Mental health and asthma control during pregnancy: Investigating underlying immune mechanisms

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Abbreviations

ACQ: Asthma Control Questionnaire

ACTH: Adrenocorticotrophic hormone

ANRQ: Antenatal Risk Questionnaire

AQLQ: Juniper Asthma Quality of Life Questionnaire

AVP: Vasopressin

BMI: Body mass index

CD: Cluster of differentiation i.e. CD14

CD14Bright: 'Classical' monocytes

CD16Bright: 'non-classical' monocytes

$CD14^{+}CD16^{+}$: 'Intermediate monocytes

CCR2: Monocyte chemoattractant protein-1 receptor

CeA: Central nuclei of the amygdala

CI: Confidence interval

CRH: Corticotrophin-releasing hormone

DC: Dendritic cell

DPBS: Dulbecco's phosphate buffed saline

EGF: Epidermal growth factor

EMT: Epithelial-mesenchymal transition

EPDS: Edinburgh Postnatal Depression Score

FACS: Flow cytometric analysis of cell surface molecules

FBS: Foetal bovine serum

FCV: Force vital capacity

FENO: Fractional exhaled nitric oxide

FEV1: Forced expiratory volume in one second

GR: Glucocorticoid receptor

HADS: Hospital Anxiety Depression Scale

HLA: Human leukocyte antigen

HPA axis: Hypothalamic-pituitary-adrenal axis

ICAM: Intercellular Adhesion Molecule

ICS: Inhaled corticosteroids

IFN: Interferon

IgE: Immunoglobulin E

IL: Interleukin

IQR: Interquartile range

IRR: Incidence rate ratio

LABA: Long acting β2 agonists

LMH: Lyell McEwin Hospital

LPS: Lipopolysaccharide

M1: Classically activated macrophage

M2: Alternatively activated macrophage

MCP: Monocyte chemoattractant protein

MeA: Medial nuclei of the amygdala

nfMLP: N-formly-met-leu-phe

NK: Natural killer cells

OCS: Oral corticosteroids

OVA: Ovalbumin

PBMC: Peripheral blood mononuclear cell

RANTES: Regulated And Normal T cell Expressed and Secreted

RR: Relative risk

SGA: Small for gestational age

Tc cells: T cytoxic cells

TGF: Transforming growth factor

Th cells: T helper cells

TNF: Tumor Necrosis Factor

T reg: Regulatory T cells

VEGF: Vascular endothelial growth factor

Abstract

Background: Asthma during pregnancy has been associated with poor pregnancy outcomes such as pre-eclampsia, small for gestational age babies and preterm birth. Depression and anxiety are associated with reduced asthma control in non-pregnant individuals. This study investigated whether depression/anxiety in combination with pregnancies complicated by asthma has a negative effect on asthma control. Potential immune mechanisms that may drive worsening asthma were also investigated.

Methods: One hundred and eighty-nine asthmatic women with and without depression/anxiety were followed throughout their pregnancies. Incidences of uncontrolled asthma and exacerbations were measured throughout gestation. At 18 and 30 weeks of gestation, monocyte inflammatory profile was examined using flow cytometric analysis of cell surface molecules (FACS) and peripheral blood mononuclear cell (PBMC) chemotaxis was also examined.

Results: The incidence of uncontrolled asthma increased in women with depression/anxiety compared to women without depression/anxiety during pregnancy (unadjusted incidence rate ratio (IRR) 1.739, adjusted IRR 1.633, CI 1.092-2.442, p=0.017). Relative risk of experiencing uncontrolled asthma during pregnancy was also increased with depression/anxiety (unadjusted RR 1.619; adjusted RR 1.538, CI 1.114-2.122, p=0.009). There was no increase in the incidence rate ratio (unadjusted IRR 0.770; adjusted IRR 0.755, CI 0.412-1.382, p=0.362) or relative risk (unadjusted RR 0.867; adjusted RR 0.859, CI 0.496-1.489, p=0.589) of asthma exacerbations during pregnancies complicated by depression/anxiety. Asthma without depression/anxiety was associated with an increase in peripheral blood total monocyte percentage at 18 but not 30 weeks gestation when compared to asthmatic women with depression/anxiety (p=0.027). There were no changes in PBMC chemotaxis at 18 or 30 weeks gestation in pregnant women regardless of the presence of asthma or depression/anxiety.

Conclusion: The presence of asthma and depression/anxiety during pregnancy is associated with an increase in uncontrolled asthma, but not a change in exacerbation risk. This increase in uncontrolled asthma in women with depression/anxiety was not a result of alterations in monocyte inflammatory profile or PBMC chemotaxis.