normalized ratio (INR), did not differ significantly between groups. This observation is consistent with studies by Uchikova and Ledjev

(2005) and Bremme (2003), which reported that routine coagulation tests often remain within normal limits despite significant hemostatic alterations in pregnancy. Similarly, Reikvam et al. (2011) emphasized the limited ability of conventional assays to assess global coagulation dynamics.

In contrast, TEG parameters demonstrated significant alterations in gestational hypertension. The reduction in reaction time (R) and clot formation time (K) observed in the present study is comparable to findings reported by Sharma et al. (2011) and Xie et al. (2020); however, the slightly greater reduction in our cohort may reflect enhanced thrombin generation and population-specific variations in endothelial and inflammatory responses.

The increased alpha angle observed in this study reflects accelerated fibrin polymerization and clot kinetics. Similar findings have been reported by Wang et al. (2019), although the magnitude of elevation in our study appears modestly higher, suggesting a more pronounced shift toward rapid clot propagation in this population. These findings are consistent with the pathophysiological mechanisms of endothelial dysfunction described by Granger et al. (2001).

Clot strength parameters, including maximum amplitude (MA) and G value, were significantly elevated in gestational hypertension, indicating enhanced clot firmness. The magnitude of MA elevation observed in the present study is comparable to that reported by Xie et al. (2020) and Macafee et al. (2012), although the slightly higher values in our cohort may reflect population-specific variations in platelet activation and fibrinogen levels.

The observed reduction in estimated percent lysis (EPL) suggests suppression of fibrinolysis, contributing to a prothrombotic state. This finding aligns with observations by Bremme (2003), who reported reduced fibrinolytic activity during pregnancy due to increased levels of plasminogen activator inhibitors. The wide variability observed in EPL in the present study likely reflects inter-individual differences in fibrinolytic activity.

Importantly, the present study extends beyond descriptive analysis by evaluating the diagnostic performance of TEG parameters. ROC analysis demonstrated that maximum amplitude (MA) and reaction time (R) exhibit moderate-to-good discriminative ability, with AUC values of 0.82 and 0.79, respectively. These findings are comparable to those reported by Wang et al. (2019), suggesting that TEG parameters have clinically relevant diagnostic utility in hypertensive disorders of pregnancy.

Correlation analysis revealed stronger associations between TEG parameters and conventional coagulation indices in gestational hypertension compared to normal pregnancy. This supports the observations of Reikvam et al. (2011) that global coagulation assays better capture dynamic interactions within the coagulation cascade than conventional tests.

A major strength of this study is the establishment of pregnancy-specific reference intervals for TEG parameters in a South Indian population. Previous studies, including Sharma et al. (2011) and Macafee et al. (2012), have highlighted the limitations of applying non-pregnant reference values. The present study addresses this gap and provides clinically relevant baseline data.

From a clinical perspective, the ability of TEG to detect early hypercoagulable changes has important implications. Its integration into clinical practice may facilitate improved risk stratification, enable targeted therapeutic interventions, and support timely decision-making in high-risk obstetric settings. However, further large-scale, multicentric studies are required to validate these findings and establish standardized clinical thresholds.

Second, TEG-guided evaluation may support individualized decision-making regarding anticoagulant therapy by identifying patients with hypercoagulable states. Third, the rapid and point-of-care nature of TEG allows its integration into early triage settings, including casualty, intensive care units (ICU), and high-dependency units (HDU), where timely assessment of coagulation status is critical for risk stratification and management.

Limitations

The present study has several limitations. First, it was conducted at a single tertiary care center, which may limit the generalizability of the findings. Second, the sample size was relatively small, potentially affecting the statistical power of the study. Third, comparison with rotational thromboelastometry (ROTEM) was not performed, which may have provided complementary insights into coagulation dynamics. Finally, the cross-sectional design precluded longitudinal assessment of coagulation changes across different stages of pregnancy.

CONCLUSION

Thromboelastography provides a comprehensive and sensitive assessment of coagulation dynamics and appear superior to conventional coagulation tests to detecting early haemostatic alterations in gestational hypertenstion, establishing pregnancy specific reference intervals enhances its clinical applicability. Incorporation of TEG into evaluation of women with gestational hypertension may facilitate earlier diagnosis, guide individualized management, and improve maternal and foetal outcome

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