

Influence of maternal stress during pregnancy and child outcomes

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ABSTRACT

Prenatal stress is an overwhelming concern in pregnancy-related care. The mother exposed to prenatal stress poses the fetus at the risk of developing many adverse health conditions. It is estimated that around 10%–20% of pregnant women suffer from mental health concerns during the perinatal period. History dates back to the tragic 1961 Thalidomide tragedy which cautions both the individual and the health professionals about pregnancy-related care. Multiple mechanisms have been put forth to link the relationship between the indwelling fetus and the carrying mother. Of them, the “Barker hypothesis” suggests the role of perinatal conditions in influencing the development of diseases in the later life of the child. Mental health issues are a growing concern during pregnancy. In recent years, there has been an increasing trend of smoking, alcohol abuse, and illicit drug use among pregnant women, which has shown to adversely affect the fetus. In the 21st century, environmental stressors are a looming threat which has now been shown to affect the pregnant population. These data emphasize the need to consider early environmental life events as etiological factors for adverse child outcomes. This review summarizes the history, background, causes of maternal stress, and the ways to improve them.

Key words: Barker hypothesis, Child outcomes, Mental health, Pregnancy

Pregnancy is an indispensable phase in every woman's life. The mother and the growing fetus have a unique and inevitable attachment. The three most addressed domains of this maternal-fetal attachment theory are the cognitive, affective, and altruistic attachments. Cognitive attachment is the desire of the mother to know the baby. Affective attachment is described as the pleasure obtained from the interaction with the baby. Finally, altruistic attachment is the constant need to protect the unborn baby. This theory sheds light on the depth of mother-child relationship from the point of conception [1]. Mental disorders are more common in women than in men. Mental health issues during pregnancy jeopardize the health of both the growing fetus and the mother. Studies have documented a prevalence of antenatal depression/anxiety from 8% to 30% [2,3]. This remains widely undiagnosed and unaddressed across various cultures and beliefs. Furthermore, the social stigma associated with mental illness complicates the situation [4].

Fetal growth is a critical period vulnerable to maternal and environmental insults. Maternal events can include both physical and psychological stressors [5]. It can have a lasting impression on the neurological and behavioral development of the child [6].

Events occurring during child development from prenatal to adolescence have a huge impact on the well-being of a child and the family system. It has a significant impact on the mental trajectory of the growing child [7].

Therefore, it is important to review the historical evidence relating to maternal stress that has excited the scientific community to grow more cautious while engaging in pregnancy care.

HISTORICAL EVIDENCE

In the early 1950s, epidemiologists believed that the fetus was a “perfect parasite” protected from the nutritional damage undergone by the mother [8]. The placenta qualified as an efficient filter guarding the fetus against harmful substances in the mother's system. Thalidomide was licensed in 1957 and used for morning sickness among pregnant women, until 1961 when an epidemic of severe birth defects with missing arms and legs set in. Soon after the Thalidomide disaster in 1961, it was realized that the placenta is not “some sort of impervious barrier” [9]. Fig. 1 represents a set of risk factors during pregnancy that lead to adverse child outcomes including birth defects. During the Dutch famine of 1944-1945, it was found that prenatal and in-utero exposure to nutritional deprivation can lead to obesity during adulthood [10].

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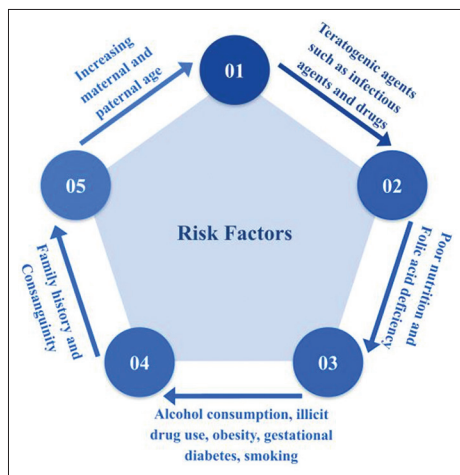


Figure 1: Risk Factors during pregnancy that lead to adverse child outcomes, including birth defects

In 1992 a British physician and epidemiologist, David J. Barker argued that adult health behaviors have a fetal origin. This theory put forward by him is known as “the developmental origins of adult disease” often known as the “Barker Hypothesis” [11]. The most widely accepted possible mechanisms under this hypothesis are altered fetal nutrition and increased glucocorticoid exposure during pregnancy. During this period, the fetus is exposed to an insult or stimulus that can have irreversible long-term effects on the development [12]. Similarly, in alliance with the above theory, Barker also proposed that during a maternal infection, the maternal energy is diverted from the fetus and can result in negative sequelae of the body’s inflammatory response [13].

PROBABLE MECHANISMS

Death of a family member, catastrophic community-wide disasters, household strain, homelessness, daily hassles, and perceived stress during pregnancy can all increase the risk of preterm birth [14]. Major life events and chronic stressors (including food insecurity, chronic illness at home, increased crowding, and unemployment) during pregnancy carry a significant burden of low birth weight [15]. An important source of chronic stress is racial discrimination which is a growing concern among African-American women [16]. Although there are no direct neural connections between the mother and the child, mechanisms exist that translate maternal psychological functioning to physiological effects. The three main mechanisms are the transport of stress-related hormones to the fetus through the placenta, alteration in maternal behavior, and reduction in blood flow to the fetus [17]. The Hypothalamus-Pituitary-Axis (HPA) has a centric role in the development of psychiatric diseases. The high cortisol levels bring about significant changes in the number of neurotransmitters released particularly dopamine, serotonin, and noradrenaline [18,19]. Maternal stress can modify the HPA axis in the developing fetus. The associated changes are increased impulsivity, elevated attention deficit, and aggression. These alterations are a part of a child’s future ability to fight intruders and predators. Consequently, these children have an increased

tendency to develop psychiatric diseases as a way of adapting to stressful situations [20,21]. Nevertheless, the exact mechanism underlying maternal stress-induced fetal HPA programming is yet to be confirmed.

In alliance with the above findings, a male partner’s behavior has a direct effect on the pregnant women’s perceived stress and acts as one of the stress-enhancing factors. A study conducted by Kainz has stated that “the child’s father becomes an important person for the mother’s well-being during childbirth” [22]. Inmate violence, emotional abuse, and physical abuse are influential factors in pregnant women’s perceived stress [23]. Therefore, male partner behavior needs adequate focus while analyzing maternal stress during pregnancy.

PREGNANCY AND MENTAL HEALTH

Most often women enter pregnancy with underdiagnosed or undiagnosed psychiatric disorders and with or without consuming psychotropic medications. Around 3.3% of pregnant women experience post-traumatic stress disorder (PTSD) which extends up to 1-year post-childbirth. Although the diagnosis of PTSD is of concern at any point time in life, it is particularly dangerous during pregnancy and may lead to negative child outcomes. PTSD is associated with neuroendocrine abnormalities and can predispose the infant to develop PTSD. In addition to the biological vulnerability of PTSD in the infant, the mother can also develop other psychiatric comorbidities such as anxiety and depression. This leads to a series of fatal events such as preterm delivery and low birth weight. Low birth weight can have an adverse impact during the developmental stages of a child. It is associated with poor academic performance, attention deficit problems, and internalizing behavioral issues [24,25].

Depression is a psychiatric illness commonly seen during pregnancy and in the postpartum period. It is generally unrecognized in prenatal care [26]. In a systematic review conducted by Gavin, depression was evaluated through a structured interview approach. As per the findings of this study, the point prevalence of depression was 11% in the first trimester and 8.5% in the second and third trimesters [27]. Depression during pregnancy can lead to unfavorable outcomes such as poor compliance to prenatal care, smoking initiation, substance and illicit drug abuse, inadequate nutrition, lack of exercise, and elevated suicidal ideation [28-30].

Maternal stress, anxiety, and depression during pregnancy have a substantial effect on the neurodevelopment of the child. As suggested, it has long-term implications with a negative effect on motor skills, learning ability, and behavior through a mechanism called “fetal programming” [17]. Psychological stress during pregnancy can also lead to life-threatening situations including stillbirth. In a prospective study conducted by Wisborg *et al.*, it was revealed that psychological stress during pregnancy increases the risk of stillbirth by 80% [31]. Prenatal distress is also associated with maternal inflammation that can in turn disrupt the brain development of the fetus [32].

Maternal anxiety during pregnancy can lead to smaller fetal head circumference. Similarly, maternal anxiety and depression can restrict the intra-uterine growth of the fetus [33]. Maternal stress has also been correlated to increased adiposity in the later life of the child. A potential mechanism is that maternal psychological distress could be a cause of low birth weight this triggers a “catch up” growth resulting in obesity and overweight [34]. Another risk factor for increased body mass index and obesity index (OI) among children is maternal smoking during pregnancy. Another probable explanation for it is the low birth weight, due to fetal malnutrition caused by maternal anorexia [35]. The severity of stress experienced by women during pregnancy can influence the development of attention deficit hyperkinetic disorder (ADHD) in children [36]. The greater the stress the higher the severity of ADHD symptoms among children [37].

PREGNANCY AND SMOKING

Maternal smoking during pregnancy is a serious public health issue as the smoke in cigarettes is detrimental to the health of both the mother and the child. A systematic review conducted by Lange with data from 100 countries has concluded that worldwide 52.9% of women who smoked daily also continued it during pregnancy [38]. Older age, less schooling, a greater number of previous gestations and abortions, low economic status, unplanned pregnancies, and exposure to passive smoking are factors that induce smoking behavior in pregnant women [39]. Maternal smoking until 7–10 months of pregnancy causes a decrease in birth weight. This is attributed to intrauterine growth retardation and not premature birth [40].

There are numerous harsh chemicals in a cloud of cigarette smoke that are: Nicotine, carbon monoxide, tar, benzene, and heavy metals. The mechanism operating behind this is – the nicotine and carbon monoxide in cigarette smoke causes vasoconstriction in the placenta followed by fetal ischemia [41]. Nicotine and its metabolite cotinine are highly lipophilic and cross the placental barrier; therefore, it can be inferred that the fetus is exposed to higher concentrations of nicotine than the smoking mother. The impending fetal ischemia deprives the fetus of adequate nutrition and oxygen thereby adversely impairing fetal development. Epidemiological studies have also implicated the fatal effects of maternal smoking during pregnancy with a significant risk of the development of behavioral and psychiatric problems in the offspring (attention deficits, hyperkinetic disorder, alcohol abuse, substance abuse, and depression) [42]. Therefore, pregnant women should be advised to quit or abstain from smoking. Under circumstances when this is not possible risks associated with maternal smoking should be translated and children born to these women must be monitored for any adverse outcomes.

ILLICIT DRUG USE DURING PREGNANCY

Illicit drug use during pregnancy is an alarming concern globally with fatal maternal and child outcomes. Prenatal drug use exposes

the underdeveloped organs of the fetus to harsh chemicals. As per the World Drug Report, 2019, more than 5% of the world population is abusing some kind of illicit drug [36]. A recent national survey conducted in the United States among pregnant women has highlighted that unmet mental health needs during pregnancy lead to illicit substance abuse among pregnant women. As per the findings of the study 6.4%, of pregnant women reported unmet mental health needs and of them, 4.5% used illicit drugs during pregnancy [43].

The use of illicit or legal drugs during pregnancy is associated with placental abruption, premature rupture of membranes, abortion, stillbirth, and increased infant mortality. In addition, use of non-sterile needles carries the risk of dangerous infections. The most commonly abused illicit drugs during pregnancy are cocaine, marijuana and opioids [44,45]. Few illicit drugs can affect the cardiovascular system of the mother, increase the heart rate, and also produce vasoconstriction. This sequence of events reduces blood flow to the uterus which eventually causes intra-uterine growth restriction [46]. Other categories of drugs that affect the maternal central nervous system can lead to congenital malformation, cause intrauterine growth disturbance, and increase the incidence of neonatal morbidity [36].

PREGNANCY AND ALCOHOL ABUSE

Alcohol use during pregnancy remains a global public health concern. Pregnant women often consume alcohol unaware of its ill effects on the developing fetus. The global prevalence of alcohol use in pregnancy from 1984 to 2014 is estimated to be 9.8% with marginal variation from one country to another depending on which area the woman resides [47]. The alcohol consumed by the mother is passed into the fetal circulation and may have the same or even higher blood alcohol concentrations. The fetus is unable to process the alcohol in the blood as efficiently as an adult and this culminates in a sequence of adverse alcohol effects. Therefore, the teratogenic effect of alcohol can persist on the fetus during fetal growth, infancy, or even later in life [48].

Although there is a dearth of scientific evidence about the degree of effects of alcohol use during pregnancy and may vary depending on dose, duration, trimester of exposure, genetic factors, maternal nutrition, and stage of the fetus at exposure. Since the degree of risk is unknown health-care professionals recommend abstinence from alcohol in women who plan to become pregnant [49]. Alcohol use during pregnancy poses a significant risk, fetal alcohol syndrome being one of the most severe outcomes. Fetal alcohol spectrum disorder (FASD) can include abnormal facial features, small head size, shorter than average height, low body weight, hyperactive behavior, poor coordination, attention deficit, poor memory, difficulty in school, learning disabilities, intellectual disability, poor reasoning and judgment skills, sleep, and sucking problems as babies and vision or hearing problems. FASD is irreversible but can be completely prevented by abstaining from alcohol during pregnancy. Other adverse health outcomes of alcohol use during pregnancy are

miscarriage, stillbirth, intra-uterine growth restriction, and preterm labor [50]. In-utero alcohol exposure has been associated with multiple fetal structural anomalies such as craniofacial abnormalities (palpebral fissures, a smooth philtrum, and a thin vermilion border of the upper lip), renal, cardiac, and other major malformations [51]. Therefore, screening pregnant mothers during antenatal health-care visits particularly, of women with a history of alcohol intake, can save the fetus from the adverse health outcomes of alcohol consumption.

PREGNANCY AND ENVIRONMENTAL STRESSORS

Distressing environmental exposure during pregnancy can also lead to poor pregnancy outcomes with increased morbidity, mortality, and health-care costs. Poor air quality during gestation is associated with low birth weight, preterm birth, intra-uterine fetal growth restriction, and infant death [52]. Ritz *et al.*, in their study conducted in Southern California, have found that increasing levels of carbon monoxide and particulate matter <2.5 micrometer in aerodynamic diameter carries a risk of preterm birth [53]. Similarly, exposure to heavy metals also increases the risk of adverse birth outcomes. Cadmium is associated with decreased birth weight [54,55] and both arsenic and lead induce low birth weight and pre-term birth [56-58]. Moreover, in the long-term, prenatal lead exposure may have cognitive effects up to 12–24 months of age [59]. Proximity to landfill sites is associated with neural tube defects, low birth weight, and very low birth weight [60]. Prenatal pesticide exposure is an unexplored area of threat. Increased exposure to dichlorodiphenyldichloroethane during pregnancy is associated with lower birth weight [61]. Maternal residence within 1000 m of agricultural applications of benomyl, methyl carbamate, organophosphorus pesticides, or pesticides classified as endocrine disruptors, cholinesterase inhibitors, or developmental toxins is associated with neural tube defects [62].

Pregnant women are also more vulnerable to heat changes in comparison to the general population. Extremely high and low levels of heat can induce maternal stress during pregnancy. Ambient temperature induces changes in the anterior hypothalamus of the mother. The anterior hypothalamus is the thermoregulatory center of the brain, it modulates the balance between serotonin and noradrenaline. These neurotransmitters have the potential to regulate mood and thereby induce maternal stress. Pregnant women also face difficulty while sleeping in high temperatures which poses an increased risk of depression. Similarly, less sunlight is a contributing factor to the development of winter depression. Therefore, it can be inferred that weather conditions have a significant impact on human psychological health, particularly during pregnancy [63].

IMPROVING PREGNANCY-RELATED OUTCOMES

Encouraging the practice of relaxation exercises during pregnancy can improve the psychological state of pregnant

women. Progressive muscle relaxation and diaphragmatic breathing are two documented techniques that have significant benefits with a reduction in the level of perceived stress and a sense of internal control during pregnancy. They are ideal non-pharmaceutical interventions, easy to accommodate, and practice in daily routine [64]. Similarly, the integration of mindfulness-based therapy is another valuable way to prepare pregnant women to confront the challenges of pregnancy, childbirth, parental role, post-partum stress, anxiety, and depression [65]. Yoga is another unexplored avenue in improving pregnancy-related outcomes by reducing stress, depression symptoms, and some adverse birth outcomes [66].

Mobile health interventions are in practice among developed nations and have shown to enhance four major psychosocial parameters: Self-efficacy, social support, anxiety, and depression. Therefore, mHealth interventions can improve pregnancy outcomes during ante-natal care [67]. In low- and middle-income countries, implementation of mobile-based interventions can improve maternal education during the perinatal period [68]. Regularly engaging in antenatal exercise is a strategic lifestyle intervention aimed to improve the short and long-term health of the mother and the child. According to the recommendations of the Improving Maternal and Progeny Risks of Obesity through Exercise trial, regular moderate-intensity exercise during the second half of pregnancy will result in improved maternal and offspring outcomes, including a reduction in birth weight and adiposity in the offspring, which may be protective against obesity in later life [69].

FUTURE DIRECTIONS

One of the major challenges of ongoing research is not only continuing to probe the mechanisms of how prenatal stress affects pregnancy outcome and offspring development, but also the extent and duration of its effects. Prenatal stress is of emerging concern especially, in the context of technology use and improved access to health care. There are multiple strategies if used effectively can curb the dangers of perinatal stress. Additional longitudinal studies are required to fully characterize the extent and significance of newer methods to reduce and tackle perinatal stress. Pregnant women exposed to physical and emotional trauma are unintentionally passing down these stressors to their developing fetus. Timely prevention can avoid future burdens both on the individual level and at the economic and health care level.

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