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| **Table ST1.** Summary of study characteristics, main findings of cross-sectional and cohort studies testing associations between maternal depression and inflammation during pregnancy and the quality of evidence according to the Newcastle-Ottava Scale criteria. | | | | | | | | | | | | | |
| **Study** | **Population** | **Sample Size** | **Study Design** | **Depression Measure** | **Time of Depression Measure** | **Inflam-mation Markers** | **Time of Inflamma-tion**  **Measure** | **Important Covari-ates** | **Results** | **Quality of evidence** | | | |
| **Selection** | **Comparability** | **Outcome** | **Overall**1 |
| **CROSS-SECTIONAL STUDIES:** | | | | | | | | | | | | |  |
| **(Scrandis *et al.*, 2008)** | Women from two Mid-Atlantic obstetric clinics and one birthing center,  USA | 27 | Cross-sectional | SIGH-SAD2 | 35-38 gw3 | IL-64  CRP5 | 35-38 gw3 | None | Higher depressive symptoms were significantly correlated with higher CRP, but not IL-6 | 3/5 | 0/2 | 1/3 | Poor |
| **(Christian *et al.*, 2009)** | Women with low socioeco-nomic status from Ohio State University Prenatal Clinic, USA | 60 | Cross-sectional | CES-D6 | Mean=15 SD=4.8 gw3 | IL-64  TNF-α7 | Mean=15 SD=4.8 gw3 | Body Mass Index | Higher depressive symptoms were significantly associated with higher IL-6 but not TNF-α. | 2/5 | 1/2 | 3/3 | Fair |
| **(Cassidy-Bushrow *et al.*, 2012)** | African American women from the Henry Ford Health System Clinics, Detroit area, USA | 187 | Cross-sectional | CES-D6 | 13.1-28.6 gw3 | IL-64  IL-1β4  IL-104  hs-CRP5  TNF-α7 | 13.1-28.6  gw3 | Body Mass Index | Higher depressive symptoms were significantly associated with higher IL-1βbut not with hsCRP, IL-6 or TNF- α levels. Body Mass Index moderated the associations: higher depressive symptoms were associated with higher IL-6 and IL-10 in women with lower Body Mass Index, while higher depressive symptoms were associated with lower IL-10 in women with higher Body Mass Index. | 3/5 | 2/2 | 3/3 | Fair |
| **(Cheng and Pickler, 2014)** | Women from a prenatal clinic of a large, urban medical center, Ohio area, USA | 12 | Cross-sectional\* | CES-D6 | ≥36 gw3 | IL-1β4  IL-54  IL-74  TNF-α7  MIP-1β8  VEGF9  MCP-110  G-CSF11 | ≥36 gw3 | None | Higher depressive symptoms were associated with higher  MIP-1β, but not with TNF-α, IL-1β, IL-5, IL-7, VEGF, MCP-1 or G-CSF. | 1/5 | 0/2 | 1/3 | Poor |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **(Simpson *et al.*, 2016)** | Women from Women’s Health Concerns Clinic, Ontario, Canada | 33 | Cross-sectional\* | EPDS12 | ≥26 gw3 | IL-64  IL-104  CRP5  TNF-α7 | ≥26 gw3 | Body Mass Index;  Exclusion criteria: hyperten-sive disorders, diabetes | No significant associations between depressive symptoms and CRP, IL-6, TNF-α or IL-10. | 2/5 | 2/2 | 2/3 | Fair |
| **COHORT STUDIES:** | | | | | | | | | | | | | |
| **(Blackmore *et al.*, 2011)** | Women at low to medium obstetric risk from the University of Rochester  Clinical Research Center, New York, USA | 130 for IL-64, 137 for TNF-α7 | Cohort | SCID13 diagnosis of major depressive disorder EPDS12 | 18 and 32 gw3 | IL-64 TNF-α7 | 18 and 32  gw3 | Body Mass Index | No significant associations of depression diagnosis or depressive symptoms with IL-6 or TNF-α at either measurement point. | 4/4 | 1/2 | 3/3 | Good |
| **(Azar and Mercer, 2013)** | Caucasian women, low to medium socioeco-nomic status from Cumber-land Regional Health Care Center, Canada | 27 | Cohort | PHQ-914 | 7-10 and  16-20 gw3 | IL-64  CRP5  TNF-α7 | 7-10 and  16-20 gw3 | Exclusion criteria: hyperten-sive disorders | Higher depressive symptoms in early pregnancy were associated with higher CRP and TNF-α in early and mid-pregnancy and with higher IL-6 in mid-pregnancy. An increase in depressive symptoms from early to mid-pregnancy was also associated with higher IL-6 in mid-pregnancy. | 1/4 | 0/2 | 3/3 | Poor |
| **(Haeri *et al.*, 2013)** | Women from Perinatal Mood Disorders Clinic and who delivered at a single tertiary hospital, Texas, USA | 200 | Cohort | Major Depressive Disorder diagnosis  EPDS12 | Major Depressive Disorder diagnosis during pregnancy  EPDS11:  12.7 gw3 | IL-64  TNF-α7 | 11-14 gw3 | Body Mass Index,  Exclusion criteria: hyperten-sive disorders, diabetes, infections | Women with depression diagnosis had higher TNF- α and IL-6 levels than controls with no depression as indicated by EPDS. | 2/4 | 2/2 | 2/3 | Fair |
| **(Gustafsson *et al.*, 2018)** | Women with familial or personal history of ADHD from large hospital clinic, Oregon, USA | 68 | Cohort | CES-D6 | 24 and 37 gw3 | IL-64  TNF-α7  MCP-110 and  a latent variable  combining all three markers | 37 gw3 | Exclusion criteria: high-risk or medically compli-cated pregnancy | Higher depressive symptoms were associated with higher IL-6 and TNF-α, but not with MCP-1. Higher depressive symptoms were also associated with the latent antenatal inflammation variable. | 0/4 | 0/2 | 2/3 | Poor |
| **(Osborne *et al.*, 2018)** | Women from Maudsley Perinatal Psychiatry Service or routine antenatal ultrasound screening at King’s College Hospital, London, UK | 106 | Cohort | SCID13 diagnosis of major depressive disorder BDI15 | major depressive disorder diagnosis 25 gw3 BDI 32 gw3 | IL-24  IL-84  IL-64  IL-104  IL-1β4  hs-CRP5  TNF-α7  VEGF9  MCP-110  EGF16 | 23.9-34.9 gw3 | Body Mass Index, exclusion criteria: gestational diabetes, hyperten-sion | Women with major depressive disorder had higher IL-6, IL-10, TNF-α and VEGF, but no differences in IL-2, IL-1β, hsCRP, TNF- α, MCP-1 or EGF. | 2/4 | 2/2 | 2/3 | Fair |
| 1 The quality of evidence assessments followed the Newcastle-Ottawa Scale (NOS)-criteria for cross-sectional (Wells *et al.*, 2014b) and cohort (Wells *et al.*, 2014a) studies. Overall quality of evidences for cross-sectional studies: Good quality: 4–5 points in the selection domain, 1–2 points in the comparability domain, and 2–3 points in the outcome domain. Fair quality: 3 points in the selection domain, 1–2 points in the comparability domain, and 2–3 points in the outcome domain. Poor quality: 1–2 points in the selection domain, or 0 points in the comparability domain, or 0–1 point(s) in the outcome domain; Overall quality of evidence for cohort studies: Good quality: 3–4 points in the selection domain, 1–2 points in the comparability domain, and 2–3 points in the outcome domain. Fair quality: 2 points in the selection domain, 1–2 points in the comparability domain, and 2–3 points in the outcome domain. Poor quality: 0–1 points in the selection domain, or 0 points in the comparability domain, or 0–1 point(s) in the outcome domain. . Quality of evidence according to the NOS-criteria were reviewed independently by Rachel Robinson and by Marius Lahti-Pulkkinen and Polina Girchenko. In cases of disagreement, they were discussed and agreed upon by consensus.  2Structured Interview Guide for the Hamilton Depression Rating Scale- Seasonal Affective Disorder  3gw refers to gestational week.  4IL refers to Interleukin-2 / Interleukin-4 / Interleukin-5 / Interleukin-6 / Interleukin-7 / Interleukin-8 / Interleukin-10 / Interleukin-1β  5hsCRP / CRP refers to high sensitivity C-Reactive Protein / C-reactive Protein  6CES-D refers to Center for Epidemiological Studies Depression Scale  7TNF-α refers to Tumor Necrosis Factor alpha  8MIP-1β refers to Macrophage Inflammatory Protein 1β  9VEGFrefers to Vascular Endothelial Growth Factor  10MCP-1 refers to Monocyte Chemoattractant Protein-1  11G-CSFrefers to Granulocyte-Colony Stimulating Factor  12EPDS refers to Edinburgh Postnatal Depression Scale  13SCID refers to Structured Clinical Interview for DSM-IV  14PHQ-9 refers to Patient Health Questionnaire-9  15BDI refers Beck Depression Scale  16EGF refers Epidermal Growth Factor  Note. Studies of Scrandis et al, 2008, Cheng and Pickler, 2014, and Simpson et al., 2016 were prospective in study design. However, all studies had only one measurement during pregnancy (prospective measurements were postpartum) and reported cross-sectional correlations of depression and inflammation during pregnancy. Therefore, these studies were classified as cross-sectional. Studies of Haeri, et al.,, 2013, and Osborne et al., 2018 were classified by the authors as case-control. However, after assessment, we judged that the studies should not be assessed as a classical case-control studies, but should be assessed using the criteria of cohort studies. Haeri, Baker, and Ruano, 2013. compared women with major depressive disorder diagnosis at any time during pregnancy with controls without clinically relevant depressive symtpoms in early pregnancy (control group was not assessed for depression at any later stage during pregnancy). Moreover, in this study inflammatory biomarkers were assessed before, at the time of or after the case-control status definition. In the Osborne et al., 2018, the cases comprised 49 women with major depressive disorder. However, 18 of the cases did not meet the diagnostic criteria for major depressive disorder when assessed during pregnancy. | | | | | | | | | | | | | |

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