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New recommendations for thromboelastography reference ranges for pregnant women

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ABSTRACT

Introduction: The target of this study was to compare thromboelastography coagulation parameters in pregnant and non-pregnant women. If appropriate, we would propose recommendations for new reference ranges for pregnant women in their third trimester.
Materials and methods: Prospective observational study, comparing, by using thromboelastography, the blood samples of 60 healthy women in third trimester of pregnancy (group GRAV) to the samples of the control group of 43 healthy non-pregnant fertile women (group NON-GRAV). Selective percentiles were used to determine new reference limits.
Results: Mean values and standard deviations (SD) in both groups were as follows (GRAV vs NON-GRAV): time *r* 4.7 min (SD 1.7) vs. 7.8 (SD 2.8); time *k* 1.5 min (SD 0.5) vs. 2,7 (SD 0,9); alpha angle 69.6° (SD 5.5) vs. 54.4 (SD 11.5); maximum amplitude 71.3 mm (SD 4.5) vs. 63.1 (SD 5.4); coagulation index 2.7 (SD 1.8) vs. -1.9 (SD 3.0); LY60 1.1% (SD 1.8) vs. 4.8 (SD 3.6). Due to statistically significant differences between both groups, we established, based on our results, these new thromboelastography reference limits for pregnant women: time *r* 2–8 min ("common" range 4–8 min), time *k* 1–3 min ("common" range 1–4 min), alpha angle 60-77° ("common" range 47-74°), maximum amplitude 64–76 mm ("common" range 55–73 mm), LY60 0–3% ("common" range 0-15%), coagulation index 0–5 ("common" range (−3) – (+3)).
Conclusions: It may not be suitable to use the same reference ranges for pregnant women as for the general population. Therefore, we suggest new reference limits for thromboelastography in pregnant women.

Introduction

During pregnancy, a physiological shift of coagulation balance occurs in terms of hypercoagulation [1–3]. The main causes of hypercoagulation during pregnancy are a slowdown of blood flow, a reduction of protein S activity, an increase in prothrombin activity and a higher concentration of some plasma coagulation factors (fibrinogen, factors VII, VIII and von Willebrand factor). There also exist some physiological compensation mechanisms such as pregnancy hemodilution and an increase in tissue factor-pathway inhibitor (TFPI) activity. Even with the existence of these compensation mechanisms hypercoagulation arises in physiological pregnancy.

Although this is common knowledge, pregnant woman coagulation levels are routinely compared to the reference ranges of the general population [4]. "Pregnancy" standards have been already established for some of the laboratory coagulation parameters [5,6].

Thromboelastography is a unique bedside method used to examine blood coagulation. The basis of this method is an in-vitro measurement of the viscoelasticity properties in blood. The thromboelastogram shows a dynamic model of the creation of coagulum from initialization through acceleration to retraction or lysis. By adding kaolin it is possible to accelerate the examination, which can be clinically important in situations with fast changes in coagulation status (life-threatening bleeding, disseminated intravascular coagulation etc.) In the past few years thromboelastography has been used more frequently for determining coagulation levels in others groups of patients [7–10].

We hypothesize that coagulation levels change significantly during pregnancy so it is not accurate to use the same reference ranges for thromboelastography examinations for pregnant women as those used for the general population. The target of this prospective observational study was to compare thromboelastography coagulation parameters in pregnant women with those of non-pregnant women. In the case of finding significant variations in the levels of coagulation between these

Abbreviations: AA, alpha angle; CI, Coagulation index; GUH, General University Hospital; k, time k; LY60, fibrinolysis at 60 minutes; MA, maximum amplitude; r, time r; SD, standard deviation; TEG, thrombelastography; TFPI, tissue factor-pathway inhibitor.

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two groups we will set new reference ranges for pregnant women based on the data collected.

Materials and methods

Study participants

The GRAV group contained a random sample of 60 healthy women who were in their third trimester of physiological pregnancy and who came for a medical check-up or for childbirth to the Department of Gynecology and Obstetrics at the General University Hospital (GUH) and 1st Faculty of Medicine, Charles University in Prague.

Inclusion and exclusion criteria

The exclusion criteria for the GRAV group were: 1) below 15 years or above 45 years of age; 2) a medical history of coagulopathy and/or thromboembolic disease; 3) anticoagulation treatment and/or treatment with anti platelet drugs during pregnancy; 4) the women who did not consent to participate in the study.

The control group (NON-GRAV group) contained 43 healthy non-pregnant women. The exclusion criteria for the NON-GRAV group were: 1) below 15 years or above 45 years of age; 2) a medical history of coagulopathy and/or thromboembolic disease; 3) anticoagulation treatment and/or treatment with anti platelet drugs in the last 30 days; 4) have used hormonal contraceptives in the last 6 months; 5) are currently pregnant; 6) have undergone delivery or abortion in the last 6 months; 7) the women who did not consent to participate in the study.

Before being admitted into the study, all of the women underwent an informative interview with a physician and expressed their written consent to participate in the study. The Ethics Committee of the GUH granted consent with the performed study.

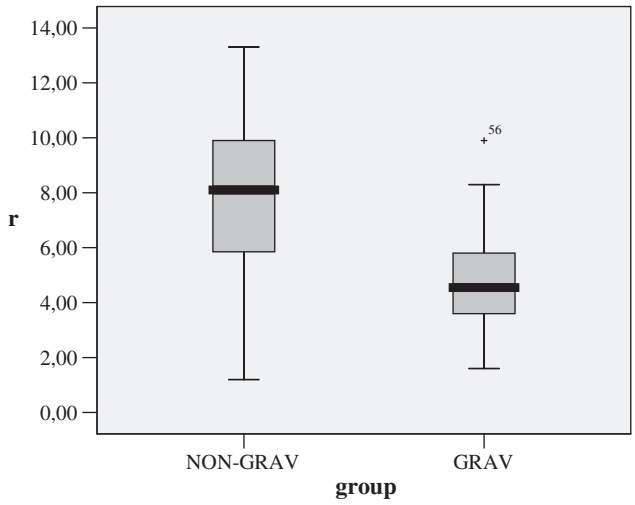
Thromboelastography

The sample of venous blood used for the study was taken prior to any infusion therapy. The venous blood was taken from the 18-20 G peripheral venous cannula using the two syringe method. Only the sample from the second syringe was used for the study, after drawing at least a three fold of the so called "dead space" using the first syringe. A 360 μL sample from 1 mL of whole, kaolin-activated blood was tested using thromboelastography (for exact procedure, see manufacturer's recommendations – Haemascope Corp., Skokie, IL, USA, www.haemoscope.com). The analysis, using the TEG® device, was performed within 4 minutes of taking the sample. The entire procedure was performed at 37 °C. The following parameters were recorded: time *r*, time *k*, alpha angle (AA), maximum amplitude (MA) and LY60 as parameter of fibrinolysis. Coagulation index (CI) was calculated from the measured results. The TEG® device was calibrated and tested daily (according to recommendations of Haemascope Corp., Skokie, IL, USA, www.haemoscope.com).

Table 1
Tromboelastographic parameters of pregnant and non-pregnant women.

	GRAV (n = 60)		NON-GRAV (n = 43)		p-value
	mean	SD	mean	SD	
r	4.75	1.74	7.81	2.76	0.001
k	1.48	0.45	2.72	0.94	0.001
AA	69.58	5.52	54.38	11.48	0.001
MA	71.33	4.45	63.06	5.4	0.001
LY60	1.15	1.78	4.83	3.64	0.001
CI	2.68	1.79	-1.91	3.01	0.001

Abbreviations:
r – r time (min), k – k time (min), AA – alpha angle (degree), MA – maximum amplitude (mm), LY60 – fibrinolysis factor (%), CI – coagulation index.



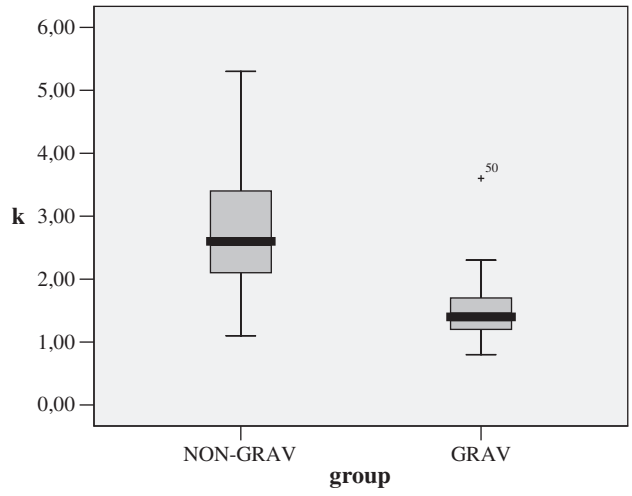
Graph 1. Time r. The bottom and top of the box represent the 25th and 75th percentile. The band inside the box shows the median. The ends of the whiskers represent the minimum and maximum of all the data except extreme value, which are plotted as a + with the identification number of the participant.

Statistical analysis

Calculations of basic statistical characteristics, i.e. mean, standard deviation (SD) and median, for continuous variables and non-parametric Mann-Whitney test were performed using the MedCals and Excel applications (www.medcalc.be/index.php). The p-value cut-off for significant difference was set at 0.01. Selective percentiles were used to determine the new reference ranges [11,12].

Results

All the women who participated in the study were healthy and had not undergone any anticoagulation and/or anti platelet drug treatment. The mean age of the women in both groups was not significantly different (the GRAV group 28.8 years, the NON-GRAV group 30.9 years). The women in the GRAV group were all in their third trimester. There was a significant difference in all the thromboelastography parameters



Graph 2. Time k. The bottom and top of the box represent the 25th and 75th percentile. The band inside the box shows the median. The ends of the whiskers represent the minimum and maximum of all the data except extreme value, which are plotted as an + with the identification number of the participant.