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Baseline parameters for rotational thromboelastometry (ROTEM®) in healthy women undergoing elective caesarean delivery: A prospective observational study in Australia

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This study was conducted at The Royal Brisbane and Women's Hospital (RBWH).

Short Title: ROTEM® baseline parameters in elective caesarean deliveries

Abstract

Background: Formal reference ranges for rotational thromboelastometry (ROTEM®) in pregnancy have not been obtained in the recommended minimum sample size of 120. This prospective observational study aimed to establish baseline parameters in an Australian population of women undergoing elective caesarean delivery. The secondary aim was to compare these reference ranges with those from prior studies and the manufacturer.

Methods: Women undergoing elective caesarean delivery at term were included if they were at term, with normal body mass index and had no conditions affecting coagulation. ROTEM® reference ranges were derived by calculating the 2.5 and 97.5 percentiles for INTEM/EXTEM/FIBTEM amplitude at 5 minutes (A5), amplitude at 15 minutes (A15), coagulation time (CT), maximum clot firmness (MCF), and clot formation time (CFT).

Results: Of 202 women screened, 132 met the inclusion criteria, having a mean age of 32.7 ± 5.0 years and median body mass index of 23.8 kg/m^2 (interquartile range 21.5-26.4). The reference ranges for selected ROTEM® parameters were as follows: FIBTEM A5 (13-28 mm), FIBTEM CT (40-74 s), FIBTEM MCF (16-34 mm), EXTEM A5 (39-66 mm), EXTEM CT (43-69 s), INTEM A5 (38-63 mm).

Conclusions: ROTEM® reference ranges for women with uncomplicated term pregnancies were reported as per the International Federation of Clinical Chemistry. The FIBTEM MCF and FIBTEM/EXTEM/INTEM amplitudes were higher in comparison to the manufacturer's reference ranges for the non-obstetric population. The EXTEM CT was shorter than the non-obstetric reference ranges. These ranges show an increase in coagulability during normal pregnancy compared to the non-pregnant reference ranges.

Keywords: Coagulation; elective caesarean deliveries; pregnancy; reference ranges; rotational thromboelastometry; ROTEM®; third trimester.

Introduction

Postpartum haemorrhage (PPH) remains the leading cause of maternal morbidity and mortality worldwide.[1, 2] In pregnancy, there is a physiological shift towards hypercoagulation,[3] despite compensatory mechanisms of haemodilution and an increase in tissue factor-pathway inhibitor (TFPI) activity.[3] However, as placental blood flow at term constitutes 15 percent of the total cardiac output, obstetric haemorrhage can be a life threatening event.[4] Rotational thromboelastometry (ROTEM®) is a point-of-care test of coagulation. ROTEM®-guided transfusion of blood products has consistently shown a significant reduction in bleeding and transfusion requirements in the trauma setting.[5-7] Its use is well established in hepatic and cardiac surgery and it is being used increasingly in obstetric care.[3, 8, 9]

Management of obstetric haemorrhage may be optimised by knowledge of ROTEM® reference ranges specific to the obstetric population, due to the hypercoagulable state in pregnancy. However, there is a lack of standardisation and data for the definition of normal ROTEM® values and controls in obstetric care. Currently, reference ranges have been obtained from the non-pregnant population and are inferred in the pregnant population. Therefore, formal baseline parameters for ROTEM® need to be established in normal pregnancy, as per the International Federation of Clinical Chemistry (IFCC). The IFCC recommends a minimum sample size of 120 for establishing reference ranges. One hundred and twenty observations are required to determine both the central 95% of the distribution, by calculating the 2.5th and 97.5th percentile, and the 90% confidence limits of both endpoints.[10, 11] There are several studies published reporting reference ranges in obstetrics,[12-16] but they report from samples of less than 120 women.[12, 14, 15]

This prospective observational study aimed to establish baseline parameters in an Australian obstetric population undergoing elective caesarean delivery at term. A secondary aim was to compare the values with reference ranges available from prior studies and the manufacturer.[17]

Methods

This manuscript adheres to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) Statement. This single-centre observational study was conducted at a tertiary referral hospital with institutional review board approval (HREC/14/QRBW/496). Written informed participant consent was obtained.

Women with singleton pregnancies were recruited from the maternity preadmission clinic if they were booked for an elective caesarean delivery at term (>37 weeks' gestation); aged 18-45 years; of body mass index (BMI) of 18.5-30 kg/m^2; and having an uncomplicated pregnancy. Women were excluded if they had pre-existing co-morbidities, pregnancy-related conditions, or were taking medications affecting coagulation. Excluded pregnancy-related conditions included the following: gestational hypertension, pre-eclampsia and HELLP (haemolysis, elevated liver enzymes and low platelet count) syndrome, as defined according to guidelines of the Society of Obstetric Medicine of Australia and New Zealand[18]); gestational diabetes mellitus, defined according to criteria of the Queensland Clinical Guidelines[19]; and anaemia, defined according to the World Health Organisation definition.[20] Women with the following conditions were also excluded: gestational thrombocytopaenia, cholestasis of pregnancy, antepartum haemorrhage, Factor V Leiden deficiency, antiphospholipid syndrome, haemochromatosis, thalassaemia and human immunodeficiency virus. Women on anticoagulant drugs for thromboembolism or on aspirin were excluded.

ROTEM® sampling occurred upon insertion of an intravenous cannula pre-operatively. Blood samples were obtained by peripheral venepuncture and placed in standard 3.5 mL Vacutainer™ collection tubes (Becton-Dickinson, North Ryde, Australia) containing 3.2% sodium citrate. The ROTEM® analysis occurred within two hours of specimen collection. The ROTEM® results were reviewed retrospectively and were not used to alter clinical management.

All ROTEM® tests were performed by trained personnel, using citrated whole blood and a ROTEM® Delta analyser (Pentapharm, Munich, Germany). The INTEM, EXTEM and FIBTEM tests were performed on three parallel channels simultaneously, using automated pipette programmes according to the manufacturer's instructions. The ROTEM® parameters of clotting time (CT), clot formation time (CFT), clot formation rate (CFR), alpha angle, maximum clot firmness (MCF), amplitude at five, 10, 15, 20 and 30 minutes (A5, A10, A15, A20, A30), the area under the curve (AUC) and the maximum velocity (MaxV) were calculated and compared to the manufacturer's reference ranges for the non-obstetric population.

A minimum sample size of 120 was targeted for establishing reference values, as per the IFCC recommendations. This minimum number provides enough data to determine both the central 95% of the distribution and the 90% confidence limits of both endpoints. With 120 observations, rank 3 is the 2.5th

percentile; rank 118 is the 97.5th percentile; ranks 1 and 7 define the 90% confidence interval of the 2.5th percentile; and ranks 114 and 120 define the 90% confidence interval of the 97.5th percentile.[10] The ROTEM® reference ranges were derived by calculating the 2.5 and 97.5 percentiles, as well as stating the minimum and maximum values for INTEM/EXTEM/FIBTEM parameters, including A5, A15, CT, MCF and CFT. Statistical analysis was performed using SPSS Statistics Software Version 23. Categorical variables were summarised by frequencies and percentages; continuous variables by means and standard deviations; and median and interquartile range (IQR) for non-normally distributed variables.

Results

Two hundred and two women were screened between January and December 2016 and one hundred and thirty-two (59%) met inclusion criteria. Fig. 1 shows the reasons for exclusion. The women had a mean age of 32.7 ± 5.0 years, a median gestation of 39 weeks (IQR 38.3-39.3), and median BMI of 23.8 kg/m^2 (IQR 21.5-26.4). Twenty-six (19.7%) women were nulliparous and 89 (67.4%) were presenting for a repeat caesarean delivery (Table 1*)*. The medians and IQRs for selected ROTEM® parameters are shown in Tables 2-4. Table 5 shows information on the study cohort for this current study and prior studies. A comparison with reference limits from previous studies is shown in Table 6.

Discussion

This is the first study to establish baseline ROTEM® parameters with the minimum number of 120 women using three different assays (FIBTEM, EXTEM and INTEM), in a cohort of healthy pregnant women at term with singleton pregnancies and a normal BMI. The study provides more reference limits than all previously published studies combined. We observed results consistent with the hypercoagulable state in pregnancy. The FIBTEM MCF was higher in comparison to the manufacturer's reference range for the non-obstetric population. Similarly, the EXTEM and INTEM MCF, were higher and narrower in range. The FIBTEM/EXTEM/INTEM amplitudes were also higher than the non-obstetric population. The EXTEM CT was shorter than the non-obstetric reference range, with the upper and lower limits differing by more than 10 percent. Narrower ranges were also demonstrated for EXTEM CFT, alpha angle, and INTEM CFT.

The manufacturer's reference ranges for the non-obstetric population are based on a study by Lang et al.[17] This was a multicentre trial across six sites and included non-pregnant individuals, blood donors, clinical personnel, and cardiac patients.

Several studies have confirmed a hypercoagulable state of pregnancy, in the form of a slightly shorter CT, and significantly greater clot firmness.[12, 13, 21, 22] These studies were designed to define reference ranges, but were of inadequate sample size and applied different exclusion criteria. Armstrong et al.[12] analysed 54 pregnant women and 54 non-pregnant women. Parturients had significantly lower haemoglobin values and platelet counts. Despite this, thromboelastometry exhibited significantly lower INTEM CT (7.3%), INTEM CFT (11.1%) and EXTEM CFT (18.0%) in the pregnant group. The MCF values were significantly higher (INTEM 10.9%, EXTEM 10.6% and FIBTEM 47.1%) in the pregnant group compared to the non-pregnant group. However, they did not analyse ROTEM® values other than CT, CFT, alpha angle and MCF.[12] The change in ROTEM® parameters has been shown to be gradual throughout the three trimesters with a significant increase in hypercoagulability by the second trimester and further increase in the final trimester.[15] This was demonstrated by Bowden et al.[15] in less than 100 women in each trimester and the control group.

An increase in EXTEM and INTEM MCF with a shorter EXTEM CT was confirmed by Duraj et al.[14] in the third trimester, in 57 non-obese healthy pregnant women with a BMI less than 30 kg/m^2. The authors did not test for the FIBTEM values.[14]

The only study to date that has met the IFCC sample size criterion for determining reference ranges is de Lange et al.[13] However, this study was limited by the inclusion of both parturients and elective caesarean participants, and those of a gestation of less than 37 weeks. They also did not discriminate based on BMI and included twin pregnancies. De Lange et al.[13] provided values for A10 and A20, but not A5, which has greater clinical utility. Our reference ranges have been established in term pregnancies, but the results are not generalisable to other pregnant women such as those with obesity, gestational diabetes mellitus, coagulopathies, anaemia and those in established labour or at earlier gestations.

The inclusion and exclusion criteria used in this study were similar to previous studies, but exclusion criteria were stricter. For example, prior studies included women with gestational diabetes mellitus, despite the tendency to develop thrombosis in this condition.[23] Patients are at increased risk of bleeding when anaemic and studies have shown a hypercoagulable appearance in thromboelastography and ROTEM®. One study analysed platelet function in anaemic blood and accelerated platelet aggregation was demonstrated at lower haemoglobin concentrations.[24]

The manufacturer recommends that each site should undergo a quality control process to generate their own normal ranges, as geography can have a significant influence on values. This process should also be repeated in the obstetric population at each institution to account for these changes. Many institutions utilise viscoelastic testing and have established their own transfusion thresholds, based on the OBS2 trial results, rather than using obstetric-specific reference ranges.[25] The OBS2 randomised controlled trial demonstrated that the infusion of fibrinogen concentrate triggered by a FIBTEM A5 value of less than 15 mm did not improve PPH outcomes.[25] However, a subgroup analysis suggest that fibrinogen is not required if the FIBTEM A5 is greater than 12 mm.[25] The reference ranges from this current study would not replace transfusion triggers, but complement their use in clinical practice. For example, an EXTEM clotting time value may appear normal if non-obstetric ranges were used, but may in fact be on the higher normal range or greater than the obstetric reference range. If a patient was still bleeding, then this knowledge would be useful in prompting the need for the transfusion of fresh frozen plasma. In contrast, if a FIBTEM A5 value appears normal based on non-obstetric ranges, the value may in fact be within the lower normal range or lower than the obstetric reference range. If the patient had ongoing blood loss, then this knowledge would be useful in prompting for the transfusion of fibrinogen.

A limitation of the study is that ROTEM® was not repeated postpartum to investigate the rate and timing of normalisation of coagulation parameters to non-pregnant levels. This would be of interest, as it has previously been shown that pregnancy-related hypercoagulability can persist for up to eight weeks postpartum.[26] Another limitation is that this was performed within one institution from one geographic area.

In conclusion, we have provided baseline reference ranges for ROTEM® values in women in our centre with uncomplicated pregnancies and who presented for an elective caesarean delivery at term. These ranges show an increase in coagulability during normal pregnancy compared to the non-pregnant population. Our study identified a difference in the obstetric population compared to the non-obstetric population and we conclude that pregnancy-specific ROTEM® reference ranges should be used for obstetric care.

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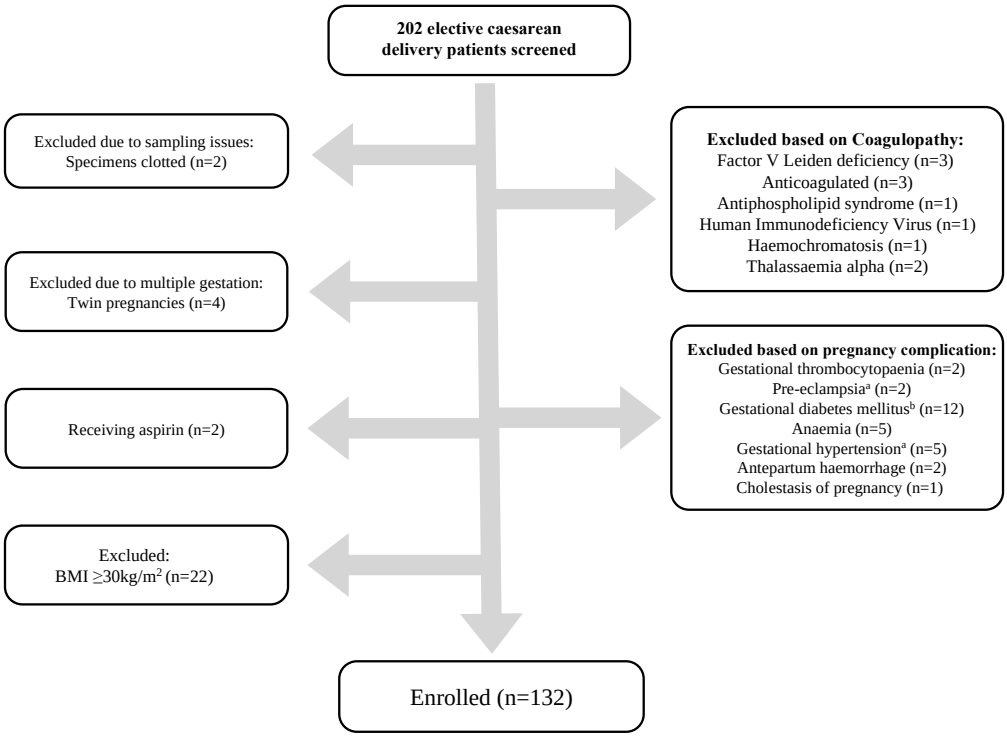
Fig. 1. Recruitment flowchart detailing participant exclusions



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[b]Gestational diabetes mellitus as described in the guidelines from the Queensland Clinical Guidelines. Sourced from The Maternity and Neonatal Clinical Guideline: Gestational diabetes mellitus, published by Queensland Health, Australia. 2015. URL:// https://www.health.qld.gov.au/__data/assets/pdf_file/0023/140099/g-gdm.pdf Accessed August 1, 2018)

Table 1. Demographic information of 132 women undergoing elective caesarean delivery at The Royal Brisbane and Women's Hospital

Characteristics (n=132)	Total n (%)
Indication for caesarean delivery	
Repeat caesarean	89 (67.4)
Other	43 (32.6)
Nulliparous	26 (19.7)
PPH	
No	121 (91.7)
Yes	11 (8.3)
Maternal age (y), mean (SD)	32.7 (5.0)
BMI (kg/m^2), median (IQR)	23.8 (21.5-26.4)
Gestation (weeks), median (IQR)	39.0 (38.6-39.3)

PPH: postpartum haemorrhage. SD: standard deviation. BMI: body mass index. IQR: interquartile range.

Table 2. Reference ranges for FIBTEM parameters established using results from 132 women delivering by elective caesarean delivery at The Royal Brisbane and Women's Hospital

Parameter	n	Min-Max	Median (IQR)	Reference range	Manufacturer's reference range
CT	132	33-75	53 (48-58)	40-74	38-62
CFR	131	67-85	77 (74-79)	67-82	-
Alpha angle	131	58-81	76 (74-78)	67-81	-
MCF	132	13-43	24 (21-27)	16-34	9-25
A5	132	10-34	20 (17-22)	13-28	6-22
A10	132	12-39	22 (19-24)	14-30	7-23
A15	130	13-41	23 (20-25)	15-32	-
A20	127	13-43	23 (20-26)	16-33	8-24
A30	124	14-43	24 (21-27)	16-34	-
AUC	132	1311-4314	2379 (2086-2639)	1634-3366	-
MaxV	132	6-47	17 (14-20)	9-27	-

ROTEM® reference ranges were derived by calculating the 2.5 and 97.5 percentiles
CT: clotting time. CFR: clot formation rate. MCF: maximum clot firmness. A5: amplitude (firmness) at 5 minutes. A10: amplitude at 10 minutes. A15: amplitude at 15 minutes. A20: amplitude at 20 minutes. A30: amplitude at 30 minutes. AUC: area under curve. MaxV: maximum velocity. IQR: interquartile range.

Table 3. Reference ranges for EXTEM parameters established using results from 132 women delivering by elective caesarean delivery at The Royal Brisbane and Women's Hospital

Parameter	n	Min-Max	Median (IQR)	Reference range	Manufacturer's reference range
CT	132	42-78	54 (49-57)	43-69	38-79
CFT	132	39-140	64 (57-71)	43-108	34-159
CFR	132	71-83	79 (77-80)	71-82	-
Alpha angle	132	67-82	77 (76-79)	69-82	63-83
MCF	132	55-80	70 (68-73)	60-78	50-72
A5	132	32-68	53 (50-57)	39-66	-
A10	132	43-75	63 (61-67)	50-73	43-65
A15	129	48-78	67 (65-70)	55-76	48-69
A20	127	51-80	69 (67-72)	57-77	50-71
A30	123	54-80	70 (68-73)	60-78	-
AUC	132	5441-7928	6964 (6766-7234)	5960-7645	-
MaxV	132	11-31	20 (18-22)	12-30	-

ROTEM® reference ranges were derived by calculating the 2.5 and 97.5 percentiles
CT: clotting time. CFR: clot formation rate. MCF: maximum clot firmness. A5: amplitude (firmness) at 5 minutes. A10: amplitude at 10 minutes. A15: amplitude at 15 minutes. A20: amplitude at 20 minutes. A30: amplitude at 30 minutes. AUC: area under curve. MaxV: maximum velocity. IQR: interquartile range.

Table 4. Reference ranges for INTEM parameters established using results from 132 women delivering by elective caesarean delivery at The Royal Brisbane and Women's Hospital

Parameter	n	Min-Max	Median (IQR)	Reference range	Manufacturer's reference range
CT	132	108-270	165 (145-185)	115-245	100-240
CFT	132	38-140	63 (53-71)	42-103	30-110
CFR	132	70-83	78 (77-80)	71-83	-
Alpha angle	132	69-82	77 (76-79)	70-82	70-83
MCF	132	54-79	69 (66-71)	59-76	50-72
A5	132	31-66	51 (48-55)	38-63	38-57
A10	132	42-74	62 (59-65)	49-70	44-66
A15	127	47-77	66 (63-69)	54-74	48-69
A20	127	50-78	68 (65-70)	57-75	50-71
A30	122	53-79	69 (66-71)	59-76	-
AUC	132	5375-7820	6858 (6588-7069)	5886-7524	-
MaxV	132	11-34	19 (17-23)	12-31	-

ROTEM® reference ranges were derived by calculating the 2.5 and 97.5 percentiles
CT: clotting time. CFR: clot formation rate. MCF: maximum clot firmness. A5: amplitude (firmness) at 5 minutes. A10: amplitude at 10 minutes. A15: amplitude at 15 minutes. A20: amplitude at 20 minutes. A30: amplitude at 30 minutes. AUC: area under curve. MaxV: maximum velocity. IQR: interquartile range.

Table 5. Study cohort information for all prior studies

Study	Our Study	Lang et al. (2005)[17] (non-obstetric ranges)	Armstrong et al. (2011)[12]	Bowden et al. (2016)[15]	Duraj et al. (2015)[14]	De Lange et al. (2014)[13]	Huissoud et al. (2009)[21]
Study size	n=132	n=155 INTEM n=202 EXTEM n=143 FIBTEM	n=108	n=316	n=112	n=161	n=104
Number of centres	Single centre	Multicentre (6 sites, 40-60 from each site)	Single centre	Single centre	Single centre	Multicentre	Single centre
Study group	Elective caesarean deliveries	Non-pregnant, blood donors, clinical personnel, heart patients (including patients with diabetes and renal insufficiency)	n=54 pregnant (elective caesarean delivery) n=54 non-pregnant	n=99 First trimester n=60 Second trimester n=80 Third trimester n=75 non-pregnant	n=55 Non-pregnant n=57 Healthy pregnant women (n=50 tested four times throughout pregnancy)	Parturients (induced and spontaneous) and elective caesarean deliveries (elective and emergency)	n=20 non-pregnant n=17 First trimester n=9 Second trimester n=58 Third trimester
Geographical location	Australia	Germany, France, Austria	United Kingdom	United Kingdom	Slovakia	The Netherlands	France
Ethnicities	75.8% Caucasian, 9.1% South East Asian, 6.8% Indian, 7.6% Other, 0.8% Indigenous Australian	-	79.6% Caucasian, 7.4% Afro-Caribbean, 13% Asian	-	-	94.4% Caucasian, 0.6% Indian/Pakistani, 0.6% African, 1.2% Mediterranean, 1.2% South American, 3.7% Other	-
Age exclusions	<18 y >45 y	-	<18 y >45 y	-	<18 y >45 years	-	-
Age (y)	32.7 (5.0)	45.4 (17.6) INTEM 43.1 (15.9) EXTEM 38.8 (14.1) FIBTEM	33.5 (5.7)	-	-	31.6 [22-43]	29 [26-33] pregnant group 30 [21-32] control group
Weight exclusions	BMI <18.5 or >30 kg/m^2	-	<50 kg >100 kg	-	BMI >30 kg/m^2	-	-
BMI	23.8 [21.5-26.4]	-	-	-	-	24.6 [16.8-41.5]	-
Gestational age (weeks)	>37 weeks included only	-	-	-	-	>24 weeks included	-
Past medical history exclusions	Personal or family history of coagulation disorders	Pregnancy and lactation	Personal or family history of coagulation disorders	Coagulopathies or conditions associated with	Haemostasis defects Thromboembolic disease	Twin pregnancies included Known bleeding	Hypertension Inflammatory syndrome Chronic disease

				coagulopathy		disorders	Coagulopathy
Other exclusions	Gestational hypertension Pre-eclampsia HELLP syndrome GDM Anaemia Gestational thrombocytopaenia Cholestasis APH HIV	Recent blood transfusion, recent surgery, raised liver enzymes	Blood transfusion or surgery within 28 days Abnormal FBC Smoking history or concurrent disease (cardiovascular, renal, malignancy, liver disease)	-	Pre-eclampsia Fetal loss Preterm delivery Inadequate blood sampling	-	-
Medication exclusions	Medications affecting coagulation	Antiplatelet medication, analgesics	Medications affecting coagulation	Medications affecting coagulation	Anticoagulation Antiplatelet	Prophylactic or therapeutic coagulation	Anticoagulation Antiplatelet

Data are mean (SD) and median [IQR]. BMI: body mass index. HELLP: haemolysis, elevated liver enzymes, low platelets. GDM: gestational diabetes mellitus. APH: antepartum haemorrhage. HIV: human immunodeficiency virus. FBC: full blood count.

Table 6 Comparison of reference limits from previous studies

Study	Our Study	Lang et al. (2005)[17] (non-obstetric)	Armstrong et al. (2011)[12]	Bowden et al. (2016)[15]	Duraj et al. (2015)[14]	De Lange et al. (2014)[13]	Huissoud et al. (2009)[21]
FIBTEM Parameters							
CT	53 (40-74)	51 (43-69)	49 (20-95)	-	-	39 (31-79)	5 [46-65]
CFR	77 (67-82)	-	-	-	-	-	-
Alpha angle	76 (67-81)	-	78 (33-86)	-	-	79 (50-83)	-
MCF	24 (16-34)	16 (9-25)	25 (15-38)	23 (8-49)	-	25 (22-28)	19 [17-23]
A5	20 (13-28)		-	18 (7-31)	-	-	16[15-20]
A10	22 (14-30)	14 (9-24)	-	-	-	22 (12-38)	-
A15	23 (15-32)	-	-	-	-	-	19 [17-22]
A20	23 (16-33)	15 (8-21)	-	-	-	24 (13-40)	-
A30	24 (16-34)	-	-	-	-	-	-
AUC	2379 (1634-3366)	-	-	-	-	-	-
MaxV	17 (9-27)	-	-	-	-	-	-
EXTEM Parameters							
CT	54 (43-69)	55 (42-74)	47 (31-80)	-	42 [39-45]	45 (41-50)	53 [47-62]
CFT	64 (43-108)	95 (46-148)	50 (34-86)	-	-	69 (62-81)	74 [66-89]
CFR	79 (71-82)	-	-	-	-	-	-
Alpha angle	77 (69-82)	72 (63-81)	80 (64-83)	-	-	77 (67-83)	-
MCF	70 (60-78)	60 (49-71)	73 (66-92)	-	71 [69-73]	71 (42-78)	67 [64-71]
A5	53 (39-66)	-	-	-	-	-	49 [47-54]
A10	63 (50-73)	53 (43-65)	-	-	-	64 (61-68)	-
A15	67 (55-76)	-	-	-	-	-	64 [62-68]
A20	69 (57-77)	59 (50-69)	-	-	-	70 (68-73)	-
A30	70 (60-78)	59 (50-69)	-	-	-		-
AUC	6964 (5960-7645)	-	-	-	-		-
MaxV	20 (12-30)	-	-	-	-		-
INTEM Parameters							
CT	165 (115-245)	184 (137-246)	140 (86-168)	-	156 [142-180]	147 (109-225)	155 [132-186]
CFT	63 (42-103)	63 (40-100)	48 (33-108)	-	-	55 (40-103)	66 [58-78]
CFR	78 (71-83)	-	-	-	-	-	-
Alpha angle	77 (70-82)	77 (71-82)	81 (71-83)	-	-	79 (70-82)	-
MCF	69 (59-76)	61 (52-72)	71 (55-79)	-	71 [68-72]	71 (63-78)	66 [63-69]
A5	51 (38-63)	-	-	-	-	-	48 [45-52]
A10	62 (49-70)	55 (44-68)	-	-	-	64(55-72)	-
A15	66 (54-74)	48-69	-	-	-	-	62 [60-66]
A20	68 (57-75)	60 (50-71)	-	-	-	70 (62-77)	-
A30	69 (59-76)	60 (51-72)	-	-	-	-	-
AUC	6858 (5886-	-	-	-		-	-

	7524)						
MaxV	19 (12-31)	-	-	-	-	-	-

Data are median and 2.5-97.5 percentiles except for column 5* and 7* which displays median [IQR]. CT: clotting time. CFR: clot formation rate. MCF: maximum clot firmness. A5: amplitude (firmness) at 5 minutes. A10: amplitude at 10 minutes. A15: amplitude at 15 minutes. A20: amplitude at 20 minutes. A30: amplitude at 30 minutes. AUC: area under curve. MaxV: maximum velocity. IQR: interquartile range.

HIGHLIGHTS

- Rotational thromboelastometry reference ranges were established in term pregnancies
- Measures of clot firmness were higher than non-obstetric reference ranges
- Times to clotting onset were shorter than non-obstetric reference ranges
- ROTEM® reference ranges in pregnant women were different to non-obstetric values