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Review Article

Women with a history of congenital anomaly: preparation for next pregnancy

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ABSTRACT

Congenital diseases are damaging to the fetus and have an influence on the length of pregnancy. Some congenital problems can still be fixed after birth, however the costs are significant. Prophylaxis is strongly advocated to reduce the risk of congenital abnormalities during preconception. The incidence of congenital anomalies in the first pregnancy is associated with a 2.5-fold increased risk of recurrence in future pregnancies. The likelihood of recurrence is more than 24 times larger for the same type of aberration, but just 1.4 times for separate anomalies. The MTHFR-folate gene polymorphism has been related to an increased frequency of neural tube anomalies. Infectious diseases and environmental teratogens have an effect on genetic or epigenetic factors. Environmental elements that are repeated such maternal diabetes, obesity, and nutritional shortages seem to increase the incidence of fetal malformations. Alcohol, nicotine, or psychotropic drugs can all be teratogens. The promotion of contraceptive usage, optimization of weight and micronutrient status, prevention and management of infectious illnesses, birth spacing and the prevention of adolescent pregnancy, screening for and the management of chronic diseases are a few of these interventions. In conclusion, the probability of recurrence is quite high in the category of congenital defects, particularly for similar anomalies. Structural abnormalities can be decreased even further with proper planning and preparation, especially in high-risk populations. Moreover, preconception intervention have the potential to minimize congenital malformations.

Keywords: Congenital abnormalities, Nutrition, Teratogens, Chronic diseases, Preconception intervention

INTRODUCTION

Population-based register data on 18,605 singleton pregnancies with congenital abnormalities that occurred in 872,493 stillbirths, live births and termination of pregnancy for indications of fetal anomalies were obtained from the Northern congenital abnormally survey, North of England, England, for 1985-2010.[1] A history of congenital abnormalities in the first pregnancy is associated with a 2.5-fold increased risk of recurrence in subsequent pregnancies, although the overall prevalence of congenital abnormalities is lower in the second pregnancy when compared to the first pregnancy. The risk of recurrence was almost 24 times higher for similar types of congenital abnormalities, whereas for different anomalies the increase was much lower by 1.4 times. With similar anomalies, a significantly higher risk of recurrence was observed for the isolated congenital anomaly group by 20-fold, whereas for those that were syndromic by 34-fold.[1]

In different anomalies, the increased risk of recurrence was much lower for isolated anomalies, namely by 1.3 times and for those that were syndromic, by 1.7 times. This is the first study to estimate the absolute and relative recurrence risk of a major congenital anomaly in siblings using population-based data derived from a high-quality congenital anomaly registry, which uses consistent, internationally agreed, and meaningful definitions, classifications, and inclusion criteria clinically.[1]

LITERATURE RESEARCH

As a source of literature in the form of articles derived from searches with PubMed and Scopus links. The material for discussion is in the form of risk factors that may influence the incidence of congenital abnormalities, as well as possible therapies and management. In addition, the results are sought and displayed in the form of alternative preconception interventions so that the incidence of congenital abnormalities does not recur.

DISCUSION

Risk factors and prevalence

The lower prevalence of congenital anomalies in second pregnancies compared to first pregnancies suggests that nulliparity is associated with a higher risk of specific congenital anomalies and need improved health and preparation for pregnancy in subsequent pregnancies.[2] Causes of multiple congenital anomalies (e.g., single gene defects, chromosomal anomalies, syndromes specific) is known, and the risk of recurrence can be estimated according to the disorder. However, in approximately 70% of non-syndromic structural anomalies (eg cardiovascular anomalies, neural tube defects and orofacial clefts), the cause is unknown and is thought to consist of a multifactorial combination of genetic, environmental and gene-environment interactions. Several genetic variants that occur frequently or which are rare may be associated with the risk of non-syndromic congenital anomalies.[3]

Polymorphisms in the methyl tetra hydro folate reductase (MTHFR)-folate associated gene have been shown to increase the risk of neural tube defects.[3] The occurrence of a similar anomaly in a second pregnancy is estimated to have a 12.4-fold, 3.6-fold, and 32.3-fold increased risk of recurrence for nervous system anomalies, cardiovascular anomalies, and cleft lip. This is greater than the effects of most known environmental teratogens, suggesting a specific mechanism, such as genetic or epigenetic exposure. Repetitive environmental exposures such as maternal diabetes, obesity and micronutrient deficiencies tend to contribute to the risk of recurrence of congenital abnormalities.[4-6] The potential risk of recurrence is higher in younger women associated with various behavioral risk factors such as smoking, drug use, alcohol consumption and unplanned pregnancy.[7-9] In addition, being older than one partner is also associated with disability.[10]

Essential vitamins and minerals are dietary components required in small quantities to support almost all metabolic activities, including cell signaling, motility, proliferation, differentiation and apoptosis which regulate tissue growth, function and homeostasis.[11] These fundamental biological roles, in early life, allowing the fetus to develop and mature into a healthy neonate. Vitamins and minerals support every stage of the interaction between mother, placenta and fetus to enable a healthy pregnancy.[12] Most vitamins and minerals are referred to as 'micronutrients'. Some essential nutrients, such as calcium, magnesium and phosphorus are considered 'macro' minerals because they are required in larger amounts. The micronutrients that receive the most attention in pregnancy, and are commonly provided as supplements, include vitamins A, D, E, folate, B12, B6, and C, iron, zinc, iodine, copper and selenium.[13] Although the other B-complex vitamins (e.g., niacin, riboflavin and thiamin) are almost always included in dietary supplements, the role of metabolism in pregnancy is still not widely known but may influence placental health.[14] Consequently, to describe the contribution of B vitamins, focus is on folate and vitamin B12, which support its function in pregnancy, especially in the formation of maternal erythrocytes and the prevention of congenital abnormalities.[15-17]

Infections and teratogens

Congenital defects present a burden by causing significant financial, social and moral problems to families and communities and some are difficult to correct and rehabilitate. Exposure to teratogenic agents and intrauterine infection are two significant causes of nongenetic anomalies present at birth.[18,19] Teratogens such as drugs, adverse maternal clinical conditions, toxins and wastes are environmental factors that cause structural and functional malformations and also mortality embryo or fetus. Teratogens can cause significant congenital anomalies if exposed during the period of organogenesis, around 3-8 weeks of fetal life, which is the stage of tissue and organ formation. Morphological and functional disturbances may occur with exposure during the first 2 weeks of fetal period. Infections of the TORCH group (toxoplasmosis, others, rubella, cytomegalovirus, and herpes) are the most serious infectious diseases during pregnancy because of poor exposure rates and possible lesions in the fetus. Other infections that can cause congenital abnormalities besides TORCH are syphilis. In addition, parvovirus often causes anemia in the fetus and causes hydrops fetalis in the end.[19-21]

Teratogens that often cause disability have been mentioned above, especially alcohol, nicotine, and psychotropics. As well as environmental exposure to waste and pesticides in contaminated food.[22] In principle similar to infection, teratogens damage the structure and metabolism of the placenta and fetus.

Maternal clinical pathology

The increased incidence of congenital abnormalities in the offspring of women with diabetes and there is a difference for pregestational DM and GDM.[23] The relative risk of overall congenital abnormalities and congenital heart disease in the offspring of women with pregestational DM is higher than that of the offspring of women with GDM.[24] Screening for diabetes in pregnant women may allow for better glycemic control, and may enable earlier identification of offspring at risk for congenital abnormalities.[25] Other maternal diseases that are at high

risk of developing congenital abnormalities are autoimmune.[26]

Diseases that can clearly affect the fetus if not treated, for example as described above in pregestational DM, namely myocardial damage, autoimmune for example Lupus can cause abnormalities in fetal heart rhythm (heart impulse block), hypothyroid conditions can cause cretinism if the mother is not treated until she reaches euthyroid, psychiatric illness, thyroid disease, etc.[27]

The increased risk of these congenital abnormalities can be caused by the disease suffered by the mother or by the administration of drugs that contribute as teratogens.[28] Psychiatric illness or epilepsy is known to cause an increase in central nervous system abnormalities, because most of the drugs given are anti-folate, so folate doses must be considered no period when the patient is pregnant.[29]

Effects of severe iodine deficiency

Severe maternal dietary iodine deficiency in pregnancy has the potential to cause maternal and fetal hypothyroidism, with the consequence that hypothyroidism can lead to cretinism if no therapy is performed on the mother until she reaches euthyroid, Severe iodine deficiency is associated with poor obstetric period outcomes including spontaneous abortion, prematurity, and stillbirth.[30,31] Thyroid hormone plays an important role in neuronal migration, myelination, and synaptic transmission and plasticity.[32] Animal models have shown that mild and transient maternal hypo-thyroxinemia during pregnancy can impair neuron migration in the fetus, resulting in ectopic neurons in different cortical layers including the subcortical white matter and hippocampus.[33] Iodine deficiency is therefore associated with adverse fetal effects including congenital anomalies, decreased intelligence, and neurological cretinism (which includes spasticity, deaf mutism, and mental deficiency).[34]

Preconception interventions

Reproductive health and pregnancy outcomes may be improved if reproductive risk assessments are assessed from the preconception period.[35] Preconception treatments may include biomedical, behavioral and social interventions to women and partners prior to conception to address health problems. Behavior can be corrected so that it can correct health problems, individual or environmental risk factors that can contribute to the death and morbidity of the mother or fetus. The main goal is to improve the output of a healthy mother and fetus.[36] Preconception care includes the period before the first pregnancy occurs, or the distance between the two pregnancies. The preconception period provides an opportunity to intervene early to optimize the health of the future mother (and father) as well as to prevent harmful exposure that can affect the developing fetus. These interventions include spacing between births and preventing teenage pregnancy, promoting contraceptive use, optimizing body weight and micronutrient status, preventing and managing infectious diseases, and screening for and managing chronic disease conditions. [37]

Through preconception treatment and counseling, qualified couples will recognize, and implement actions to improve preconception health. In the end, it is expected to have a significant impact on improving the health status of mothers and fathers. Pre-pregnancy mother's weight is an important factor in the preconception period, when underweight contributes to a 32% higher risk of premature birth, and obesity conditions increase the risk of preeclampsia and diabetes. Women who are overweight increase to the possibility of undergoing a cesarean delivery, have a higher chance of becoming a neural tube defect or congenital heart defect. Among nutrition-specific interventions, preconception folic acid supplementation has evidence it can prevent 69% of recurrent neural tube defects. Multiple micronutrient supplementation shows hope for reducing occurrence of congenital anomalies and the risk of preeclampsia.

Preconception behavioral interventions significantly decreased reinfection or new sexually transmitted infection rates by 35% (95% CI: 20-47%). Furthermore, condom use has been shown to be an effective way to prevent HIV (85% protection in prospective studies) through sexual intercourse. Preconception vaccination against tetanus prevented a large number of neonatal deaths when compared to placebo in women who received more than 1 dose of the vaccine (OR 0.28; 95% CI: 0.15-0.52); (OR 0.02; 95% CI: 0.00-0.28) respectively.[38]

The mother's preconception caffeine intake of > 300 mg/d significantly increased the risk of subsequent fetal loss by 31% (95% CI: 8-58%). On the other hand, the consumption of preconception alcohol led to an increase in the risk of spontaneous abortion by 30% (RR 1.30; 95% CI: 0.85-1.97). Preconception counseling about the dangers of alcohol can significantly reduce alcohol consumption during the first trimester (OR 1.79; 95% CI: 1.08-2.97). Smoking periconception is associated with an almost 3-fold increased risk of congenital heart defects (OR 2.80; 95% CI 1.76-4.47). Preconception environmental in female workers exposed to radiation before conception showed an increased impact in the risk of fetal death. [39]

The treatment of diabetes in preconception mothers was a significant intervention to reduce the occurrence of congenital abnormalities by 70% (95% Confidence Interval (CI): 59-78%) and perinatal mortality by 69% (95% CI: 47-81%). Therapy for groups of mothers with chronic disorders and conducting therapy will improve the better discharge of the mother and fetus. Preconception management of women with epilepsy and phenylketonuria is very important and can optimize the outcome of pregnancy, fetus and neonatal if given before conception.

Changes in antiepileptic drug therapy should be carried out at least 6 months before the planned conception.[40]

CONCLUSION

In conclusion, the relative risk of recurrence is very high for different groups and subtypes of congenital abnormalities, especially for similar anomalies with unidentified genetic factors. Structural anomalies, such as neural tube defects, can be further reduced with the help of planning and preparation before pregnancy, especially in high-risk groups such as women with diabetes, thyroid disease, and autoimmune. In addition, pre-conception interventions have the potential to reduce congenital defects, especially the treatment of clinical abnormalities in the mother and periconceptional folate and iodine supplementation. A review of the types of drugs given to treat diseases in the mother as well as advice on types of diet and nutrition during pregnancy preparation, tends to reduce the risk of adverse pregnancy outcomes including congenital abnormalities.

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