

Effect of Prenatal Maternal Stress on Foetal Outcome and its Long Term Consequences: A Review of Literature

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Received: October 21, 2016; **Published:** January 20, 2017

Abstract

It is known since ancient times that maternal stress has a strong negative effect on foetal outcomes. The maternal stress during pregnancy not only causes poor development of foetus but it also affects the cognitive and behavioural development of children in their later life. It is usually associated with language, cognitive, behavioural and emotional problems in children. Such an impact of stress varies in function with type of stress, gestational period during which it occurs. Hence, the present review was conducted to have a better idea of how prenatal maternal stress causes poor foetal outcome as well as poor neurological development of children exposing them to increased risk for various neuro-developmental problems.

Methods: The literature regarding effects of prenatal maternal stress on foetal outcomes was obtained from numerous English language journals and peer-reviewed articles on Pubmed, MEDLINE, Embase and Google Scholar till 2016.

Keywords: Anxiety; Depression; Foetus; Pregnancy; Stress

Introduction

Stress is a complex state that includes conditions like mild stress, distress, anxiety and depression that can occur from a range of phenomena including daily hassles, poor relationships, and adversity [1]. Various human developmental studies have shown that pregnancy is considered as starting point of life, suggesting that majority of psychological and behavioural development of foetus starts in-utero [2]. It is now obvious that environmental effects on foetal development are important with regard to emotional, behavioural and cognitive outcomes of child. Furthermore, many animal studies have proven that stress during pregnancy can result into long term effects on neurodevelopment of offspring [3].

According to recent studies approximately 29% of pregnant women suffer from antenatal anxiety or some form of stress [4]. There are many stressors that can affect pregnant women, some of which are: low income, complicated employment conditions, big families, household responsibilities, poor relationship, and complicated pregnancy [5]. Another major reason for stress, especially in various developing countries of the world is sex discrimination and preference for sons rather than daughters which significantly contributes to anxiety among pregnant women [6].

It is now proven that anxiety during pregnancy is associated with prematurity and lower birth weight, and long term effects on infant development [7].

Citation: Naina Kumar and Harkiran Preet Kalsi. "Effect of Prenatal Maternal Stress on Foetal Outcome and its Long Term Consequences: A Review of Literature". *EC Gynaecology* 3.6 (2017): 432-438.

How Maternal Stress Affects Growing Foetus?

For last few years, numerous studies have shown that maternal psychological distress is an important cause for poor pregnancy outcomes [8] as well as it also results in disruptions of postnatal development of offspring in animals [9-11].

But still, the exact cause of such negative effect of human maternal stress on foetal outcome is poorly understood till date. It was found that the foetal brain is very sensitive to even small changes in intrauterine milieu which can result from various internal and/or external factors [12]. The mechanisms underlying all these events are just beginning to be understood; one recent hypothesis suggests that altered placental function due to stress allows passage of more of stress hormone cortisol to the foetus, leading to all negative effects on foetal outcome [13].

It was observed that maternal psychological stress is similar to a potent teratogenic agent that can cause deleterious perinatal and/or developmental outcomes [14]. In fact a study has reported that small amount of stress is needed for foetal motor and cognitive development [15]. Hence, it is mainly the difference in ways that the foetus is affected resulting into different foetal outcomes, that is; prenatal stress may cause either a more progressive physical development or a more anxious child [16].

It has been proposed by numerous recent studies that emotional stress or insult incites an adaptive response involving the hypothalamic-pituitary-adrenal axis, with release of various immune (Interleukins 1, 6, and Tumor Necrosis Factor-alpha), hormonal (prostaglandins) and neurohormonal (corticotrophin-releasing hormone, hence cortisol and catecholamines) mediators [17-21]. This systemic pro-inflammatory state occurring as a response to excessive maternal stress was found to be very much similar to that resulting from exposure to various non-emotional situations that cause heavy production of free radicals or reactive oxygen species (ROS) such as; trauma, infections, ionizing radiation, heat injury, obesity, smoking and environmental pollution, etc [22,23].

If the defensive antioxidant activity of body fails to balance this overproduction of ROS, oxidative stress will occur, causing oxidation of essential macromolecules and DNA. This in turn will result in alteration of vital cell functions along with systemic inflammatory state, causing long term effects [23]. Furthermore, the placenta also produces free radicals due to presence of heavy metals like iron [24,25], hence pregnancy itself represents, mostly by second trimester onwards, a stressful condition. An additional insult (emotional or non-emotional) further enhances release of various stress mediators, that in turn result in wide spread visceral damages, changes in sub-decidual angiogenesis, increased materno-fetal transfer of stress substances and also reduction in intrauterine blood flow [22,24,26]. All these changes, then ultimately result in increased myometrial irritability and foetal inflammatory climate [27], responsible for higher rates of pregnancy losses [28], preterm deliveries, intrauterine growth restriction, low birth weight babies [17-19,29-32] and neonatal intravascular hemorrhage [24].

Another recent study proposed that the elevated prenatal maternal cortisol is one of the strongest predictor of these neonatal outcomes. Newborn babies of depressed mothers usually show a biochemical profile that is very much similar to their mother's prenatal biochemical profile with high cortisol levels and decreased dopamine and serotonin levels [33].

Despite of all these recent studies many things still remain unclear, such as what types of stress, and at what level, it effects the developing foetus, which needs to be addressed in near future for better understanding of patho-physiology of maternal stress.

Effects of Prenatal Stress on Foetus

The belief that maternal stress and anxiety can have deleterious effects on developing foetus has its origin in old tradition and folklore. Various studies have shown that the harmful effects of antenatal stress and depression on the developing foetus include; preterm birth [34], low birth weight [35], reduced cognitive ability, increased fearfulness [36], and an increased incidence of respiratory and skin illnesses in early life [37]. It was also reported that depressed women are at higher risk of delivering prematurely, and often have neonates requiring intensive care for postnatal complications as compared to normal pregnant women [38]. Furthermore, these women also carry

an increased risk of having low birth weight (< 2500 g), small for gestational age babies (< 10th percentile) [39], higher rates of placental abnormalities, pre-eclampsia, and spontaneous miscarriage [40].

Another recent study reported that foetal heart rate, foetal activity, sleep patterns and movements, which are all indicators of foetal neurobehavioral development, were drastically affected by maternal stress, depression, and anxiety [41].

On contrary to this a recent meta-analytic review, found that psychosocial stress during pregnancy was weakly related to neonatal weight and risk for low birth weight [42]. Similar findings were reported by another meta-analysis of 50 studies which found no relationship between anxiety symptoms during pregnancy and poor perinatal outcomes [43].

Hence, it is yet to be understood that it is not only toxic or extreme prenatal stress that are important, but the environment and circumstances prevailing around pregnant women such as daily hassles, pregnancy specific anxiety [44] or relationship strains [36], etc all carry adverse effects on developing foetus.

Long Term Consequences of Prenatal stress in Children

Various studies in recent years have shown that maternal stress not only carries complications for foetus in-utero, but also have long term effects on the cognitive and behavioural development of children later in their lives [45,46].

The women's anxiety during pregnancy can extend into childhood and adolescence, affecting the hypothalamic-pituitary-adrenal axis, causing attention deficit hyperactivity disorder (ADHD) symptoms in 8 – 9 year old children [47]. Furthermore, the maternal stress was found to be directly linked with lower cognitive and language ability [48], more difficult, inhibited, or emotionally reactive temperament [49], behavioural problems [16] and poorer neuro-developmental outcomes in children [50].

It was found that if a mother is stressed, anxious or depressed during pregnancy, her child is at increased risk for having a range of problems that includes; emotional problems, conduct disorder and impaired cognitive development later in life [45]. Hence, both altered brain structure [51] and its function [52] were found to be associated with prenatal stress.

More recently, studies have found that maternal antenatal anxiety and/or depression can cause increased risk for neuro-developmental disorders in children, and also confer them for increased risk of future mental illness. They also reported that elevated levels of antenatal depression and anxiety were associated with poor emotional adjustment in young children [53], increased risk for mixed handedness, autism and affective disorders [45]. Such children were also found to be at increased risk of developing schizophrenia, especially those who were exposed to extreme stress in their first trimester [54].

On contrary to above findings some studies also report that prenatal psychological distress can cause faster neural and behavioural maturation in children [15,55].

Future Implications for Parents, Health Care Services and Policy makers

There is lot of research still going on related to effects of maternal stress on foetal outcomes. Though the physical care of pregnant women has drastically improved over the past 100 years, especially in developed countries; however, little attention is being paid towards emotional care of pregnant women. This is also the most neglected area of obstetric care, as most of us fail to enquire about the emotional status of women [56].

We can improve the present scenario by creating awareness amongst community about the detrimental effects of maternal stress on foetal outcome. This can be achieved by imparting public health education about this issue, as well as by encouraging pregnant women to take care of them emotionally and to seek help whenever needed.

The major problem in today's era is that most of the anxiety and depression in pregnant women goes undetected and untreated or is taken very casually by family members. This can be tackled to some extent by making sure that pregnant women are sensitively ques-

tioned in privacy on their first contact with health professionals, especially about their emotional history and current status. Appropriate intervention and prevention programs should be initiated at an early stage to identify such women who are at risk of having stress at different periods of gestation.

Furthermore, it is very important to counsel both the parents that it is not only diagnosable disorders that can affect foetal development, but there is range of symptoms of stress, anxiety and depression, that includes poor relationship with partner also. Parents should be given opportunity to have knowledge and understanding of their own child's development, they should be appropriately counselled by health professionals about the way that maternal stress can affect intrauterine environment and subsequent development of foetus. Health care providers and psychosocial workers should receive adequate training about how to communicate to parents about prevention and management of stress during antenatal period. Appropriate personalized counselling of each woman to tackle stressful conditions during pregnancy can definitely help in preventing a number of neuro-developmental disorders that occur in a substantial proportion of kids in their later part of life.

Various programs targeting reduction of anxiety, depression and stress in pregnant women should be motivated everywhere so as to reduce the risk of low birth weight babies, prematurity and long term neurological consequences. These programs should include policies related to maternal education and employment that will help in building the confidence of women.

Hence, by helping women tackle her stress we can think of better future for children and protect them from having various neurological deficits.

Acknowledgement

I would like to acknowledge and thank Dr. Namit Kant Singh for his advice and expertise.

Conflicts of Interest

There are no conflicts of interest.

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Volume 3 Issue 6 January 2017

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