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Pregnancy Related Complications Due To Lifestyle Modification.

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Abstract

Worldwide, there are so many maternal deaths per year. Pregnancy-related problems are a major cause of death for women. Unfortunately, pregnancy-related complications are a common occurrence for women, and they necessitate evaluations, because they have an effect on both the mother and the embryo or foetus. An important modifiable risk factor for pregnancy problems is the unhealthful lifestyle decisions made by obstinate mothers. Smoking, drinking alcohol, and caffeine use are among the worst lifestyle choices for mothers. Maternal age is also seen as a modifiable risk factor for unfavorable pregnancy outcomes, while not being directly tied to lifestyle. The foetus is affected by maternal behaviors, sedentary lifestyle i.e. lack of exercise and diet. With a focus on the effects on birth outcomes, this article's objective is to quickly summaries the most recent research on the consequences of stress exposure and adverse emotional states (thus, anxiety and depression) during pregnancy. The focus of this review is on the connection between maternal lifestyle and unfavorable pregnancy outcomes.

1. Introduction

A normal pregnancy is supported and developed by a variety of hormones. Around two weeks into the menstrual cycle, the pituitary glands secrets luteinizing hormone (LH) and follicular stimulating hormone (FSH) cause egg maturation and ovulation. Corpus luteum that produces progesterone and oestrogens develops after ovulation. FSH and LH levels fall during a typical menstrual cycle without egg fertilization, which causes the corpus luteum to ovulate, progesterone and oestrogen levels to fall, and menstruation to occur. If the egg is fertilized and implants in the endometrium, the hormone hCG helps to keep the corpus luteum producing oestrogen and progesterone. The serum beta human chronic gonadotropin (hCG) level rises as the embryo develops, peaking at 150,000-200,000 mI U/mL at 10-12 weeks of embryo gestational age. As hCG levels fall, the placenta secretes a variety of hormones, including progesterone, oestrogen, and human placental lactogen, to keep the pregnancy going. In a nonviable pregnancy, low levels of oestrogen and progesterone cause embryo involution and menstruation.(1)

2. Embryonic Development and Foetal Physiology:

The ovum is fertilized in the Fallopian tube over the course of 5–6 days before making its way to the uterus. In this stage, the fertilized ovum's rapidly dividing cells go through blastulation, in which the zygote's cells create a fluid-filled structure with distinct external and internal cellular components. The resulting blastocyst is composed of an inner cell mass that will eventually become the embryo and a surrounding membrane structure, as well as external cells that will interact with the uterine endometrium to produce the placenta. The blastocyst enters the uterine canal roughly a week after fertilization and implants in the uterine endometrium (endometrium) on average 9 days after fertilization, though it can occur as early as 6 days and as late as 12 days after fertilization. Within 8–10 days after conception (days 22–24 of a 28-day menstrual cycle), trophoblast (placental) cells secrete human chorionic gonadotropin (hCG), which is initially detectable in pregnant women's urine and blood. (2)

The syncytiotrophoblast is an invasive, multinucleated syncytium formed by the blastocyst's most exterior trophoblastic cells in contact with the endometrium.

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The synctyiotrophoblast must be separated from the more distant, single-cell cytotrophoblastic cells. As the developing embryo and amniotic cavity are supported by the synctyiotrophoblast, it thickens and creates vacuolar gaps. The placental villi and intervillus spaces are the resultant matrix of cellular trabeculae and vacuolar spaces. The foetal villus vasculature begins to form in the third week following conception. During majority of the first 10 weeks of pregnancy, the lacunae of the developing placenta are filled with transparent fluid without an actual link between embryonic circulations and maternal. During this phase, intervillus space oxygen values are at 20 mm Hg, and gas and nutrient exchange with embryonic tissues is passive. However, there has been a remarkable transformation in the spiral arterioles, the terminal portions of the uterine arteries that enter the decidualized endometrium, where fibrinoid has replaced the smooth muscle and elastic fibers of the vascular wall. As a result, the terminal arteriolar structure is dilated and non-muscular.

During the first few weeks of pregnancy, other significant alterations in the maternal vasculature have taken place. Under the impact of pregnancy-related hormones, the more distal portions of the spiral arteries widen as well, and overall maternal blood supply to the uterus begins to decrease. There have been further major changes to the maternal vasculature. The more distal sections of the spiral arteries widen as well under the influence of pregnancy-related hormones, and overall maternal blood flow to the uterus starts to significantly increase.

At 10–12 weeks of gestation, the cellular congestion of the terminal spiral arterioles starts to dissipate, allowing maternal blood to penetrate the intervillus space and rinse the foetal villi. As a result, the intervillus gap's oxygen tension increases. Concurrent villi maturation and foetal generation of capable (non-nucleated) erythrocytes completing the prerequisites for full placental circulation. The intervillus space is under pressure that is lower than that of the foetal villous vasculature because of the comparatively high volume and low velocity of this circulation. As a result, oxygenated maternal blood is able to penetrate the intervillus space and bathe the delicate foetal villi without harming or collapsing them. The blastocyst comprises approximately 200 cells at the time of implantation. The trophoblastic cells of the blastocyst can be separated from the inner cell mass, also known as the embryonic disc. Within a few days, the embryonic disc separates into the primitive ectoderm and the overlaying endoderm, two cell layers. The "embryonic period" of development begins the third week following fertilization, or the fourth menstrual week. All important organs of the embryo are created throughout the next 8 weeks, while more organ development happens during the later foetal period (tenth menstrual week).

The sequence of events from the embryonic disc to a fully developed embryo with all of its major organs present is clearly complex. As an example, consider cardiac development. The formation of a splanchnic mesodermal layer of cells in the fifth menstrual week permits the embryonic vasculature to grow. The primitive heart tube develops when two neighboring midline endothelial tubes combine in the fifth menstrual week. A myoepicardium mantle is created by the condensing of the surrounding splanchnopleuric mesoderm. The connective tissue between the myoepicardial mantle and the endocardium of the primitive heart tube forms subendocardial tissue. By the end of the fifth menstrual week, this fundamental structure is pulsatile and starts to contract in the early fifth menstrual week. In five locations along its length, the tubular structure bulges, each of which will give rise to an adult cardiac structure. Future atrial and sinus venous tissues, however, will lie caudal to future ventricle and major artery outflow tissues. The tubular heart structure loops rightward, forcing the future ventricular and atrial areas into adult connections, with the atrial tissues lying cranial to the ventricular structures. After then, complex tissue partitioning happens in a specific order, resulting during the seventh menstrual week in a 4-chambered heart. When this process goes wrong, it can lead to detectable neonatal heart abnormalities.

Truncus arteriosus persists when a barrier between the aorta and the pulmonary trunk does not form, while disorders such transposition of the main arteries or tetralogy of Fallot result from incomplete or irregular division. Failure of the primitive atrial septal division results in atrial septal defects. During the foetal stage, critical organ development occurs. The foetal period begins at the end of the ninth or early tenth menstrual week. The embryo-foetus is about 4 cm long, all major organs are established (though many are immature), and skeletal structures can be easily

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identified. By the fourteenth week, a visual examination of the genital area can reveal the sex of the foetus. After the seventh gestational week, foetal lungs acquire significant branching and vascularisation. In the 22nd to 24th week, the gas-exchanging segments of the respiratory tree begin to emerge, and alveolar expansion continues into childhood. Before this stage, it is challenging to survive outside the uterus due to the inability to exchange oxygen and carbon dioxide. The foetus weighs about 300 g and develops some scalp hair by 20 weeks. (4)

Beginning with this phase of linear foetal growth, glucose is the main resource used by the developing foetus for oxidative metabolism. Glucose is absorbed through the placenta's facilitated transfer process. In its aerobic metabolism, the foetus also utilizes lactate and amino acids. Human placental lactogen circulates in the mother's bloodstream, inhibiting the uptake of glucose by maternal tissues and leaving it available for the placenta (as well as predisposing genetically predisposed individuals to maternal glucose intolerance).(5) Glycerol, free fatty acids, and free amino acids also pass through the placenta and are used by the foetus.

Foetal adipose tissue deposition occurs predominantly in the third trimester of pregnancy, growing gradually from about 26 to 32 weeks and more rapidly after that. Environmental influences on foetal growth, particularly gene imprinting, are of great interest nowadays.(6) The foetal circulation is one of the most fascinating aspects of foetal physiology. These venous structures enter the inferior vena cava, which is located high within the abdominal cavity, in a way that facilitates the flow of well-oxygenated blood along the inferior vena cava's medial aspect as it returns to the heart. When it reaches the right atrium, the configuration of the foetal upper atrial septum shunts the well-oxygenated blood through the patent foetal foramen ovale into the left ventricle from which it is directed to the systemic arterial circulation. Through the tricuspid valve, blood that is less well-oxygenated and returning to the right atrium via the inferior and superior vena cava is diverted to the right ventricle. A foetal artery leading to the descending aorta called the ductus arteriosus is where the majority of blood discharged from the right ventricle travels. Only a small part of the right ventricular outflow is sent to the pulmonary circulation, which has a relatively high resistance.

The foetal hypogastric arteries connecting to the umbilical arteries return right ventricular blood to the placenta after entering the descending aorta through the ductus arteriosus. At birth, these distinctively foetal circulatory components undergo significant changes: the foramen ovale, ductus arteriosus, and ductus venosus all close or constrict. At birth, the lungs expand and the pulmonary circulation resistance dramatically decreases. Prioritizing the pulmonary circuit, right ventricular outflow travels there to receive oxygen before returning to the left atrium.(7)

3. Maternal Habits and Lifestyle that Adversely Affect the Pregnancy Or Foetus:

Maternal habits and lifestyle also affect pregnancy and growth of foetus and health. This review focus on following habits and conditions:

- Psychological stress and anxiety.
- OTC Drugs
- Smoking, alcoholism and caffeine consumption
- Age.
- Over weight and obesity
- Psychological stress and anxiety:

Pregnancy-related psychiatric research mostly focuses on diagnosable mental diseases, particularly anxiety and depressive disorders and posttraumatic stress disorder like the wake of traumatic life events or delivery experiences. Low monetary resources, bad employment conditions, significant family and domestic responsibilities, strain in intimate relationships, and pregnancy problems are factors that frequently impact women during pregnancy.(8) A positive feedback loop between chronic stress and unfavorable pregnancy outcomes is possible. Due to the stress sensitivity of the immune system and the neuroendocrine interplay between the mother and foetus, birth outcomes may be impacted. Cortisol release is related to maternal stress.(9)

High cortisol levels reduce lymphocyte sensitivity to glucocorticoids by binding to glucocorticoid receptors; hence, when steroid resistance is created, there is an increased production of proinflammatory cytokines. The proinflammatory cytokines interleukin

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(IL)-6, IL-1, and tumors necrosis factor, as well as the anti-inflammatory cytokine IL-10.1, are all affected by maternal stress on the levels of circulating inflammatory indicators.(10) These inflammatory indicators hinder the immune system's response, making pregnant women more vulnerable to complications like preterm birth (PTB). By binding to glucocorticoid receptors, high cortisol levels decrease lymphocyte sensitivity to glucocorticoids; hence, when steroid resistance is developed, there is an increase in the production of proinflammatory cytokines.(11) Worse pregnancy outcomes, such as preeclampsia, spontaneous PTB, low birth weight and neonatal morbidity have all been linked to acute and chronic stress. In turn, PTB (regardless of indication) is linked to a higher risk of long-term complications among survivors (such as neurodevelopmental delay, vision issues, cerebral palsy, and hearing loss), as well as short-term neonatal morbidities (including pulmonary, neurologic, cardiovascular, immune, gastrointestinal, and metabolic complications) (12-14).

Pregnancy-related depression and anxiety are fairly prevalent. (15, 16) Furthermore, 1 in 5 women will experience an anxiety disorder during pregnancy, and 10% to 14% of women in the general obstetrical population meet the criteria for major depression during pregnancy.(17) The impact of stress on LBW and/or birth weight of infants. Evidence suggests that' major life events' moderately predicted birth weight or foetal growth as reported in the literature. In one study, low-income women's risk of LBW was predicted by unemployment and crowding. Infant birth weight and maternal depression symptoms are directly connected.(18) Through potentially impacting the physiological and behavioral of the mother, depression may be a significant mechanism through which the consequences of exposure to chronic stress influence foetal growth and birth weight.(19)

- **OTC Drugs:**

Numerous studies have shown that self-medication and substance use during pregnancy have an impact on the fetus's health. Some OTC products have questionable safety, despite the fact that most have great safety profiles. Although it is believed that only 10% of all birth abnormalities are caused by a teratogenic agent, the embryo is sensitive to the teratogenic effects of some medications or other substances throughout the time of organogenesis.(20)

The Food and Drug Administration (FDA) of the United States has developed a plan to help ensure safe drug usage during pregnancy. Sort medications into one of the five broad categories A, B, C, D, or X based on the possibility of foetal harm.(20) The majority of medications are categorized into category C due to a lack of data, which states that the treatment should only be administered if potential benefits outweigh potential dangers to the foetus, as opposed to categories D and X, which indicate evidence of foetal harm.(21) Prenatal drug exposure can result in low birth weight, lengthier hospital stays, preterm birth, feeding and breathing issues, and more. According to a USFDA survey, medication exposure during pregnancy causes 10% or more birth defects. Due to ethical concerns, many medications have not undergone controlled trials and likely won't.(22)

Table no 1: FDA Classification of Drug Safety during Pregnancy (22)

Sr .No.	Category	Drugs
1	**B and C**	**Analgesics & Antipyretics**
2	B	Phenacetin
3	B	Acetaminophen
4	C	Aspirin
5	**B and C**	**Antiemetics**
6	B	Cyclizine
7	B	Dimenhydrinate
8	B	Doxylamine
9	B	Meclizine

According to a recent survey, the majority of pregnancy-related medications fell under USFDA category A, which includes vitamins and mineral supplements. The category B medications, which were prescribed for illnesses that could occur during pregnancy, were then prescribed. These included

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paracetamol, ibuprofen, diclofenac sodium, antacids, dicyclomine, pantoprazole, ranitidine, omeprazole, ampicillin, cephalosporins, amoxicillin, metronidazole, and methyldopa. Nifedipine, clotrimazole, fluconazole insulin, chloroquine, digoxin, isoxsuprine, phenobarbitone, betamethasone, and carbamazepine were some of the category C and D medications used for certain situations to prevent the complications of various diseases. Progesterone, the only medication in Category X, was recommended in situations including threatening miscarriages, missed abortions, and preterm labour (16)

Table No 2

Sr No.	Category	Drugs
1	**B, C and D**	**Antibiotics**
2	B	Erythromycin
3	B	Cephalosporins, Cloxacillin
4	B	Penicillin, Ampicillin, Amoxycillin,
5	C	Gentamicin
6	C/D	Amikacin
7	B/D	Sulphonamides
8	D	Streptomycin
9	D	Tetracyclines
10	**B**	**Amoebicides**
11	B	Metronidazole
12	**B**	**Anthelmentics**
13	B	Mebendazole
14	B	Piperazine

Table no 3

Sr No.	Category	Drugs
1	**A**	**Vitamins**
2	A	B,C,D,E,folic acid
3		**Hormones**
4	A	Thyroxin
5	X	Androgens
6	X	Estrogens
7		**Progestogens-**
8	D	Hydroxyprogestrone
9	D	Medroxyprogestrone
10	X	Norethindrone
11	X	Norgestrel

Table no 4

Sr No.	Category	Drugs
1	**B and C**	**Anti TB Drugs**
2	B	Ethambutol
3	C	PAS
4	C	Pyrazinamide
5	C	Rifampicin
6	C	INH

Table no 5 A list of some of the medications used often during pregnancy, along with a categories of each medication's as per FDA classification (23)

Category A	There is no evidence of a risk to the foetus in later trimesters according to controlled research in women, and the likelihood of foetal injury seems small.
Category B	Either there are no controlled studies in pregnant women, but animal reproduction studies have not shown a foetal risk, or animal reproduction studies have shown

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	a negative effect (other than a reduction in fertility), but this effect has not been confirmed in controlled studies in first-trimester women (and there is no risk in later trimesters).
Category C	There are either no controlled studies in women, or studies in women and animals are not available. Studies in animals have shown harmful effects on the foetus (teratogenic, embryocidal, or other). Only if the possible benefit justifies the potential risk to the foetus should medication be administered.
Category D	Although there is evidence that using a drug while pregnant poses a risk to the foetus, there may be benefits to doing so (for example, if the drug is required in a circumstance where life is at risk or for a major illness when safer treatments cannot be used or are ineffective).
Category X	The risk of using the drug while pregnant obviously outweighs any potential benefit as studies in animals or humans have shown foetal abnormalities or there is evidence of foetal risk based on personal experience. Women who are pregnant or who might become pregnant should not take the drugs.

- **Age:**

Women are delaying having children all around the world for various reasons better contraception, a longer life expectancy, more education, or other financial or career objectives. Over-35-year-old pregnant women are regarded as being of advanced age and are more likely to experience problems childbirth and during pregnancy. It is commonly accepted that women over 35 have a higher risk of pregnancy problems.(24) The majority of age-related risk variables, however, only have a tenuous connection to age due to their correlation with age-dependent confounders such diabetes, hypertension, high parity, uterine myomas, and a history of infertility. Among them, hypertension and diabetes will be treated individually because they have significant effects on pregnancy in addition to having a high prevalence in the ageing population.(23, 25)

The outcome of pregnancy and its relationship to maternal age differs between women who conceive naturally and those who do so through assisted reproductive technology. Because assisted reproductive technology users tend to be older women >35 years, they are more likely to experience spontaneous abortion, ectopic pregnancy, placenta previa, pre-gestational diabetes, eclampsia, pregnancy-induced hypertension, Caesarean section, and induction of labour.(26) With rising maternal age, prenatal, neonatal, and stillbirth mortality rates also rise. Some of these obstetrical complications seem to be caused solely by getting older, while others are thought to be caused by coexisting factors like multiple pregnancies, higher parity, and underlying chronic medical conditions (such as diabetes mellitus, hypertension, and other chronic diseases) that are more common as people get older. Older women have a greater rate of spontaneous abortions, which increases the risk of some non-chromosomal birth abnormalities. (27)

It has been found that these foetal losses increase with maternal age and often occur between 6 and 14 weeks of gestation. Most spontaneous abortions in older women are caused by chromosomally defective embryos, primarily autosomal trisomies. Maternal age >35 years is linked to a 4- to 8-fold increased risk of ectopic pregnancy compared to younger women.(28)

- **Smoking, alcoholism and drugs consumption:**

One of the most critical and modifiable risk factors linked to poor prenatal outcomes is smoking during pregnancy. Smoking increases the risk of miscarriage, stunted growth of the foetus, low birth weight, preterm delivery, preeclampsia, placental complications, impaired infant lung function, respiratory illness, cancer, stunted growth, and the emergence of behavioural issues. Smoking is thought to be the cause of 15% of premature deliveries, 20% to 30% of low birth weight newborns, and a 150% increase in overall prenatal mortality.(29)

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The psychiatric conditions that include generalized anxiety disorder, bipolar disorder, oppositional disorder, substance misuse or dependency, and attention deficit hyperactivity disorder may all be associated with maternal prenatal smoking.(30) An increased risk of preterm delivery, miscarriage, or severe physical defects is associated with cannabis usage during pregnancy. However, it has been noted in numerous studies that babies born to moms who used cannabis six or more times per week had gestational ages that were reduced by about one week.(31) According to the findings of several studies, there may be a dose-response association between cannabis use during pregnancy and birth weight, with higher usage being notably linked to lower birth weight. According to a prior study, cannabis usage during pregnancy substantially predicted birth outcomes that were unfavorable, such as preterm birth, low birth weight, small size for gestational age, and admission to the neonatal critical care unit. These impacts were unrelated to the mother's sociodemographic traits, her use of alcohol, cigarettes, or other illegal drugs.(32)

It has been commonly held that maternal smoking during pregnancy increases the chance of LBW. Birth weight decreases in response to the use of cigarettes, and children of smokers are 150–250 grams–lighter at birth than children of nonsmokers.(33)

Both alcohol and cigarette use during pregnancy have been linked to a range of negative consequences on the development of the child's brain and behavior. As early as the 19th century, alcohol's teratogenic potential was firmly acknowledged. Even an infant's risk of developing acute myeloid leukemia has been drastically increased by a mother's alcohol use during pregnancy.(34)

- **Overweight, Obesity and Neonatal Health:**

A number of health hazards for the foetus or newborn are also linked to maternal obesity and overweight. Stillbirth, foetal discomfort, babies who are too big for their gestational age (called macrosomia), neonatal death, and congenital abnormalities are all complications. Large birth size is linked to both delivery problems, such as an increased risk of caesarean or medically assisted vaginal delivery, and related dangers, including foetal distress and harm.(35) Even while women without gestational diabetes frequently have large children, it appears that maternal obesity and overweight are linked to high birth weight (36).

Additionally connected to congenital anomalies, such as heart problems, skeletal malformations, and neurological diseases like spina bifida, are maternal overweight and obesity during and throughout pregnancy. Additionally, newborn skinfold thickness is higher in children born to obese moms, indicating that the newborn's increased weight is the result of a larger fat mass(37). Macrosomia increases the risk of perinatal death, shoulder dystocia, birth damage, and low Apgar scores. Macrosomic infants born by caesarean section experience fewer birth traumas, but the perinatal mortality rate is unaffected.(38)

4. Conclusion:

Women must be aware of hazards related to gestation and their habits, as well as the medical staff who are treating them during gestation, in order to improve women's health and reduce risks. Smoking, drinking alcohol, and caffeine use are among the worst lifestyle choices for mothers can ultimately affect growth of foetus and gives adverse delivery outcomes. Numerous therapies, like as dietary changes, meditations, weight loss, and increased physical exercise, seem to be successful in reducing these risks. Smoking increases the risk of miscarriage, stunted growth of the foetus, low birth weight, preterm delivery, preeclampsia, placental complications, impaired infant lung function, respiratory illness, cancer, stunted growth, and the emergence of behavioral issues. It is evident that several obstetric issues are linked to a higher risk of long-term maternal morbidity also. Maternal age is also seen as a modifiable risk factor for unfavorable pregnancy outcomes like neonatal death, and congenital abnormalities are all complications

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