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Application of DOHaD hypothesis to the Effect of Stress Levels in Pregnant Women on the Fetus and Baby's Mental Health: A Literature Review

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ABSTRACT

Introduction: *According to the research of Cadzow et al., on antepartum and postpartum mental health, weak attachment bonding between the fetus and mother during pregnancy was associated with postpartum depression and anxiety. Sugishita et al. found that postpartum depression decreased when attachment to the fetus was higher during the antepartum period. Attachment to the fetus during pregnancy was associated with maternal mental health and was associated not only during pregnancy but with postpartum depression and blood cortisol levels, which are stress indicators, cross over the placenta and have been correlated with maternal and fetal levels. It has been afraied that strong psychological stress during pregnancy has some effect on the fetus and causes mental development in children, and the fetal programming hypothesis is pointed out in the background. However, there has been no previous research on the relationship between mental health such as stress in pregnant women and the fetal programming hypothesis. The purpose of this study is to examine the relationship between stress in pregnant women and the fetal programming hypothesis through literature.*

Methods: *The databases used in the literature search are Pubmed, CINAHL, Cochrane Library, and Google Scholar. The search range is from 2000 to 2020. The criteria for adopting the document are 'DoHaD' x 'Mental Health', 'DoHaD' x 'Stress', and 'DoHaD' x 'Depression' in the English original article registered in the retrieved database. Among the retrieved articles, duplicate documents were excluded as a result of animal experiments and genome analysis. As a result, 13 articles were selected.*

Results & Conclusion: *As a result of conducting a literature review, it was found that when the stress of the pregnant woman is physically and psychologically high, the stress of the child is high. In particular, fetal dysfunction is likely to occur during labor if you spend pregnancy period when pregnancy complications and anxiety are strong. It is still necessary to examine the relationship between the child's growth and mental illness and the stress she received as a mother at the time of the fetus.*

Keywords

Stress levels, Pregnant woman, Child abuse, Mental health.

Introduction

Child abuse is a highly important societal issue that is worsening with time and requires urgent resolution. Most childhood deaths from abuse are in children younger than 1 year, among whom deaths of children less than 24 hours after birth account for 25%. More than 90% of the perpetrators of deaths in infants less than 24 hours after birth are the biological mothers, and the motive is most commonly unwanted pregnancy or denial of the existence of the child.

Regarding antepartum and postpartum mental health, Cadzow et al. have reported an association of weak attachment bonding between the fetus and mother during pregnancy with postpartum

depression and anxiety [1]. Sugishita et al. found that levels of postpartum depression were lower in mothers who had stronger attachment to the fetus during the antepartum period [2]. Attachment to the fetus during pregnancy has been associated with maternal mental health, not only during pregnancy but also with regard to postpartum depression and anxiety [3,4]. Blood cortisol, a stress indicator, can cross the placenta, and a correlation between the maternal and fetal levels has been reported [5]. The DOHaD hypothesis is that adaptive responses occur due to various environments during the fetal period and newborn baby, and are involved in future disease risk [6]. According to the DOHaD hypothesis strong psychological stress during pregnancy can affect the fetus and cause abnormal mental development in children. However, there has been no previous research regarding the relationship between mental health, such as stress, in pregnant women and the DOHaD hypothesis. The purpose of this study is to examine the relationship between stress in pregnant women and the DOHaD hypothesis through a literature review.

Methods

The Pubmed, CINAHL, Cochrane Library, and Google Scholar databases were used in a literature search of articles published between 2000 and 2020. The criteria for adopting the document were 'DoHaD' x 'Mental Health', 'DoHaD' x 'Stress', and 'DoHaD' x 'Depression' for original articles published in English and registered in the database. Among the retrieved articles, duplicate documents and those reporting animal experiments and genome analysis were excluded. Following assessment of the relevance of the research theme and the impact of the research theme to fetuses and newborns in the remaining 18 articles, a final total of 13 articles were included in the analysis.

Results

Among the 13 papers, the effects of the pregnant woman's mental health on their baby were divided into those due to complications and those due to lifestyle. The 13 papers are listed in Table 1.

Table 1: Literature List.

	Author	Year	Title	Main Results
[complications factors]				
1	Horsch A., Gilbert L., Lanzi S., et al.	2018, BMJ Open	Improving cardiometabolic and mental health in women with gestational diabetes mellitus and their offspring: study protocol for MySweetHeart Trial , a randomised controlled trial	GDM, life cycle, **mental health**, maternal obesity and child obesity are associated.
2	Lewis AJ., Austin E., Knapp R., et al.	2015, Health Care	Perinatal Maternal Mental Health, Fetal Programming and Child Development.	Maternal mental disorders may affect fetal development through **programming effects**. A stressful pregnancy experience is associated with increased emotional and behavioral problems by age 5 and increased risk of anxiety that persists into puberty.
3	MonkC., Lungo-Candelas C, Trumpff C., et al.	Epub, 2019	Prenatal Developmental Origins of Future Psychopathology: Mechanisms and Pathways	**Maternal prenatal distress is only one of many**, many influences on children's futures; distress during pregnancy is typically a modifiable facto.
4	Mervi Vanska., Raijya-Leena Punamaki., Jallu Lindblom., et al.	2017, Family Relations	Parental Pre- and Postpartum Mental Health Predicts Child Mental Health and Development	**Mothers' symptoms alone (separate mother model) predicted child internalizing symptoms,** whereas joint parental symptoms (additive model) predicted problems in executive function.
5	Claes S.	2020, J Mol Sci	Neuroepigenetics of Prenatal Psychological Stress	**Psychological stress in pregnant women can have many negative effects** on the child's physical and psychological functioning.
6	Takeo Kubota.	2018, Adv Exp Med Biol.	Preemptive Epigenetic Medicine Based on Fetal Programming	Several lines of evidence suggest that **prenatal environmental stress alters the epigenetic state of genes, causing persistent gene dysregulation** and may be associated with postnatal disease.
7	Pathik D. Wadhwa., Claudia Buss.,, Sonja Entringer.	2010, Semin Reprod Med.	Developmental Origins of Health and Disease: Brief History of the Approach and Current Focus on Epigenetic Mechanisms	Findings suggest that the effects of **prenatal stress and maternal placental hormones** on the developing fetus may persist postnatally, as assessed by measures of temperament and behavioral reactivity in the first years of life.

8	Pathik D. Wadhwa.	2005, Psychoneuro endocrinology	Psychoneuroendocrine processes in human pregnancy influence fetal development and health	Findings suggest that the influence of maternal prenatal stress in the etiology of prematurity-related outcomes is mediated in part by the maternal-placental-fetal neuroendocrine axis, particularly placental corticotropin- releasing hormone. The effects of prenatal stress and **maternal-placental hormones on the developing fetus** may persist postnatally, as assessed by measures of temperament and behavioral reactivity during the first years after birth.
[lifestyle factors]				
9	Fukuoka H.	2016, Jpn. J. Hyg	Environmental Effect In Utero for Adult Disease	**Overweight and obese** people are increasing. Therefore, perinatal overnutrition and excesses of specific nutrients should also be investigated.
10	Fukuoka H., Sata F.	2016, Jpn. J. Hyg	Molecular Mechanism of Developmental Origins of Health and Disease (DOHaD)	Postnatal life changes during development are **caused by exposure to the harsh environment in the womb.** Endocrine disruptors, severe psychological stress, undernutrition or overnutrition.
11	Carolina DW.	Development and Psychopathology. 2018; 30: 1129-1144.	Prenatal stress and the development of psychopathology: Lifestyle behaviors as a fundamental part of the puzzle	The analysis of the literature led to the conclusion that **sleep, diet, and exercise during pregnancy,** may have fundamental roles as mediators between prenatal stress and maternal pregnancy physiology.
12	Romy G., John W., Vincent WV	2019, J Dev Orig Health Dis	Lifestyle intervention strategies in early life to improve pregnancy outcomes and long- term health of offspring: a narrative review	Adverse maternal lifestyle factors, including **overweight, unhealthy diet, sedentary behavior, smoking, alcohol consumption and stress** in the preconception period and during pregnancy, are the most common modifiable risk factors leading to a suboptimal in-utero environment for fetal development.
13	Blaker LS., Van Dammen L., Leeflang MMG., et al.	2020, Meuroscience & Biobehavioral Reviews	Hypothalamic-pituitary-adrenal axis and autonomic nervous system reactivity in children prenatally exposed to maternal depression: A systematic review of prospective studies	Study results imply that certain factors are likely to mediate and moderate associations between prenatal exposure to **high maternal depressive symptoms** and HPA axis and ANS reactivity in children, such as **partner support, postnatal depression and caregiving behavior**

According to the DOHaD hypothesis, high-risk pregnancies with obvious complications have affect to fetus and child. In particularly Gestational Diabetes Mellitus (GDM) or diabetes (DM), extreme stress, and mental illness [7,8]. It has been found that when a pregnant woman is under high physical and psychological stress, the stress levels in the child are also high [9-12]. In particular, fetal dysfunction is most likely to occur during labor in women who had complications of pregnancy and high levels of anxiety during gestation. The literature review revealed that damage caused by such maternal stress affects the fetus and infant. Furthermore, strong hormonal fluctuations during pregnancy have an impact on the mental health of the fetus and newborn [13-15].

Regarding the effects of lifestyle on pregnant women's mental health, overnutrition, harsh environment in the womb, and lack of exercise have been identified as important factors [16]. Sleep, diet, and exercise during pregnancy may have fundamental roles as mediators of prenatal stress during pregnancy [17]. Adverse maternal lifestyle factors, including smoking, alcohol consumption, and stress in both the preconception period and during pregnancy, are the most common modifiable risk factors leading to a suboptimal in-utero environment for fetal development [18,19]. Prenatal exposure to poor partner support and high levels of maternal depression, such as postpartum depression, are highly associated with HPA (Hypothalamus-Pituitary-Adrenal)-axis and ANS (autonomic nervous system) reactivity in children [20].

Discussion

The effects of depression, anxiety, and stress in pregnant women on their fetuses and newborns can be considered in terms of the Developmental Origins of Health and Disease (DOHaD) theory. The DOHaD proposes that the environment from the embryonic stage to early childhood influences future health and development of disease [21]. Current research investigating the link between DOHaD and perinatal mental health is particularly relevant to understanding how early life experiences shape our biology and psychology. Other important research areas in the field of DOHaD include the roles of psychological stress, environmental chemicals, and artificial reproductive technology on fetal health.

Complication-related factors affecting pregnant women's mental health that were identified in the literature search included malnutrition, which may be associated with type2 diabetes; and psychological stress, which may be associated with neurodevelopmental disorders. Recent studies have shown that some drugs and early intervention are effective in preventing epigenetic disorders. Therefore, preventive and pre-emptive care is possible against disorders that are caused by prenatal and early fetal program changes [8].

Some pregnant women have poor living conditions that are ongoing, from the time the baby is in the womb conditions that are ongoing throughout the pregnancy. An unhealthy lifestyle, including high calorie intake, lack of exercise, and stress, increases the risk to the fetus. Stress during pregnancy also poses a risk for neuropsychiatric disorders in the child that are related to the number and severity in the pregnant woman [22]. In the case of high-risk pregnancies with complications, early intervention is necessary to minimize the impact on the fetus.

It has been reported that the risk of mental developmental disorders in the child can be reduced by detecting stress caused by depression and anxiety and providing support to the woman early in pregnancy [23]. Lifestyle changes (e.g., with regard to excess weight, lack of exercise) can be made with guidance from midwives [24,25]. Fetal dysfunction during labor is more likely in women who experience complications and strong anxiety during pregnancy. It is important for midwives to provide appropriate health guidance to pregnant women according to their gestational age.

The future challenge is still necessary to examine the relationship between the child's growth and mental illness and the stress she received as a mother at the time of the fetus.

Conclusion

The major finding of this literature review was that when a pregnant woman experiences high physical and psychological stress, the child also experiences high stress. Fetal dysfunction during labor is most likely to occur in women who had complications of pregnancy and experienced high levels of anxiety during pregnancy. Further study is required to understand the relationship between stress experienced by the fetus in the womb and growth abnormalities and mental illness in the child.

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