Blood Rheology during normal pregnancy – Results of a single center investigation

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Introduction

- The course of normal pregnancy goes along with a marked increase of blood volume to upto 1.5 liter in favour to a plasma/cell ratio of 2:1 resulting in physiologic hemodilution that is most pronounced in the 2\textsuperscript{nd} trimester.

- In a previous study we found increased erythrocyte aggregation (38 ± 7.9) and a plasma viscosity in the upper range (1.32 ± 0.8 mPa s) in a total of 3,959 women with normal pregnancy at the end of the 3\textsuperscript{rd} trimester within two days before delivery.

- Moreover, among women with different pathologic pregnancy outcomes (n=1,026) pre-eclampsia (n=428) was associated with significant higher erythrocyte aggregation and hematocrit as compared to normal pregnancy.
Erythrocyte aggregation *in stasis* and *low shear*
Plasma viscosity

- normal pregnancy
- pre-eclampsia
- birth weight < 2500g
- IUGR
- early birth (<37 SSW)

25-75% inter quartile, means, medians

n.s. p<0.0001 n.s. p=0.003
Objectives of the study

Longitudinal assessment of blood rheological parameters prior to and within each trimester during normal pregnancy with particular emphasize to Red Blood Cell deformability
Laboratory Methods

Blood rheological parameters:

- **Plasma viscosity:** Capillary tube viscometer (KSVP-4)  
  Fresenius, Bad Homburg Germany

- **RBC aggregation:** Aggregometer (MA1)  
  Myrenne, Roetgen, Germany

- **RBC deformability:** Rheodyn SSD shear stress diffractometer  
  Myrenne, Roetgen, Germany
Design of Investigation

- two center investigation
  Acquisition periode II: June 2015 ongoing.
- Inclusion criteria: Women who visit for routine pregnancy check-ups
- Exclusion criteria:
  - severe or chronic disease
  - development of severe pregnancy related complications such as preeclampsia, HELLP-Syndrome, IUGR, a.s.o
  (data will be analyzed separately)
- Signed informed consent.
- Anonymized data acquisition via questionnaire.
- Vote of Ethik Kommission (Maximillians University – Würzburg, Germany)
Statistical Analysis

- Descriptive analysis.
- None parametric analysis (Friedmann test).
- Two-sided Pearson’s correlation.
- $P$ values $< 0.05$ were considered statistically significant.
- SPSS 17.0.
- Institute for Clinical Epidemiology and Biometry; Maximillians-University Würzburg.
Results – number of studied women and

Total number of pregnant women: \( n = 801 \)

Women with normal pregnancy (included): \( n = 730 \)

Number of women with rheological results prior to their pregnancy: \( n = 124 \)

Total blood rheological estimations: \( n = 1,756 \)

Investigations per pregnant women: \( 2.5 \)
Plasma viscosity

Blood Rheology before and during pregnancy

Before pregnancy

1.15 ± 0.1

n.s.

Trim

1.18 ± 0.08

1.18 ± 0.08

1.18 ± 0.1
Blood Rheology before and during pregnancy

Erythrocyte Aggregation

**stasis**

*Before pregnancy*

*Trim 1*

*Trim 2*

*Trim 3*

**low shear**

*Before pregnancy*

*Trim 1*

*Trim 2*

*Trim 3*
Blood Rheology before and during pregnancy

RBC Deformability - Low shear forces

1.2 Pa

Before pregnancy

<table>
<thead>
<tr>
<th>Trim</th>
<th>Deformability</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>11.2±2.9</td>
</tr>
<tr>
<td>2</td>
<td>8.0±2.6</td>
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<tr>
<td>3</td>
<td>7.8±2.4</td>
</tr>
<tr>
<td>4</td>
<td>10.4±3.3</td>
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</table>

P<0.001

3.0 Pa

Before pregnancy

<table>
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<tr>
<th>Trim</th>
<th>Deformability</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>22.5±3.4</td>
</tr>
<tr>
<td>2</td>
<td>18.3±4.2</td>
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<tr>
<td>3</td>
<td>17.9±4.2</td>
</tr>
<tr>
<td>4</td>
<td>21.1±4.5</td>
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</table>

P<0.001

P=0.04
Blood Rheology before and during pregnancy

RBC Deformability - moderate shear forces

6.0 Pa

<table>
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<tr>
<th>Trim</th>
<th>Before pregnancy</th>
<th>Before pregnancy</th>
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<tbody>
<tr>
<td>1</td>
<td>30.6±3.3</td>
<td>30.6±3.3</td>
</tr>
<tr>
<td>2</td>
<td>26.6±5.4</td>
<td>26.0±5.2</td>
</tr>
<tr>
<td>3</td>
<td>29.2±4.3</td>
<td>29.2±4.3</td>
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P<0.001 P<0.001 P=0.006

12.0 Pa

<table>
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<tbody>
<tr>
<td>1</td>
<td>36.9±3.2</td>
<td>32.6±5.1</td>
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<td>2</td>
<td>32.0±5.9</td>
<td>32.0±5.9</td>
</tr>
<tr>
<td>3</td>
<td>35.3±4.4</td>
<td>35.3±4.4</td>
</tr>
</tbody>
</table>

P<0.001 P<0.001 P=0.003
Blood Rheology before and during pregnancy

RBC Deformability – high shear forces

30.0 Pa

Before pregnancy

Trim

% 43.3±3.3 38.8±7.0 38.2±7.2 41.4±4.6

P<0.001 P<0.001 P=0.001

60.0 Pa

Before pregnancy

Trim

% 46.8±3.5 41.7±7.6 41.3±7.5 44.7±4.9

P<0.001 P<0.001 P<0.001
Trend of Blood Rheology results according to gestational age

Plasma viscosity

\[ r = 0.01; p=0.5 \]
Trend of Blood Rheology results according gestational age

Erythrocyte Aggregation

*stasis*  
*low shear*

$r = -0.02; p=0.3$

$r = 0.12; p<0.001$
Trend of Blood Rheology results according to gestational age

RBC Deformability - Low shear forces

1.2 Pa  
3.0 Pa

r = 0.27; p<0.001
r = 0.12; p<0.001
Trend of Blood Rheology results according gestational age

RBC Deformability - moderate shear forces

6.0 Pa

12.0 Pa

\[ r = 0.25; p<0.001 \]
\[ r = 0.27; p<0.001 \]
Trend of Blood Rheology results according gestational week

RBC Deformability – high shear forces

30.0 Pa

60.0 Pa

\[ r = 0.22; p<0.001 \]

\[ r = 0.23; p<0.001 \]
Summary

- The current investigation provides some surprising results:

  1) Aggregability of erythrocytes within the first 12 weeks of pregnancy is significantly increased as compared to the values found in the same women before pregnancy.

  2) In the first trimester Deformability of the erythrocytes is significantly lower as compared to the findings before pregnancy.

  3) The course of Plasma viscosity is neither different at the estimation time points in the first trimester nor thereafter compared to the results under non pregnant conditions.

  4) After the first and throughout the 2nd trimester erythrocyte aggregation shows a further significant increase while deformability remains unchanged compared to the values in the 2nd trimester.

  5) A trend towards lowering erythrocyte aggregation and further improvement of their deformability is present at the end of pregnancy.
Conclusion

The most marked changes in blood rheological properties seem to manifest early during pregnancy in the first trimester and are linked to an increase of the viscous properties of the Red Blood cells.

Surprisingly, developing hyper coagulability in the course of normal pregnancy has no effect on plasmatic viscosity which has long been assumed.

The onset of physiologic plasmavolume expansion at the beginning of the 2nd trimester may compensate hyper coagulability and dilutes the up to 3 fold increase of most coagulation factor concentrations (e.g. fibrinogen) which would explain uneffected plasma viscosity.

In a number of trials, pregnancy related diseases such as pre-eclampsia, thrombosis and placental insufficiency coincide with „abnormal“ (impaired ?) rheological properties. Rheological parameters may help to clarify the risk for such pathologic events.
Thank you for your attention