

Baseline rotational thromboelastometry (ROTEM) values in a healthy, diverse obstetric population and parameter changes by pregnancy-induced comorbidities

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ABSTRACT

Background: Point-of-care testing provides a representation of the patient's coagulability status during effective postpartum hemorrhage management. Baseline values of rotational thromboelastometry (ROTEM) have not yet been reported in a heterogeneous obstetric population. This study aimed to establish a baseline for a diverse population representative of the United States. The secondary aim was to evaluate the association of these hematologic parameters with comorbidities, race, and socioeconomic factors.

Methods: The study was a retrospective review of collected ROTEM values of women undergoing vaginal or cesarean delivery with a history of or at risk for postpartum hemorrhage. Patients were divided into healthy and comorbid groups. Exclusion criteria for both groups included active or recent bleeding, receipt of blood products or clot-enhancing factors, and liver disease. Mean values of ROTEM by race and comorbidities were included. Median values were reported for intrinsic pathway thromboelastometry (INTEM), extrinsic pathway thromboelastometry (EXTEM), and fibrin polymerization thromboelastometry (FIBTEM) amplitude at 10 minutes (A10) and 20 minutes (A20), coagulation time, clot formation time, and maximum clot firmness.

Results: A total of 681 records were reviewed; 485 met inclusion criteria, and 267 met healthy criteria. The mean (standard deviation) demographics for maternal age (years), body mass index (kg/m²), and gestational age (weeks) were 32.2 (5.7), 34 (7.3), and 35.4 (5), respectively. The median INTEM, EXTEM, and FIBTEM A10 were 63, 65, and 23 mm. The mean for INTEM, EXTEM, and FIBTEM A10 was increased for those who were Black or obese, whereas a decreased FIBTEM and EXTEM A10 was noted in those who were Asian or those who had the hemolysis, elevated liver enzymes, low platelet syndrome.

Conclusions: Our heterogeneous population presents ROTEM values within the interquartile range of those previously reported in European studies. Black race, obesity, and preeclampsia were associated with hypercoagulable profiles.

KEYWORDS HELLP syndrome; hypercoagulability; point-of-care viscoelastic testing; rotational thromboelastometry

Postpartum hemorrhage remains a worldwide leading cause of maternal morbidity and mortality.¹ Decades of research have identified fibrinogen as an early biomarker to predict postpartum hemorrhage (PPH). A plasma fibrinogen level ≤ 2 g has been shown to have a 100% predictive value for progression to severe PPH.^{2–5} Hence, early recognition and replacement of this factor is critical for PPH management.^{3–7} Over the last

decade, obstetric anesthesiologists have relied on fibrinogen values to indicate an increased risk, and thus preparation, for bleeding.^{2,3,5,8} For each 1 g/L decrease in fibrinogen, the odds ratio for PPH was 2.63 (1.66–4.16; $P < 0.0001$).² With the emphasis on early recognition, some experts have scrutinized the efficiency of the laboratory Clauss fibrinogen, which can have a turnaround of 45 to 60 minutes.⁹ Clinically, the inability of early recognition may result in

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improper management of hemorrhage, with either underutilization providing insufficient control or overutilization increasing risk for transfusion-related reactions.^{10–12} The rotational thromboelastometry (ROTEM[®]) generates results within 15 minutes, which is seemingly more practical for point-of-care assessment relative to its gold standard counterpart, Clauss fibrinogen. As a result, ROTEM has become widely accepted in practice for PPH, and several PPH algorithms utilize ROTEM for guiding blood product management in cases of PPH.^{3,9,12–14}

Despite the heavy algorithm-based utilization of ROTEM, baseline parameters from a population representative of the diversity in the United States have not been established.^{9,15} Baseline values from studies in Europe^{16–18} and Australia⁹ that did not analyze the study sample by race/ethnicity, body mass index (BMI), and gestational comorbidities are not generalizable to our heterogeneous obstetric population. In addition, previously reported studies exclude comorbid conditions like gestational thrombocytopenia, gestational hypertension (gHTN), and obesity from their study design when reporting baseline values. However, obesity puts a patient at a 3 to 4 times greater risk of developing gestational diabetes (gDM) and preeclampsia,¹⁹ and 39% of parturients were obese in 2018.²⁰ The exclusion of these patients increases healthy bias risk and excludes a vast proportion of pregnant women in the United States. Thus, further review of reference ranges for ROTEM values is needed in not only healthy patients but also those at increased risk for needing it.²¹

The primary aim of this retrospective observational study was to establish baseline ROTEM parameters in our obstetric patient population. The secondary aim was to evaluate the hematologic association of ROTEM values with race and gestational comorbidities, including HELLP (hemolysis, elevated liver enzymes, and low platelet) syndrome, thrombocytopenia, obesity, gHTN, and gDM.

METHODS

This retrospective observational study was approved by our institutional review board (IRB #2000029087). Charts were retrospectively reviewed for pregnant women undergoing vaginal or cesarean delivery at our institution from December 2015 to December 2020 who received blood draws for ROTEM and Clauss fibrinogen values. Patients with a high risk for hemorrhage were excluded. High risk for hemorrhage was defined according to institutional practice as the presence of any of the following: history of PPH; repeat cesarean delivery (\geq tertiary); prior placenta accreta spectrum; macrosomia; prolonged oxytocin use in the setting of intrapartum cesarean delivery; multiple gestation pregnancies; antepartum hemorrhage or first ROTEM obtained for PPH management; receipt of medications affecting coagulation (e.g., heparin, low-molecular-weight heparin); and known Factor V Leiden deficiency, antiphospholipid syndrome, hemochromatosis, or thalassemia.

All patients meeting inclusion criteria were screened for the following: reason for obtaining ROTEM; demographic information including median income based on zip code; self-reported race (White, Black, Asian, Hispanic/Latino, Pacific Islander, other); BMI; gravidity and parity; gestational age; American Society of Anesthesiologists score; mode of delivery; indication of delivery; and comorbidities such as gHTN, HELLP syndrome, preeclampsia, gDM, gestational thrombocytopenia, and intrahepatic cholestasis of pregnancy. Socioeconomic status (SES) was classified according to post-code and corresponding median income. Incomes were defined as low for \leq \$56,000, medium for \$57,000 to \$79,000, and high for \geq \$80,000, as previously described by Chatterjee et al.²¹

Two researchers reviewed the electronic medical records and assigned patients to the healthy cohort (for baseline analysis) or the group with at least one comorbidity. If there were disagreements regarding placing a parturient in one of the groups, a third member of the research team reevaluated inclusion criteria and determined the patient's cohort. This study adhered to the Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) statement.

Physicians trained in use of ROTEM delta (Tem International, Munich, Germany) obtained all the samples stored in our database. All blood samples were placed in standard 3.5 mL BD Vacutainer collection tubes containing 3.2% sodium citrate (Franklin Lakes, NJ, USA). The samples were analyzed in parallel channels for intrinsic pathway thromboelastometry (INTEM), extrinsic pathway thromboelastometry (EXTEM), and fibrin polymerization thromboelastometry (FIBTEM) tests after warming the reagents and pipetting, as recommended by the manufacturer. The parameters derived from the test included clotting time (CT), clot formation time (CFT), maximum clot firmness (MCF), and amplitude at 10 and 20 minutes (A10 and A20) for each of the three channels (INTEM, EXTEM, and FIBTEM).

All values, besides the demographic characteristics in *Table 1*, are reported as ROTEM values in mm for amplitude and seconds for CT. Unadjusted means of ROTEM values for patients with comorbidities versus healthy patients were determined with Welch's *t* tests. Adjusted means by each comorbidity group, adjusting for age and gestational age, were reported using regression analysis with robust Huber-White standard error estimates. Age-adjusted pairwise comparisons were conducted to compare preeclamptic patients with/without severe thrombocytopenia (platelet count $<100,000 \times 10^9/L$) against patients without preeclampsia and severe thrombocytopenia. Similarly, pairwise comparisons were performed by race-dependent cohorts, using White as a reference group for Black, Asian, and other race. The baseline reference ranges were reported as medians and interquartile ranges for selected characteristics (per International Federation of Clinical Chemistry recommendations). All non-baseline characteristics were reported as means (standard deviations) with two-sided *P* values (alpha

Table 1. Demographic information of 485 patients included in statistical analysis before exclusion of comorbidities for obtaining the baseline parameters for our tertiary care unit in the United States

Characteristics	Mean (SD)					
Maternal age (years)	32.2 (5.7)					
BMI (kg/m ²)	34 (7.3)					
Gestation (weeks)	35.4 (5)					
Mode of delivery	Total n (%)					
Vaginal delivery	103 (22.4%)					
Cesarean delivery	376 (77.7%)					
Socioeconomic status	Total n (%)					
High (>\$80,000)	134 (28%)					
BMI >35	40 (29.9%)					
Medium (\$57,000–\$79,000)	155 (32%)					
BMI >35	57 (36.8%)					
Low (<\$56,000)	196 (40%)					
BMI >35	81 (41.3%)					
Comorbidities n (%)						
Race	n (%)	BMI >35	gHTN	gDM	PEC	HELLP
White	261 (53.8%)	84 (32%)	66 (25.3%)	29 (11.1%)	40 (15.3%)	15 (5.7%)
Black	110 (22.7%)	58 (52.7%)	42 (38.2%)	21 (19.1%)	30 (27.3%)	7 (6.4%)
Asian	22 (4.5%)	2 (9.1%)	2 (9.1%)	7 (31.8%)	0	0
Other	92 (19%)	34 (37%)	25 (27.2%)	16 (17.4%)	17 (18.5%)	2 (2.2%)

BMI indicates body mass index (kg/m²); gDM, gestational diabetes mellitus; gHTN, gestational hypertension; HELLP, hemolysis, elevated liver enzymes, and low platelets; PEC, preeclampsia; SES, socioeconomic status.

value = 0.05). The sample sizes for power analysis were determined by the recommendations of the Clinical Laboratory and Standard Institute, which state that N = 120 sufficiently determines upper and lower confidence intervals.^{9,22} All analyses were conducted using Stata (version 16.0; Stata Corp., College Station, TX, USA) statistical package.

RESULTS

A total of 681 ROTEM samples from pregnant women were collected between December 2015 and December 2020, out of which 485 samples met inclusion criteria. Two hundred and sixty-seven were included in the healthy baseline cohort, while 218 were included in the comorbidity analysis. *Figure 1* depicts the indications for exclusion.

As noted in *Table 1*, the average maternal age of our total population (N = 485) prior to comorbidity exclusion was 32.2 years (standard deviation = 5.7 years) with an average BMI of 34 (7.3 kg/m²) presenting at 35 + 2.8 (5 weeks) gestational age. Most women (77.7%) had a cesarean delivery and were of low SES (41.3%). The frequency of class II and

III obesity, defined as BMI 35 kg/m², was inversely proportional to SES, with a prevalence of 29.9%, 36.8%, and 41.3% within high, medium, and low SES, respectively.

The majority of our patients were White (53.8%), while 22.7% were Black, 4.5% were Asian, and 19% were other race. In White patients, 32% had a BMI >35, 25.3% had gHTN, 11.1% had gDM, 15.3% had preeclampsia, and 5.7% had HELLP syndrome. In Black patients, 22.7% had BMI >35, 38.2% had gHTN, 19.1% had gDM, 27.3% had preeclampsia, and 6.4% had HELLP syndrome. In Asian patients, 9.1% had BMI >35, 9.1% had gHTN, 31.8% had gDM, and none had preeclampsia or HELLP syndrome. In patients of other races, 37% had BMI >35, 27.2% had gHTN, 17.4% had gDM, 18.5% had preeclampsia, and 2.2% had HELLP syndrome.

Our healthy cohort baseline values (N = 267), which includes patients without any comorbidities, are summarized and presented with two previously published baseline values in *Table 2*. Median (interquartile range) values for INTEM A10, EXTEM A10, and FIBTEM A10 were 23 (20–26), 65 (61–68), and 63 (59–67), respectively. The medians reported from our sample were within range of those presented in the studies by Lee et al⁹ and De Lange et al.²³

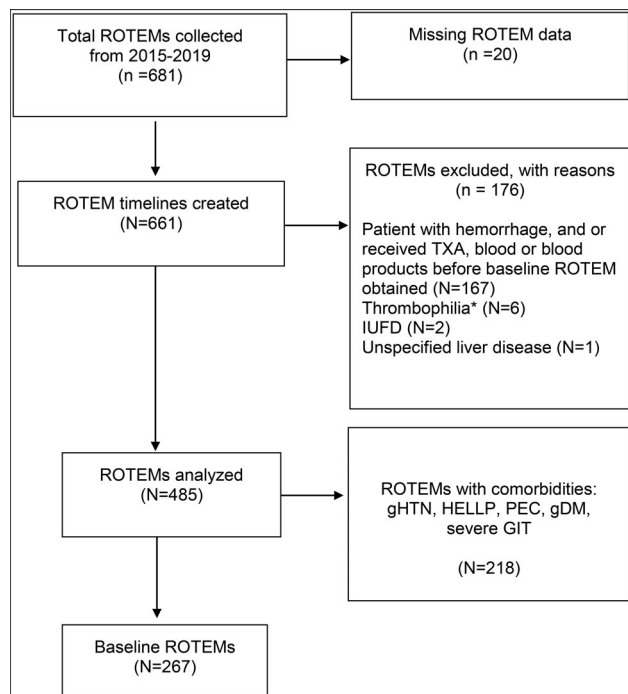


Figure 1. Flowchart detailing participant exclusions. *Thrombophilia: patients with Factor V Leiden, antiphospholipid/systemic lupus erythematosus, Von Willebrand disease, deficiencies in protein C and S. gDM, gestational diabetes mellitus; gHTN, gestational hypertension; GIT, gestational-induced thrombocytopenia; HELLP, hemolysis, elevated liver enzyme, low platelet syndrome; IUFD, intrauterine fetal demise; PEC, preeclampsia; ROTEM, rotational thromboelastometry.

After adjusting for age and gestational age, we found that the presence of class II obesity, preeclampsia, and HELLP syndrome resulted in statistically significant changes when compared to the healthy cohort. *Table 3* summarizes the comorbid variables that demonstrated at least one ROTEM parameter that was statistically different when compared to the baseline cohort, which includes obesity, HELLP syndrome, and preeclampsia. Obese patients had higher INTEM A10 (62.6 mm [8.3] vs. 60.8 [7.3]), EXTEM A10 (64.7 mm [7.8] vs. 62.6 mm [7.0]), and FIBTEM A10 (25.5 mm [5.7] vs. 22.6 mm [5.6]) when compared to patients with BMI < 35 kg/m². Patients with preeclampsia had higher FIBTEM A10 (24.9 mm [6.3] vs. 23.4 mm [5.6]) than healthy patients. On the other hand, HELLP syndrome patients varied from healthy patients with lower INTEM A10 (53.4 mm [9.2] vs. 61.9 mm [7.4]) and EXTEM A10 (55 mm [10.1] vs. 63.8 mm [6.9]).

Table 4 summarizes the ROTEM values into cohorts of preeclampsia diagnosis and subgroups by platelet count $100 \times 10^9/L$. We found significantly lower FIBTEM, EXTEM, and INTEM A10 values in those with preeclampsia and platelet counts $\leq 100 \times 10^9/L$ when compared to the remaining subgroups, including preeclampsia and platelet counts $> 100 \times 10^9/L$.

As summarized in *Table 5*, Black patients demonstrated statistically significant higher FIBTEM A10, INTEM A10, and EXTEM A10 compared to White patients. Asian

patients were associated with lower FIBTEM A10 and INTEM A10 when compared to their White counterparts.

DISCUSSION

Establishing baseline parameters requires a proper representative sample of a population. Prior studies from Europe^{17,23} and Australia⁹ reported ROTEM parameters of mainly White patients (75%–94%) and excluded obesity and other comorbidities. In contrast, our study presents a population diverse in race, SES, and comorbidities, with only 53.8% of White patients. With an estimated 50% of pregnant women meeting overweight or obese criteria in the United States,^{24,25} excluding these patients from analysis would leave almost half of the US population without any reference ranges when managing for PPH. In our sample, 67% and 36.7% met criteria for class II and class III obesity, respectively, more accurately representing the obesity epidemic, and its effects on coagulability, present in the US population. While healthy populations are typically reported for baseline populations, ROTEM can be applied in a more individualized, patient-based manner with baseline values matched appropriately by the patient's risk stratification. Arguably, these patients are at increased risk for PPH, only escalating a need for further study. Baseline studies should be focused on nonhealthy populations, who may present greater need for practical reliance on such algorithms.

Our study is also one of the few ROTEM baseline parameter studies in an obstetric population that meets the International Federation of Clinical Chemistry recommendations of a sample size with at least 120 patients to account for regional variability.^{9,23} Several other studies reporting baseline parameters have included 54 to 80 parturients for analysis.^{9,16,17,23,26} Like the two largest published obstetric baseline parameter studies, our results corroborate that the normal values of pregnancy are higher than those proposed by the ROTEM manufacturer, which was established in nonobstetric populations.^{9,23} Despite the differences in demographic information and exclusion criteria, our median results are comparable to those previously reported (*Table 2*). The smaller interquartile ranges in our results could be attributed to racial heterogeneity or greater sample size and power.^{9,17,23} However, as most algorithms published utilize subphysiological levels of fibrinogen as triggers for early recognition and goals for replacing blood products,^{9,17,23} these differences are unlikely to have clinical relevance.

Although previously reported baseline parameters in obstetric literature well defined their geographical location and racial and ethnic composition, they did not evaluate their impact on whole blood viscoelastic testing.^{9,17,23} After adjusting for patient and gestational ages, we found that Asian patients demonstrate lower FIBTEM and EXTEM A10 values when compared to White patients. The lower FIBTEM/EXTEM A10 values suggest a relative hypocoagulable state, possibly secondary to the decreased prevalence of comorbidities like obesity and hypertension seen within the

Table 2. ROTEM baseline values in our study and comparison studies^a

	Our study	Lee et al (2021)	De Lange et al (2014)
FIBTEM parameters		Median (IQR)	
CT	54 (20–26)	53 (40–74)	39 (31–79)
Alpha angle	77 (73–79)	76 (67–81)	79 (50–83)
MCF	25 (22–29)	24 (16–34)	25 (22–28)
A10	23 (20–26)	22 (14–30)	22 (12–38)
A20	24 (22–28)	23 (16–33)	24 (13–40)
EXTEM parameters		Median (IQR)	
CT	59 (54–65)	54 (43–69)	45 (41–50)
CFT	65 (56–78)	64 (43–108)	69 (62–81)
Alpha angle	77 (75–79)	77 (69–82)	77 (67–83)
MCF	72 (69–74)	70 (60–78)	71 (42–78)
A10	65 (61–68)	63 (50–73)	64 (61–68)
A20	70 (67–73)	69 (57–77)	70 (68–73)
INTEM parameters		Median (IQR)	
CT	159 (137–180)	165 (115–245)	147 (109–225)
CFT	60 (49.5–73)	63 (42–103)	55 (40–103)
Alpha angle	78 (75–80)	77 (70–82)	79 (70–82)
MCF	69 (66–73)	69 (59–76)	71 (63–78)
A10	63 (59–67)	62 (49–70)	64 (55–72)
A20	68 (65–72)	68 (57–75)	70 (62–77)
Geographical location	United States	Australia	The Netherlands
Study size	267	132	161
Weight exclusion	No	Yes	No
Race distribution	<ul style="list-style-type: none"> ● 53.8% White ● 22.7% Black ● 4.5% Asian ● 19% other 	<ul style="list-style-type: none"> ● 75% White ● 9.1% SE Asian ● 6.8% Indian ● 7.6% other ● 0.8% Indigenous Australian 	<ul style="list-style-type: none"> ● 94.4% Caucasian ● 0.6% Indian/Pakistani ● 0.6% African ● 1.2% Mediterranean ● 1.2% South American ● 3.7% other

^aROTEM reference parameters were derived by calculating the 2.5 and 97.5 percentiles.

A10 indicates amplitude at 10 min; A20, amplitude at 20 min; CT, clotting time; EXTEM, extrinsic pathway thromboelastometry; FIBTEM, fibrin polymerization thromboelastometry; INTEM, intrinsic pathway thromboelastometry; IQR, interquartile range; MCF, maximum clot firmness; ROTEM, rotational thromboelastometry.

Asian subgroup. On the contrary, Black parturients demonstrated a higher FIBTEM, INTEM, and EXTEM A10, suggesting a hypercoagulable propensity compared to White parturients. Our results reflect several population-based studies showing higher and lower incidences of venous thromboembolism in Black and Asian populations, respectively.^{27,28} With a relative hypocoagulable state, Asian patients may require more transfusions, as concluded by Bryant et al,^{27,28} who found that Asian race is an independent significant risk factor for blood transfusions or hysterectomies.

Our results on hyper- or hypocoagulability by race-dependent cohorts should be analyzed in consideration of

the complex role of SES in health and even the clotting cascade. Before discussing our SES-related results, it is important to highlight that life stressors (e.g., unemployment) and several health issues (e.g., obesity), including preeclampsia, have been associated with inflammation, which may result in hypercoagulability.^{29–32} Hence, the complex intertwinement of race, SES, and cultural differences, which may include diet and relative levels of support, are all variables that may to a certain extent impact the coagulation profile of our patients. Our study noted an inverse correlation between SES and class II obesity (BMI > 35 kg/m²): patients of low SES were more likely to be obese. Additionally, Black

Table 3. Comorbidities that maintained a statistical impact on ROTEM parameters after adjusting for age

Parameters	BMI (n)		P value	HELLP (n)		P value	Preeclampsia (n)		P value
	≤35 (308)	>35 (178)		Yes (24)	No (461)		Yes (87)	No (398)	
FIBTEM									
CT	57.1 (16.0)	59.1 (15.4)	0.20	54.7 (10.1)	58.0 (16.0)	0.13	61.8 (28.3)	57.0 (11.3)	0.12
Alpha angle	74.8 (4.8)	76.6 (4.4)	<0.001	74.6 (4.8)	75.5 (4.7)	0.35	75.9 (5.7)	75.4 (4.5)	0.46
MCF	24.8 (6.3)	27.7 (6.6)	<0.001	24.9 (8.4)	25.9 (6.4)	0.54	27.5 (7.3)	25.5 (6.3)	0.022
A10	22.6 (5.6)	25.5 (5.7)	<0.001	21.8 (6.2)	23.7 (5.8)	0.12	24.9 (6.3)	23.4 (5.6)	0.035
A20	24.2 (5.8)	27.4 (6.3)	<0.001	23.6 (7.1)	25.4 (6.1)	0.24	26.9 (7.0)	25.0 (5.9)	0.025
EXTEM									
CT	61.6 (21.8)	63.8 (37.0)	0.46	59.0 (9.3)	62.6 (29.0)	0.13	66.5 (40.5)	61.5 (24.9)	0.28
CFT	74.3 (26.1)	68.0 (33.4)	0.032	104.7 (55.1)	70.2 (26.1)	0.002	73.5 (31.1)	71.6 (28.7)	0.61
Alpha angle	76.0 (3.6)	77.2 (5.0)	0.004	74.4 (5.3)	76.5 (4.1)	0.046	76.3 (4.9)	76.4 (4.0)	0.86
MCF	69.9 (5.7)	70.9 (7.6)	0.11	63.4 (8.4)	70.6 (6.2)	<0.001	70.0 (6.5)	70.3 (6.5)	0.62
A10	62.6 (7.0)	64.7 (7.8)	0.003	55.0 (10.1)	63.8 (6.9)	<0.001	63.1 (8.4)	63.4 (7.1)	0.77
A20	68.5 (6.2)	70.5 (5.9)	<0.001	62.3 (9.8)	69.6 (5.7)	<0.001	68.6 (7.2)	69.4 (5.9)	0.36
INTEM									
CT	165.0 (39.0)	161.8 (38.4)	0.39	159.2 (31.8)	164.1 (39.1)	0.46	168.3 (45.2)	162.8 (37.2)	0.30
CFT	70.5 (30.5)	67.6 (34.7)	0.36	98.4 (44.7)	67.9 (30.6)	<0.001	70.0 (29.8)	69.3 (32.6)	0.86
Alpha angle	76.2 (4.6)	77.0 (4.9)	0.051	73.5 (5.1)	76.6 (4.7)	0.003	76.7 (4.2)	76.4 (4.8)	0.69
MCF	67.8 (6.2)	68.9 (8.4)	0.11	61.8 (8.0)	68.5 (6.9)	<0.001	68.5 (6.9)	68.1 (7.2)	0.71
A10	60.8 (7.3)	62.6 (8.3)	0.014	53.4 (9.2)	61.9 (7.4)	<0.001	61.3 (8.2)	61.5 (7.7)	0.86
A20	66.9 (6.6)	68.3 (7.3)	0.035	60.5 (8.7)	67.8 (6.6)	<0.001	67.1 (7.4)	67.5 (6.8)	0.73

A10 indicates amplitude at 10 min; A20, amplitude at 20 min; BMI, body mass index (kg/m²); CT, clotting time; EXTEM, extrinsic pathway thromboelastometry; FIBTEM, fibrin polymerization thromboelastometry; HELLP, hemolysis, elevated liver enzyme, low platelet syndrome; INTEM, intrinsic pathway thromboelastometry; MCF, maximum clot firmness; ROTEM, rotational thromboelastometry.

patients were more likely to meet the class II obesity definition (53%) than the White (32%), other (37%), and Asian (9%) cohorts. Hypercoagulability is dependent on factors like the patient's diet, exercise levels, and family history—factors impacted by race, which itself is influenced by culture. Our findings concerning obesity corroborate the results from other researchers that suggest that obesity leads to a hypercoagulable state.^{33,34} The increase in plasminogen activator-1, fibrinogen, von Willebrand factor, thrombin-anti-thrombin complexes, and leptin has been proposed as the culprit of the increased venous thromboembolism risk in the obese population, secondary to its hypercoagulable state.^{33,34} In contrast to our findings, several point-of-care viscoelastic testing studies have failed to demonstrate a statistically significant difference in the hypercoagulable state between the pregnant obese and the nonobese.^{31,35}

Besides the modifiable (e.g., BMI) and unmodifiable (e.g., race) risk factors, obstetric patients may experience several comorbidities unique to pregnancy, some of which have a clinically significant impact on coagulation.^{33,34} In accordance with previous studies, our results showed a

difference between the coagulation parameters of healthy patients and those with preeclampsia or HELLP syndrome.^{36,37} Sharma et al³⁶ described that patients with preeclampsia maintain a hypercoagulable state until they develop severe thrombocytopenia (platelet count <100 × 10⁹/L), at which point preeclampsia leads to hypo-coagulability. Likewise, we reported decreased coagulation in patients with preeclampsia and platelet count <100 × 10⁹/L. As one would expect, this finding suggests that thrombocytopenia plays a role in the coagulation profile changes of preeclampsia. Simultaneously, recognizing the complexity and dynamic process of preeclampsia is essential. Several studies have suggested an inverse correlation between thrombocytopenia and severity of preeclampsia (e.g., preeclampsia with severe features).³⁸ With this information, one could infer that platelets and their contribution to the preeclampsia coagulation profile may serve as a marker. Hence, downtrending INTEM and EXTEM A10 values at 55 mm, a 5 mm difference from mean ROTEM values of patients with severe thrombocytopenia, may serve as an early warning of the progression of the disease. This

Table 4. Effect of preeclampsia, by platelet count, on ROTEM parameters

Parameters	Platelet count ($\times 10^9/L$)				P value
	Preeclampsia		No preeclampsia		
	≤ 100	>100	≤ 100	>100	
FIBTEM					
CT	72.3 (35.5)	59.4 (26.9)	58.2 (9.9)	56.6 (11.5)	0.23
Alpha angle	75.0 (5.4)	76.0 (6.0)	73.8 (4.6)	75.6 (4.4)	0.11
MCF	24.1 (6.0)	28.4 (7.5)	22.7 (6.7)	25.8 (6.1)	<0.001
A10	21.7 (5.4)	25.8 (6.4)	20.0 (4.6)	23.8 (5.6)	<0.001
A20	23.6 (5.9)	27.8 (7.2)	21.6 (5.3)	25.4 (5.8)	<0.001
EXTEM					
CT	95.3 (86.7)	59.7 (15.1)	60.9 (10.2)	61.6 (26.5)	0.37
CFT	115.3 (45.4)	64.5 (17.1)	103.0 (39.8)	68.1 (24.7)	<0.001
Alpha angle	71.1 (7.4)	77.4 (3.3)	73.9 (3.4)	76.7 (4.0)	<0.001
MCF	61.9 (9.1)	71.8 (4.1)	62.8 (7.4)	71.1 (5.8)	<0.001
A10	51.7 (10.8)	65.6 (5.2)	53.5 (8.1)	64.5 (6.0)	<0.001
A20	59.4 (9.7)	70.8 (4.3)	61.0 (8.2)	70.2 (4.7)	<0.001
INTEM					
CT	192.5 (69.1)	162.6 (37.3)	171.4 (30.2)	160.8 (35.5)	0.057
CFT	105.9 (44.3)	62.8 (18.4)	105.5 (36.1)	64.8 (29.4)	<0.001
Alpha angle	73.3 (5.5)	77.3 (3.6)	71.4 (4.6)	77.1 (4.5)	<0.001
MCF	60.7 (9.6)	70.0 (4.9)	59.8 (7.2)	69.1 (6.5)	<0.001
A10	51.4 (11.2)	63.3 (5.5)	51.0 (7.4)	62.8 (6.6)	<0.001
A20	58.4 (10.3)	69.0 (4.8)	58.2 (7.9)	68.4 (5.9)	<0.001

A10 indicates amplitude at 10 min; A20, amplitude at 20 min; CT, clotting time; EXTEM, extrinsic pathway thromboelastometry; FIBTEM, fibrin polymerization thromboelastometry; INTEM, intrinsic pathway thromboelastometry; MCF, maximum clot firmness; ROTEM, rotational thromboelastometry.

evaluation of HELLP corroborates the hypocoagulable state and propensity toward hemorrhagic complications described previously about this syndrome.³⁹

Our study has several limitations. First, as a retrospective study, our study was not as strongly powered as a randomized controlled trial. Our descriptive study was not designed to prove causation nor definitively identify the key confounding factors for our significantly different results by race and comorbidities. Additionally, as our inclusion criteria were designed to be a representative depiction of our patient population, our sample size was more lenient than in previous studies, allowing for more heterogeneity. Despite this, we had smaller interquartile ranges than earlier, more racially homogenous studies. Also, while our study was designed to be inclusive, the sample size of patients with gDM, HELLP syndrome, and preeclampsia with and without severe thrombocytopenia was relatively small, not meeting the sample size recommendation by the International Federation of Clinical Chemistry in our subgroups. Similarly, <120 Asian and other race patients were evaluated. Thus, future work should

include larger sample sizes for Asian populations and those with comorbidities. Additionally, when comparing the race variable on whole blood analysis, BMI was not controlled. Hence, the hypercoagulable propensity in Black patients cannot be determined to be secondary to obesity or race, although the current literature suggests that both factors are independent predictors of venous thromboembolism.^{40,41} Lastly, race is a social construct dependent on culture, language, family history, SES, education level, structural differences, and legislation and was self-reported. The fidelity of our patients to their race variable cannot be confirmed.

In conclusion, the ROTEM delta, since its introduction at our institution in 2015, has shifted from a tool for exclusive active hemorrhage management to an inclusive device for preemptive assessment of patients considered at high risk for hemorrhage. To properly manage PPH with this developing technology, we describe the largest baseline reference range values for ROTEM from a US institution to reflect the diversity in race, SES, BMI, and comorbid conditions that makes up this population. Despite differences in

Table 5. Effect of race on ROTEM parameters^a

Parameters	Race				P value
	White	Black	Asian	Other	
FIBTEM					
CT	58.0 (18.6)	57.5 (13.1)	57.0 (9.2)	58.1 (10.1)	0.96
Alpha angle	75.2 (4.8)	76.3 (5.0)	72.8 (4.5)	75.8 (4.0)	0.007
MCF	25.5 (6.0)	27.4 (7.8)	21.7 (5.1)	26.2 (6.2)	<0.001
A10	23.0 (5.4)	25.6 (6.7)	19.7 (5.0)	24.1 (5.2)	<0.001
		2.67 (0.73), [1.23, 4.11], P< 0.001	-3.38 (1.09), [-5.43, -1.13], P= 0.003	NSS	
A20	24.8 (5.6)	27.3 (7.3)	21.3 (5.0)	25.7 (5.7)	<0.001
		2.60 (0.80), [1.03, 4.17], P= 0.001	-3.50 (1.10), [-5.66, -1.34], P= 0.002	NSS	
EXTEM					
CT	63.3 (37.3)	61.7 (12.9)	60.6 (7.1)	61.2 (9.7)	0.80
CFT	74.7 (33.3)	63.8 (17.6)	85.5 (24.5)	70.7 (26.3)	<0.001
Alpha angle	76.2 (4.5)	77.5 (3.6)	73.8 (3.2)	76.6 (4.0)	<0.001
MCF	70.1 (6.1)	70.7 (7.5)	67.8 (5.2)	71.0 (6.3)	0.083
A10	62.7 (7.5)	65.0 (6.5)	59.5 (6.4)	64.2 (7.8)	<0.001
		2.40 (0.78), [0.87, 3.93], P= 0.002	-3.30 (1.41), [-6.08, -0.52], P= 0.020	NSS	
A20	68.9 (6.0)	70.3 (5.8)	66.3 (5.8)	69.7 (6.8)	0.013
		1.56 (0.67), [0.23, 2.89], P= 0.021	-2.68 (1.27), [-5.19, -0.18], P= 0.036	NSS	
INTEM					
CT	164.1 (39.7)	159.6 (34.9)	172.2 (28.9)	166.0 (42.4)	0.30
CFT	73.2 (37.4)	63.3 (21.7)	80.2 (33.7)	63.3 (22.1)	0.001
Alpha angle	76.0 (5.2)	77.3 (3.8)	74.1 (5.0)	77.5 (3.7)	<0.001
MCF	67.7 (6.8)	68.6 (8.4)	66.0 (6.1)	69.6 (6.2)	0.027
A10	60.4 (7.9)	63.2 (7.2)	58.1 (7.2)	63.1 (7.3)	<0.001
		2.85 (0.86), [1.16, 4.54], P= 0.001	NSS	2.69 (0.92), [0.87, 4.50], P= 0.004	
A20	66.6 (7.0)	68.7 (6.5)	64.2 (6.7)	68.9 (6.6)	0.001
		2.08 (0.79), [1.16, 4.54], P= 0.008	NSS	2.29 (0.86), [0.60, 3.99], P= 0.008	

^aMean (standard deviation) shown on first line. Difference of means (standard error) [95% confidence interval], P value added for some comparisons. A10 indicates amplitude at 10 min; A20, amplitude at 20 min; CT, clotting time; EXTEM, extrinsic pathway thromboelastometry; FIBTEM, fibrin polymerization thromboelastometry; INTEM, intrinsic pathway thromboelastometry; MCF, maximum clot firmness; NSS: not statistically significant; ROTEM, rotational thromboelastometry.

inclusion and exclusion criteria, sample size, and geographical genetic composition, our healthy baseline medians reflect those previously reported. Based on subanalyses by

comorbidities, our study suggests that obesity and pre-eclampsia may increase whole blood coagulation and HELLP syndrome may decrease it. Lastly, Asian and Black patients

may present with hypocoagulable and hypercoagulable states, respectively, likely due to the complex interweaving of race, environment, nutrition, and healthcare access.⁴² As obstetric anesthesiology progresses to individualized, patient-centered care, our results provide reference ranges for the diverse array of patient presentations in the United States, allowing for more personalized care with contextualization of each patient's unique risk factors.

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