EDITORIAL

COVID-19 pandemic and maternal mental health: Can adverse foetal brain programming be averted?

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Covid-19 pandemic and its impact

COVID-19 has been the world's gravest public health challenge of this century. Since its declaration as a pandemic by World Health Organization (March 2020), 228 countries have been affected, with over 600 million confirmed cases and over 6.5 million deaths.[1] The most severely affected countries include the United States of America, India, Brazil, France, Germany, the United Kingdom and Russia.[1] In line with the global scenario, the impact of the pandemic has been most severely seen among Low- Middle-Income Countries, including Pakistan, Bangladesh, Afghanistan, Indonesia, Philippines, and Nepal,[1] where every aspect of human life, including physical health, mental well-being, education, and undeniably the economic conditions have deteriorated.[2]

To curtail the spread of infection, lockdowns were imposed, resulting in transitory closure of schools, businesses and offices, confinement to homes, and often loss of income, especially for those on daily wages. Disruption of livelihoods and interruption in the ability to earn a living decreased access to basic needs and health services, burdening the household stress. Maternal and childcare services, in particular, were severely underutilized as hospitals became stigmatized places for contracting COVID-19.[2,3]

Covid-19 pandemic and maternal mental well-being

Although social distancing benefitted the population in curbing the virus spread, it produced several negative consequences simultaneously, as compromised social support and human connection undermined our ability to cope with challenging situations and develop resilience. The impact of isolation on mental well-being was determined by earlier studies which reported a high prevalence of psychological symptoms of distress.[4] During the pandemic, financial concerns and social stressors combined with uncertainty and heightened fear through COVID-19 related information from social media intensified psychological anguish and poor mental health.[5] Among pregnant women, COVID-19 induced psychological stress has resulted in an increased prevalence of depression (37%) and anxiety (56.6%), intensifying maternal mental health needs.[5] Also, thoughts of self-harm were reported among women with symptoms of depression in a multi-centre cross-sectional survey conducted in China,[6] which were pronounced among underweight, primiparous, age below 35 and middle-income women working full-time.[6] Poor sleep associated with mental anxiety and depression has been demonstrated to raise the risk of postpartum depression and preterm births.[5] Additionally, women with severe depressive symptoms showed a decreased bond to their unborn children.[7] Similar outbreaks in the past, such as Severe Acute Respiratory Syndrome and Middle East Respiratory Syndrome, have shown that pregnant women are more prone to be mentally affected.[4]

As pregnant women during the pandemic remained surrounded by homebound male family members most of the time, the risk of domestic and intimate partner violence also increased.[8] In a lifetime, 30% of women worldwide are subjected to physical or sexual violence inflicted by their intimate partners. Such violence seems to increase in frequency and intensity during pregnancy, humanitarian crises, and disasters. Furthermore, victims' capacity to detach themselves from abusers and seek outside help is hampered by isolation and physical distancing.[2] Premature babies born to such victims are not only more likely to suffer from poor neonatal outcomes but they may experience several social and behavioural problems including insecure attachments, increased aggressiveness and internalizing problems, as a result of possible altered programming of the developing foetal brain.[9]

Foetal brain development and maternal mental stress

The development of brain is a lifelong process and pregnancy provides the most sensitive period for foetal brain programming where it undergoes a very long phase of anatomical development that starts about 2 weeks after conception and lasts until early adulthood. The normal phase of development is marked by the process of

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millions of neurons migrating from the centre of the brain to the periphery where they organize, get connected and create basic neural networks that serve as a platform for normal cognitive function during the postnatal period and early childhood.[10] Part of this process requires signals from its environment, providing a unique window of opportunity for the foetal brain to develop properly.[10]

In line with the concept of Developmental Origins of Health and Disease, during the critical prenatal phase of growth and development, exposure to an adverse in-utero environment can significantly affect the short- as well as the long-term health of an individual.[11] The developing foetus, if exposed to an unfavourable intrauterine milieu, will adapt to continue its viability at the cost of altered programming at cellular and endocrine levels. Adaptive developmental plasticity implies that the in-utero environment forecasts the future conditions that the foetus will subsequently inhabit after being born.[12] Consequently, a mismatch between the two, results in an increased risk of various chronic diseases of adult life.[11]

Maternal stress is considered one of the developmental teratogens[13] and has been linked to an increased risk of emotional, behavioural, and cognitive disorders among children. These include anxiety and depression symptoms, attention deficit hyperactivity disorder, behaviour and personality disorders, cognitive difficulties, and autism spectrum disorders.[12] Adverse interaction between maternal environmental stressors and the formation of the foetal brain could lead to its altered programming in the womb.[13] Studies have demonstrated that children exposed to maternal anxiety reported decreased volume of the hippocampus. Similarly, children born to mothers who lived through stressful life events during pregnancy manifested decreased volume of the anterior cingulate cortex in adulthood.[12] Further, altered foetal brain imaging depicting changes in limbic and fronto-temporal networks and their functional and microstructural connections have been attributed to maternal stress. Hypothalamic-pituitary-adrenal (HPA) axis is reported to play a key role in mediating the consequences of maternal stress on the developing foetal brain.[12] However, HPA axis is particularly vulnerable to early life programming and growing evidence suggests that prenatal stress programmes both the HPA axis and behaviour, impairing developing brain's plasticity, eventually exhibiting as impaired coping and increased anxiety among adults.[14] Not only that, but prenatal stress may influence the behavioural development of infants by altering the epigenetic fingerprints of stress-related genes. A longitudinal cohort study that assessed the behavioural and epigenetic implications of COVID-19-related prenatal stress among mothers and infants found that the neonates born to mothers who experienced greater prenatal COVID-19-related stress showed heightened SLC6A4 gene methylation at seven cytosine and guanine loci, which was negatively associated with the temperament of infants at three months.[15] These observed brain changes associated with the biological covariates and the mediators of prenatal stress form the basis of many of the behavioural, emotional, and cognitive problems encountered later in life.[12,16]

Strategies to combat maternal mental stress during Covid-19 pandemic

Living amid the pandemic can be stressful. Hence, the coping mechanisms to adapt to this reality must be employed by pregnant women to reduce their stress. Meditation is one way to help reduce perinatal stress and the risk of postpartum depression by enhancing improved peace of mind and better sleep.[17] Developing resilience is another protective strategy against stress.[18]

Talking to the baby in the womb through singing or reading is recommended to stimulate the baby's intellectual state. By the end of the second trimester, the baby begins to hear the mother's voice as well as noises from the external environment.[19] Therefore, if a pregnant woman talks to the baby with certain feelings and emotions, the baby may associate them with similar emotions once born, fostering affection and bonding with the mother. Likewise, the mother can also de-stress and extend her warmth and love to the growing foetus. This subconscious learning can favourably influence foetal brain growth and development.[19]

Supportive social relationships influence mental health by fostering adaptive health behaviours, increasing optimistic feelings, and boosting the regulation of emotions.[5] In addition, adopting a healthy lifestyle during pregnancy plays a significant role in promoting healthy foetal brain programming. This includes attention to a balanced diet and adequate water intake, adequate sleep, opting for moderate weight gain (depending on pre-pregnancy weight), practicing regular moderate physical exercise (such as running/walking or yoga), continuing regular antenatal visits and maintaining good work-life balance.[20]

Elimination of violence and discrimination against women are recognized under Sustainable Development Goal 5. The availability of prompt support to address domestic violence from government and non-governmental organizations deserves attention in disrupting the intergenerational cycle of violence for improved maternal and neonatal health. Some examples

of upstream interventions in preventing violence include the provision of microfinance to women to support their families and the nurse-family partnership when nurses pay home visits to women during antenatal and postnatal periods.[9] Such interventions could disrupt the intergenerational cycle of violence and will safeguard the health of women and their children.

In conclusion, the uncertainty surrounding the pandemic is taxing as no one can predict how long it will last. By encouraging pregnant women to take their holistic health into account, adopting health promotion strategies and following the recommendations from the health organizations, the impact of prenatal psychological stress on the developing foetal brain can be minimized.

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