Increased CD14++CD16-CCR2+ monocyte-platelet aggregates in pregnant women with previous hypertension

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Introduction
Monocytes derive from bone marrow and circulate in the blood. They phagocytose, produce cytokines and present antigen. Individual monocyte subsets play distinct roles in the pathogenesis of cardiovascular disease, but their implications in hypertension in pregnancy are unclear. Monocytes combine with platelets to form monocyte-platelet aggregates (MPAs). Our objective was to examine the difference in MPAs between pregnant women with or without previous gestational hypertension (GH) or preeclampsia (PET) and non-pregnant controls.

Methodology
Monoclonal antibodies against cell surface receptors and flow cytometry were used to detect MPAs. CD14++CD16-CCR2+ (MPA1), CD14++CD16+CCR2+ (MPA2) and CD14+CD16+CCR2- (MPA3) monocyte-platelet aggregates were analysed in 17 pregnant women with previous hypertension in pregnancy, 42 pregnant women without previous gestational hypertensive disease and 27 healthy, non-pregnant controls. All women had normal blood pressure <140/90mmHg at the time of the study. Ethical approval was obtained.

Table
Counts of monocyte-platelet aggregates. Data expressed as median (interquartile range).

<table>
<thead>
<tr>
<th>Monocyte-platelet aggregates (cells/μl)</th>
<th>Pregnant; Hypertension in previous pregnancy (n = 17)</th>
<th>Pregnant; No previous hypertension (n = 42)</th>
<th>Non-pregnant controls (n = 27)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>MPA1</td>
<td>40 (33-62)†</td>
<td>35 (26-47)</td>
<td>32 (23-38)</td>
<td>0.02</td>
</tr>
<tr>
<td>MPA2</td>
<td>2 (1-6)</td>
<td>3 (1-6)</td>
<td>4 (2-5)</td>
<td>0.99</td>
</tr>
<tr>
<td>MPA3</td>
<td>6 (4-8)</td>
<td>5 (4-9)†</td>
<td>3 (2-5)</td>
<td>0.002</td>
</tr>
<tr>
<td>Total</td>
<td>51 (43-69)†</td>
<td>47(34-66)†</td>
<td>41 (26-46)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Dunn’s post hoc testing; *p<0.05 vs group without previous hypertension; †p<0.05 vs non-pregnant controls.

Results
The groups were well-matched for age, body mass index and ethnicity (p>0.05 for all). The pregnant women were studied at 13±1 weeks gestation. MPA1 counts were higher in women with a history of GH or PET compared to other groups (p<0.05 for both) (Table). MPA3 and total MPAs were higher in both groups of pregnant women compared to non-pregnant controls (p<0.01). Blood pressure and parity were significantly higher in the group with previous GH/PET. A previous pregnancy affected by GH/PET was the only significant predictor of increased MPA1 count (B±SE 0.49±21.1, p<0.001).

Discussion
It is unclear whether phenotypic differences in monocytes are the cause of effect of disease. The pathophysiology of PET has been related to abnormal placentation and endothelial dysfunction. Women affected by hypertension may have a heightened pro-inflammatory state in pregnancy. Differences in peripheral blood monocytes may be mirrored by the macrophages in the placental bed. MPAs are a marker of monocyte and platelet activation and physical interaction between platelets and monocytes may influence their function.

Conclusion
MPA1 is increased at the beginning of the second trimester of pregnancy in women with a previous hypertensive pregnancy. MPAs are increased in pregnancy irrespective of a history of hypertension. Possible (patho)physiological and clinical effects of the changes in monocytes subsets and their cross talk with platelets in pregnancy will need to be established in the future.

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Conflicts of interest: none declared

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