

## Supplementary Data

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Table S1: Classifications and definitions of HDP

<p><b>Hypertension in pregnancy</b><sup>24-26</sup></p>	<p>Hypertension in pregnant women is defined as systolic blood pressure (SBP) greater than or equal to 140 mmHg and/or diastolic blood pressure (DBP) greater than or equal to 90 mmHg on two or more occasions at least four hours apart.</p>
<p><b>Gestational hypertension (GH)</b><sup>24, 25</sup></p>	<p>Hypertension developing after 20 weeks of gestation in previously normotensive women. The hypertension normalizes within 12 weeks postpartum.</p> <ul style="list-style-type: none"> <li>• No biochemical or haematological abnormalities.</li> </ul>
<p><b>Preeclampsia (PE) &amp; HELLP-syndrome</b><sup>24, 25</sup></p>	<p>PE is the development of hypertension after 20 weeks of gestation in combination with uteroplacental dysfunction (foetal growth restriction) and/or any of the following maternal organ dysfunctions:</p> <ul style="list-style-type: none"> <li>• Thrombocytopenia (<math>&lt; 100 \times 10^9/L</math>)</li> <li>• Pulmonary oedema</li> <li>• Impaired liver function (elevated AST, ALT to twice the upper limit of normal concentration)</li> <li>• Renal insufficiency (serum creatinine <math>&gt; 1.1 \text{ mg/dL}</math>)</li> <li>• Proteinuria (<math>\geq 300 \text{ mg/24 h}</math> urine or protein/creatinine ratio <math>\geq 0.3 \text{ mg/dL}</math> or dipstick reading of 2+)</li> <li>• New onset headache or visual changes</li> </ul> <p>HELLP-syndrome is characterized by microangiopathic haemolytic anaemia (elevated lactate dehydrogenase levels (LDH)), liver damage (elevated aspartate aminotransferase (AST) and alanine aminotransferase (ALT)) and thrombocytopenia (<math>&lt; 100 \times 10^9/L</math>). It is considered as a severe form of PE rather than a distinct hypertensive disorder of pregnancy.</p>
<p><b>Chronic hypertension (CH)</b><sup>24, 26</sup></p>	<ul style="list-style-type: none"> <li>• Hypertension before conception</li> </ul> <p>OR</p> <ul style="list-style-type: none"> <li>• Hypertension before 20 weeks of gestation</li> </ul> <p>OR</p> <ul style="list-style-type: none"> <li>• The persistence of hypertension beyond 12 weeks after delivery</li> </ul> <p>OR</p> <ul style="list-style-type: none"> <li>• The use of antihypertensives before pregnancy</li> </ul>
<p><b>Superimposed preeclampsia (SPE)</b><sup>24, 26</sup></p>	<p>An impairment of chronic hypertension with maternal organ dysfunction, the same as described in the definition of PE.</p>

Table S2: Search strategy

<b>'Biomarker'</b>	Biomarker* [MeSH] OR Biomarker* [ti/ab] OR Serum marker* [ti/ab] OR Cardiovascular marker* [ti/ab] OR Biological marker* [ti/ab] OR Biologic marker* [ti/ab] OR Biochemical maker* [ti/ab] OR Laboratory marker* [ti/ab] OR Circulating marker* [ti/ab] OR Cardiac protein* [ti/ab] OR Agents, angiogenesis inducing [MeSH] OR Agents, angiogenesis stimulating [MeSH] OR Angiogenic factor* [ti/ab] OR Angiogenic marker* [ti/ab] OR Angiogenic biomarker* [ti/ab] OR Antiangiogenic agents [MeSH] OR Antiangiogenic factor* [ti/ab] OR Antiangiogenic marker* [ti/ab] OR Antiangiogenic biomarker* [ti/ab] OR Anti-angiogenic factor* [ti/ab] OR Anti-angiogenic marker* [ti/ab] OR Anti-angiogenic biomarker* [ti/ab] OR Micro RNA [Mesh] OR MicroRNA* [ti/ab] OR miRNA* [ti/ab]
<b>AND</b>	
<b>'CVD'</b>	Cardiovascular disease* [MeSH] OR Cardiovascular disease* [ti/ab] OR Cardiovascular risk* [ti/ab] OR Cardiovascular risk factor* [ti/ab] OR Cardiovascular sequel* [ti/ab] OR Cardiac [ti/ab] OR Hypertension [MeSH] OR Hypertension [ti/ab] OR Vascular disease* [MeSH] OR Vascular disease* [ti/ab] OR Coronary artery disease* [MeSH] OR Coronary artery disease* [ti/ab] OR Myocardial infarction* [MeSH] OR Myocardial infarction* [ti/ab] OR Myocardial infarct* [ti/ab] OR Cardiovascular stroke* [ti/ab] OR Heart attack* [ti/ab] OR Endothelial dysfunction [ti/ab] OR Heart disease* [MeSH] OR Heart disease* [ti/ab]
<b>AND</b>	
<b>'HDP'</b>	Hypertension, pregnancy induced [MeSH] OR Pregnancy induced hypertension* [ti/ab] OR Hypertensive pregnancy disorder* [ti/ab] OR Hypertensive disorder of pregnancy [ti/ab] OR Hypertensive disorders of pregnancy [ti/ab] OR Hypertensive complicated pregnancy [ti/ab] OR Pre-eclampsia [MeSH] OR Preeclampsia* [ti/ab] OR Pre-eclampsia* [ti/ab] OR HELLP syndrome [MeSH] OR HELLP syndrome [ti/ab] OR HELLP-syndrome [ti/ab] OR HELLP [ti/ab] OR Hellp [ti/ab] OR Gestational hypertension [MeSH] OR Gestational hypertension* [ti/ab] OR Pregnancy transient hypertension* [ti/ab]
<b>AND</b>	
<b>'Future/previous'</b>	Later in life [ti/ab] OR In later life [ti/ab] OR Later [ti/ab] OR Future [ti/ab] OR Future risk [ti/ab] OR Long term [ti/ab] OR Long-term [ti/ab] OR Postpartum [ti/ab] OR Post-partum [ti/ab] OR Past [ti/ab] OR Previous [ti/ab] OR History [ti/ab] OR After delivery [ti/ab] OR After [ti/ab]

Table S3: Study characteristics

Author, date, country	Study design*	Exposure or Disease under investigation (n)	Controls (n)	Follow-up: time of biomarker analysis	Studied biomarkers
Chambers et al., 2001, England <sup>42</sup>	Case control study	PE (113)	NT (48)	3 Y	sICAM-1, sE-selectin, Hcy
Sattar et al., 2003, Scotland <sup>48</sup>	Case control study	PE (40)	NT (40)	15-25 Y	sICAM-1, sVCAM-1, sE-selectin
Vickers et al., 2003, Scotland <sup>65</sup>	Case control study	PE (392) GH (297)	NT (163)	33-52 Y	Fibrinogen, VWF
Freeman et al., 2004, Scotland <sup>57</sup>	Case control study	PE (40)	NT (40)	15-25 Y	IL-6, IL-10, IL-6/IL-10, TNF- $\alpha$ , sICAM-1, sVCAM-1
Wolf et al., 2004, United States <sup>31</sup>	Case control study	PE (29)	NT (32)	18 M	sFlt-1, VEGF
Girouard et al., 2007, Canada <sup>56</sup>	Cohort study	PE (63) GH (105)	NT (168)	7.8 Y	IL-6, TNF- $\alpha$ , PAI-1, Hcy
Hamad et al., 2007, Sweden <sup>43</sup>	Case control study	s-PE (18)	NT (17)	1 Y	sICAM-1, sVCAM-1, sE-selectin, PAI-1, VWF, fibrinogen, tPA
Gaugler-Senden et al., 2008, The Netherlands <sup>67</sup>	Case control study	s,e-PE (20)	NT (20)	5.5 Y	Hcy
Portelinha et al., 2008, Portugal <sup>45</sup>	Case control study	PE (58)	NT (49)	6 Y	sICAM-1, sVCAM-1
Van Rijn et al., 2008, The Netherlands <sup>46</sup>	Case control study	e-PE (144)	NT (70)	0.7 Y	IL-6, VWF, fibrinogen, sICAM-1
Portelinha et al., 2009, Portugal <sup>64</sup>	Case control study	PE (65)	NT (54)	6 Y	Fibrinogen, D-dimer, tPA, PAI-1
Noori et al., 2010, England <sup>34</sup>	Cohort study	e-PE (6), I-PE (10) GH (7)	NT (79)	12 W	sFlt-1, PIGF, sEng
Vitoratos et al., 2010, Greece <sup>52</sup>	Cohort study	PE (17)	NT (16)	12-14 W	IL-6, TNF- $\alpha$
Yinon et al., 2010, Canada <sup>35</sup>	Case control study	e-PE (15), I-PE (9)	NT (16)	6-24 M	sFlt-1, PIGF, VEGF, sEng
Kvehaugen et al., 2011, Norway <sup>30</sup>	Case control study	PE (26)	NT (15)	5-8 Y	sFlt-1, PIGF, VEGF, sEng, Calprotectin
Papakonstantinou et al., 2011,	Cohort study	s-PE (7), m-PE (5)	NT (10)	3-6 D	sE-selectin, VE-cadherin

Greece <sup>51</sup>		10 (GH)		12-14 W	
Drost et al., 2012, The Netherlands <sup>11</sup>	Cohort study	e-PE (339)	NT (332)	10 Y	Fibrinogen
Gaugler-Senden et al., 2012, The Netherlands <sup>37</sup>	Case control study	s,e-PE (16)	NT (18)	9.5 Y	sFlt-1, PlGF, VEGF
Sugulle et al., 2012, Norway <sup>63</sup>	Cohort study	PE (14)	NT (11)	5-8 Y	MR-proANP
Östlund et al., 2013, Sweden <sup>38</sup>	Cohort study	PE (15)	NT (16)	11 Y	sICAM-1, sVCAM-1, sFlt-1, PlGF, PTX3, TNF-receptor 1, NT-proBNP cystatin C, cathepsin B, cathepsin S, Hcy
Sandvik et al., 2013, Norway <sup>39</sup>	Case control study	PE (89)	NT (69)	9-11 Y	TNF- $\alpha$ , fibrinogen, sFlt-1, PlGF, VEGF sVCAM-1, ADMA, SDMA, l-arginine, homoarginine, neopterin
White et al., 2013, United states <sup>68</sup>	Case control study	PE + GH (401)**	NT (1825) NP (216)	Decades	Hcy
Blaauw et al., 2014, The Netherlands <sup>44</sup>	Case control study	e-PE (17)	NT (16)	4.5 Y	sICAM-1, VWF, Hcy, superoxide dismutase
Drost et al., 2014, The Netherlands <sup>23</sup>	Cross sectional study	e-PE (339)	NT (332)	10 Y	sE-selectin, sICAM-1, sVCAM-1, PAI-1, PAPP-A
Lampinen et al., 2014, Finland <sup>71</sup>	Case control study	PE (28)	NT (20)	6 Y	Norepinephrine, endothelin-1
Visser et al., 2014 <sup>50</sup>	SR & meta-analysis	HDP	NT	-	sICAM-1, sVCAM-1, sE-selectin, fibrinogen, VWF, PAI-1, endothelin, tPA, D-dimer, IL-6, IL-10, TNF- $\alpha$ , VEGF, sFlt-1, Hcy
Ehrenthal et al., 2015, United states <sup>54</sup>	Cohort study	PE + GH (31)	NT (40)	12-18 M	IL-6, TNF- $\alpha$
Murphy et al., 2015, Canada <sup>76</sup>	Cohort study	m-PE (7), s-PE (6)	NT (17)	During pregnancy 1 Y PP	miRNA
Murphy et al., 2015, Canada <sup>53</sup>	Case control study	PE (35)	NT (28)	5-7 M	TNF- $\alpha$ , IFN- $\gamma$ , GM-CSF, IL-1 $\beta$ , IL-2, IL- 4, IL-5, IL-6, IL-8, IL-10, IL-17 $\alpha$ , IL-23, MIP-1 $\alpha$ , fractalkine
Tuzcu et al., 2015, Turkey <sup>33</sup>	Case control study	m-PE (10), s-PE (6)	NT (24)	4.5 Y	sE-selectin, sICAM-1, sVCAM-1, sFlt-1

Visser et al., 2015, The Netherlands <sup>69</sup>	Cohort study	PE (74) GH (15)	NT (85)	2.5 Y	Hcy
Grand'Maison et al., 2016 <sup>40</sup>	SR & meta-analysis	HDP	NT	-	sFlt-1, VEGF, sICAM-1, sVCAM-1
Van Rijn et al., 2016, The Netherlands <sup>55</sup>	Cohort study	s,e-PE (44)	NT (29)	1.5-3.5 Y	IL-1 $\beta$ , IL-4, IL-5, IL-6, IL-8, IL-10, IL-13, IL-18, TNF- $\alpha$ , IFN- $\gamma$ , myeloperoxidase, fibrinogen
Akhter et al., 2017, Sweden <sup>32</sup>	Cohort study	PE (48)	NT (58)	1 Y	sFlt-1, PIGF
Akhter et al., 2017, Sweden <sup>59</sup>	Cohort study	PE (55)	NT (64)	1 Y	PTX3
Alma et al., 2017 <sup>61</sup>	SR & meta-analysis	Shared biomarkers between HFpEF and PE		-	NT-proBNP, BNP, c-Tnl, ADM, MRproADM, CA-125
Bokslag et al., 2017, The Netherlands <sup>60</sup>	Cohort study	e-PE (131)	NT (56)	9-16 Y	NT-proBNP
Zoet et al., 2017, The Netherlands <sup>77</sup>	Cohort study	e-PE (338)	NT (327)	10 Y	Pro-NT, pro-RLX2
Alma et al., 2018, The Netherlands <sup>41</sup>	Case control study	I-PE (47) GH (142)	NT (17)	2.5 Y	sICAM-1, sE-selectin
Bokslag et al., 2018, The Netherlands <sup>47</sup>	Cohort study	e-PE (131)	NT (56)	9-16 Y	sICAM-1, sE-selectin, IL-6, TNF- $\alpha$
Dayan et al., 2018, Multi-country <sup>72</sup>	Case control study	PE (30) (+ ACS)	NT (146) + (ACS)	14-20 Y	miRNA
Escouto et al., 2018, England <sup>36</sup>	Cohort study	PE (288) GH (94), CH (51), SPE (30)	NT (14)	6-7 W	PIGF, BNP, NGAL
Mohseni et al., 2018 <sup>74</sup>	Review	PE	Cardiac remodeling	-	miRNA
Shahul et al., 2018, United states <sup>79</sup>	Case control study	PE (32)	NT (25)	Antepartum 1 Y	Activin A
Tanz et al., 2018, United states <sup>49</sup>	Cohort study	PE + GH (2241) PE + GH (1117)	NT (249) NT (114)	17 Y	IL-6 sICAM-1
Wu et al., 2018, China <sup>58</sup>	Case control study	PE (47)	NT (58)	1 Y	TNF- $\alpha$
Benschop et al., 2019, The Netherlands <sup>27</sup>	Cohort study	Pregnant women (5474)***	-	Mid-pregnancy 6 Y	PIGF
Hromadnikova et al., 2019,	Cohort study	m-PE (24), s-PE (77)	NT (89)	3-11 Y	miRNA

Czech <sup>73</sup>					
Hromadnikova et al., 2019, Czech <sup>66</sup>	Cohort study	m-PE (25), s-PE (77)	NT (89)	3-11 Y	Hcy
Wu et al., 2019, China <sup>70</sup>	Cross sectional study	PE + high Hcy (31)	PE + normal Hcy (137)	5 Y	Hcy
Garrido-Gimenez et al., 2020, Spain <sup>28</sup>	Cohort study	PE (43)	NT (21)	During pregnancy 12 Y PP	sFlt-1, PIGF, sEng, sVCAM-1, NT-proBNP, BNP, Troponin T
Meeusen et al., 2020, The Netherlands <sup>78</sup>	Cross sectional study	e-PE + subclinical CAD (12)	e-PE, no subclinical CAD (78)	10-20 Y	Neutrophil count & (re)activity
Muijsers et al., 2020, The Netherlands <sup>62</sup>	Cohort study	e-PE (177)	NT (162)	9-10 Y	hc-cTnl
Neuman et al., 2020, The Netherlands <sup>29</sup>	Cohort study	PE + HT (23)	PE, no HT (57)	During pregnancy 1 Y	sFlt-1, PIGF
Schlosser et al., 2020, Multi-country <sup>75</sup>	Cohort study	ACS subjects, 18 PE and 17 NT	Non-ACS subjects, 20 PE and 20 NT	10-30 Y	miRNA
Jacobsen et al., 2021, Norway <sup>80</sup>	Cohort study	e-PE (29), l-PE (98), 57 GH	NT (137)	During pregnancy 1 Y, 3 Y	sHLA-G

\* Many studies did not specify the name of their study design. In those cases, the study design is based on the method section, but sometimes it was debatable and therefore not all may be correct.

\*\* 'PE + GH' means the study used a combined cohort, no separate results for PE were present.

\*\*\* Combined cohort of women with complicated (PE + small for gestational age + spontaneous preterm birth, n=811) and uncomplicated pregnancy (n=4664)

SR = systematic review; PE = preeclampsia; GH = gestational hypertension; CH = chronic hypertension; SPE = superimposed preeclampsia; HDP = hypertensive disorders of pregnancy; s = severe; m = mild; e = early; l = late; NT = normotensive; NP = nulliparous; ACS = acute coronary syndrome; HT = hypertension; HFpEF = heart failure with preserved ejection fraction; CAD = coronary artery disease; Y = year; M = months; W = weeks; D = days

sFlt-1 = soluble fms-like tyrosine kinase-1; VEGF = vascular endothelial growth factor; PIGF = placental growth factor; sEng = soluble endoglin; sICAM-1 = soluble intercellular adhesion molecule-1; sVCAM-1 = soluble vascular cell adhesion molecule-1; sE-selectin = soluble E-selectin; sP-selectin = soluble P-selectin; VE-cadherin = vascular endothelial cadherin; IL = interleukin; TNF- $\alpha$  = tumor necrosis factor alpha; IFN- $\gamma$  = interferon gamma; PTX3 = pentraxin 3; NGAL = neutrophil gelatinase-associated lipocalin; MIP-1 $\alpha$  = macrophage inflammatory protein-1; GM-CSF = granulocyte-macrophage colony-stimulating factor; BNP = brain natriuretic peptide; NT-proBNP = n-terminal prohormone

*brain natriuretic peptide; MR-proANP = midregional pro-atrial natriuretic peptide; hs-cTnI = high sensitivity cardiac troponin I; VWF = von Willebrand factor; Hcy = homocysteine; PAI-1 = plasminogen activator inhibitor-1; tPA = tissue plasminogen activator; miRNA = micro ribonucleic acid; sHLA-G = soluble human leukocyte antigen G; PAPP-A = pregnancy associated plasma protein A; pro-NT = pro neurotensin; pro-RLX2 = prorelaxin 2; CA-125 = cancer antigen 125; ADMA = asymmetric dimethylarginine; SDMA = symmetric dimethylarginine; MR-proADM = midregional pro adrenomedullin; ADM = adrenomedullin.*



**Table S4: Results miRNA's**

<b>Dayan et al.</b> <sup>72</sup>	Observed a significant decrease in circulating levels of miR-122-5p, miR-126-3p and miR-146a-5p in women with premature ACS who reported a history of PE compared to women with a prior normotensive pregnancy. These miRNAs have been connected to the atherogenic process. A history of PE may therefore potentiate disturbance in multiple atherogenic pathways by alterations in these miRNAs.
<b>Hromadnikova et al.</b> <sup>73</sup>	Examined differences in postpartum (4-5 years) expression of miRNAs, known to be involved in the pathogenesis of cardiovascular and cerebrovascular diseases, in cases and controls. Upregulation of miR-1-3p, miR-17-5p, miR-20b-5p, miR-29a-3p, miR-126-3p and miR-133a-3p were associated with a history of early, late, severe and/or mild PE.
<b>Mohseni et al.</b> <sup>74</sup>	Searched for miRNAs differentially expressed in both cardiac remodeling and PE and found five miRNAs upregulated (miR-18, miR-21, miR-125b, miR-195 and miR-499-5p) and two miRNAs downregulated (miR-1 and miR-30), suggesting common pathogenic mechanisms.
<b>Schlosser et al.</b> <sup>75</sup>	Assessed overlapping alterations in miRNAs in women with a history of PE, ACS and current PE and found miR-206 in the intersection.
<b>Murphy et al.</b> <sup>76</sup>	Evaluated the expression of 20 miRNA's, known to be involved in the pathogenesis of PE, and found reduced expression of miR-221-3p one year postpartum in cases, which may suggest some persistence of inflammation.

*miRNA = micro ribonucleic acid; ACS = acute coronary syndrome; PE = preeclampsia;*