



Genetic Polymorphisms Implicated in Major Pregnancy Complications: a Review

Georgios Dryllis, Panagiota Liakou, Marianna Politou

Hematology Laboratory-Blood Bank, Aretaieion Hospital, National and Kapodistrian University of Athens, Athens, Greece

Corresponding author: Marianna Politou, Hematology Laboratory-Blood Bank, Aretaieion Hospital, Medical School, National and Kapodistrian University of Athens, 76 Vasilissis Sofias Ave., 11528, Athens, Greece; E-mail: mariannapolitou@gmail.com; Tel.: +30 210-7286238

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Abstract

Pregnancy short- or long-term complications may involve the mother's health, the fetus's health, or both. A systematic literature review was performed, including studies up to October 2018 from Medline (PubMed), Science Direct, Web of Science and Google Scholar. The following inclusion criteria were applied: studies published until 2018 concerning the genetic background of pregnancy complications such as high blood pressure, gestational diabetes, preeclampsia, pregnancy loss, endometrial death, placental abruption, premature labor, and intrauterine growth retardation which may render pregnancy a high risk condition.

We identified 164 articles that met the inclusion criteria and reviewed and analyzed them. The results so far are contradictory and the pathogenicity of these pregnancy complications remains unclear. For most of the polymorphisms studied so far, data refer to small studies size but research is on-going.

The identification of genetic polymorphisms with strong correlations with certain pregnancy complications could provide us with useful tools which could be incorporated in diagnostic algorithms that could facilitate early detection and treatment of major pregnancy complications.

Keywords

genetic polymorphisms, gestational diabetes, intrauterine growth retardation, obstetric complications, placental abruption, preeclampsia, premature labor

INTRODUCTION

Pregnancy is a normal condition with a desirable outcome in most of the cases. Sometimes though, complications may occur even in women who were healthy before getting pregnant which may involve the mother's health, the fetus' health, or both.¹

Most common of them are: high blood pressure, gestational diabetes, infections, preeclampsia, pregnancy loss, endometrial death, placental abruption, premature labor, and intrauterine growth retardation. All these complications may render pregnancy a high risk condition.²

Over the past years many genetic polymorphisms that affect pregnancy outcome, have been described. Their im-

plication in the pathogenicity of high risk pregnancies remains unclear. We reviewed genetic predisposition in main obstetric complications such as: intrauterine growth retardation, placental abruption, premature labor, gestational diabetes and preeclampsia.

MATERIALS AND METHODS

A literature search was carried out including studies up to October 2018, in the following databases: Medline (PubMed), Science Direct, Web of Science, Google Scholar.

All articles were initially screened for title and abstract and full texts of eligible articles were subsequently selected.

Systematic reviews, uncontrolled prospective, retrospective and experimental studies were included for each specific subject (n=164).

The following inclusion criteria were applied: studies concerning pregnancy complications such as high blood pressure, gestational diabetes, preeclampsia, pregnancy loss, endometrial death, placental abruption, premature labor, and intrauterine growth retardation.

All studies concerning the genetic background of the above mentioned pregnancy complications were included.

RESULTS

Delay of intrauterine growth

Intrauterine growth retardation (IUGR) is a common but complex challenge in obstetrics. The American College of Obstetricians and Gynecologists defines IUGR as any embryo with a weight below the 10th percentile for a specific age of gestation. Research into the understanding and prevention of IUGR is of great importance for public health, as the limitation of intrauterine development is related not only to fetal mortality and neonatal morbidity, but also to adverse long-term consequences, such as cardiovascular diseases.³

Many factors have been associated with an increased risk of IUGR. For example, environmental agents such as smoking, alcohol abuse and poor nutrition play a significant role in limiting the fetal development.

Genetic predisposition to the occurrence of IUGR also exists and genetic mutations that result in a hypercoagulable phenotype are the most common.³ Inherited thrombophilic mutations have been assumed to increase the probability of IUGR due to an increased risk of thrombosis of the placenta. This has been considered to adversely affect maternal blood flow and to lead to poor fetal development. Regarding the most common causes of inherited thrombophilia, Facco F et al.³ found out a significant correlation only between Factor V Leiden and IUGR, while MTHFR C677T and PT G20210A mutations do not seem to correlate significantly with IUGR.

Haider S and Knöfler M⁴ confirmed that pre-inflammatory cytokines and their polymorphisms are also assumed to play an important role in the pathophysiology of IUGR, since 308G(A) mutation of the TNF- α gene has been involved in IUGR.

Proper cytokine function plays a key role in the process of trophoblast and placenta development. As a result, cytokine functional deregulation is likely to be involved in the occurrence of pregnancy complications. The correct expression of TNF- α has a beneficial role in the initial phase of pregnancy affecting the maturation of the placenta. Giannubilo SR and Tranquilli AL⁵ showed that the presence of TNF- α is important for the processes that take place in the placenta, such as the onset of inflammatory response,

stimulation of apoptosis, cell proliferation, differentiation and cell migration.

TNF- α reverses the development of trophoblast and its migration to the walls of the spiral arteries and disrupts the development of the placenta. Also, it is toxic to vascular endothelial cells.⁶ Additionally, TNF- α interferes with the anticoagulant mechanism and may cause thrombosis in the placental vessels. Therefore, it can directly contribute to the emergence of IUGR.⁷ The gene that encodes TNF- α is located in 6p 21.33 on chromosome 6, between the genes HLA-B and HLA-DR. It is a small gene compared to other cytokines (3 KB), and contains 3 introns and 4 exons, of which the last exon produces 80% of the final protein product.⁷ A past study⁸ showed that the mutation 308G(A) of the TNF- α gene is implicated in the etiology of IUGR.

The insulin growth factor 2 plays an important role in the development of the fetus, while it is much less active after birth. Studies suggest that it promotes cell growth and cell proliferation in many tissues. IGF2 is part of a group of genes that are found in the Short Strand (p) of chromosome 11. The IGF2 gene encodes insulin-growth factor 2, IGF2R gene encodes for the growth factor 2 receptor, while H19 is an untranslatable gene that lies approximately 100 Kb far from IGF2 and operates competitively to IGF2. Single nucleotide polymorphisms (SNPs) in IGF2, H19, IGF2R genes have been associated with birth weight. Specifically, SNPs in IGF2R (rs8191754, maternal genotype), in IGF2 (rs3741205, newborn genotype) and in the 5' area of H19 (rs2067051, rs2251375 and rs4929984) have been linked to the birth weight. In most tissues, only the paternal inherited copy of the IGF2 gene is active, while the maternal inherited one remains inactive (genomic imprinting).⁹

Polymorphisms in genes CCNL1 (cyclin L1), LEKR1 (leucine glutamate and lysine rich 1) and ADCY5 (adenylyl cyclase 5) also play a role in birth weight. The ADCY5 belongs to a family of enzymes, which are responsible for the composition of cAMP (cyclic adenosine monophosphate). Rs11708067 allele of ADCY5, is in linkage disequilibrium with the C allele of rs9883204, leading to weight reduction and it is associated with a higher risk of type 2 diabetes, higher fasting glucose and an incidence of insulin secretion. Fetal insulin is a basic embryonic growth factor, which explains the correlation of ADCY5 with birth weight.¹⁰

Fetal development is based on the effective supply of nutrients from the mother to the fetus through the placenta. This nutrient supply is influenced by a complex interdependence between environmental agents and genetics. The phenomenon of "gene imprinting" is extremely interesting – it is the case where only one allele, of maternal or paternal origin, is expressed. "Gene imprinting" is almost exclusively found in mammalian placenta.¹¹

This theory is explained by the assumption that gene expression of paternal origin promotes fetal development and ensures the inheritance of the paternal genome in future generations, while a recent study¹¹ showed that the expression of maternal genes restricts fetal development aiming at the survival of the mother so that reproduction process

can be repeated. Additionally, new genomic studies using chromosomal micro-array analysis (CMA) on amniotic fluid cells, showed that a 1.06-Mb duplication in 19q13.42 inherited from the healthy father and containing 34 genes including ZNF331 (a gene encoding a zinc-finger protein) is specifically imprinted (paternally expressed) in the placenta. This means that this genetic cluster is exclusively expressed from the paternal allele in the placenta. According to this finding, another study¹² has already confirmed that a duplication of the maternally imprinted ZNF331 gene could represent a new genetic cause of severe intrauterine growth retardation (IUGR).

PHLDA2 encodes the Pleckstrin homology-like domain, family A, member 2 protein, which shows the phenomenon of “gene imprinting” in one of the most extensively studied areas, the chromosomal area 11p 15.5. PHLDA 2 is expressed in many tissues, but is mainly expressed in the chorionic cytotrophoblast of the placenta during pregnancy and its expression is significantly increased in the placenta of the IUGR neonates.¹³

EDNRA (endothelin receptor type A) and PRKAA1 or known as AMPK α 1 (alpha-1 catalytic subunit of adenosine monophosphate activated protein kinase) genes play a role in the pathophysiology of residual embryonic growth associated with high altitude (>2500m). High altitude can be involved in the emergence of IUGR, as chronic hypoxia restricts fetal development, with a mechanism similar to hypertensive disorders of pregnancy.¹⁴

In particular, newborns which are born from women originated from the Andes and Tibet present half of the decrease in weight compared to women of European or Chinese origin living at the same altitude. This evidence indicates the existence of genetic factors affecting birth weight and the increased susceptibility to IUGR appearance. In clinical studies, genes involved in high-altitude adjustment have been identified in various populations.¹⁵ A significant correlation between birth weight and maternal SNPs near EDNRA and PRKAA1 gene has also been documented. The results of the studies suggest that polymorphisms in maternal genes lead to physiological reactions in pregnancy that contribute to the development of the embryo by providing genetic adjustment at high altitude.¹⁶

Placental abruption

Placental abruption is a life-threatening obstetric complication, affecting 1% of all pregnancies. The main pathophysiological mechanisms involved in placental abruption are uterine ischemia, oxidative stress and chronic hypoxia. Although placental abruption is a multifactorial disorder of complex origin. It tends to appear in women of the same family, indicating the existence of genetic predisposition, which is supported by studies, showing that the heredity of the placental detachment is approximately 16%.¹⁷

Circadian rhythm plays an important role in various aspects of female reproduction, including ovulation, fetal implantation and childbirth. Changes in maternal circadian

an rhythm, as is the case in shift work, have been associated with pregnancy complications, such as premature childbirth, delayed intrauterine growth and preeclampsia. There is evidence linking genetic polymorphisms of the circadian rhythm genes with placental detachment.¹⁸

Chunfang Q et al.¹⁹ showed that SNPs in circadian rhythm genes, such as BAMI1 (BMI1 Proto-Oncogene), PER1-2 (Period Circadian Protein Homolog 1 Protein), CRY1-2 (Cryptochrom Circadian Regulator 1-2), CLOCK (Clock Circadian Regulator), RORA (RAR-related orphan receptor alpha), RORB (RAR-related orphan receptor beta), BMAL1 (Brain and Muscle ARNT-Like 1), NPAS2 (Neuronal PAS Domain Protein 2), DEC1 (Deleted In Esophageal Cancer 1) have all been found to be related to placental detachment.

More recent studies¹⁷ have shown that SNPs known to regulate mitochondrial biogenesis (MB) like: CAMK2B (Calcium/Calmodulin Dependent Protein Kinase II Beta), NR1H3 (Nuclear Receptor Subfamily 1 Group H Member 3), PPARG (Peroxisome Proliferator Activated Receptor Gamma), PRKCA (Protein Kinase C Alpha), and THRB (Thyroid Hormone Receptor Beta) and oxidative phosphorylation (OP) like: COX5A (Cytochrome C Oxidase Subunit 5A) and NDUF (ubiquinone oxidoreductase core subunits) family of genes were also associated with significant risk for placental abruption ($p < 0.05$).

Premature labor

Premature labor (defined as childbirth before the completion of 37 weeks of gestation) affects over 15 million pregnancies each year throughout the world. It is the leading cause of death of newborns and children under the age of 5 (WHO 1977). The majority of preterm births (60%) occur in Africa and South Asia, but the problem also affects developed countries with a prevalence of around 6-7%. Among the developed countries USA shows the highest prevalence (10%).²⁰

In addition to the short-term direct effects of prematurity in the first month of the newborn, it also has many long-term consequences for the lives of infants, their families and the whole population, which makes it a serious public health concern.^{20,21}

Premature newborns are more prone to complications, such as hypoglycemia, jaundice, sepsis, pulmonary dysfunction, eye disorders, long-term neurological deficits. The frequent need for hospitalization is associated with tremendous emotional, but also financial burden.^{20,21}

Infants born prematurely are at greater risk of death during early childhood, but also at the age of 18-36 years due to cardiovascular, respiratory and endocrinal complications. Even premature newborns born at 34-36 weeks of gestation have a higher risk than the full-term neonates (37-42 weeks).^{17,20}

Depending on the severity, early births are classified into extremely premature (under 28 weeks), which account for about 5%, severe or very premature (28-31 weeks), which

make up about 15%, moderate premature (32-33 weeks), which are approximately 20%, while the majority (60-70%) are the mature early-born or last-month infants.²² From the whole number of early births, approximately 70% occur spontaneously due to the premature rupture of the hymen (PPROM-preterm premature rupture of membranes), while the remaining 30% are due to a decision of the obstetrician to induce premature childbirth due to adverse and worsening conditions for the fetus in the uterine environment.^{20,23}

Premature birth is a multifactorial syndrome and its exact cause remains unknown to up to 50% of the cases. Factors that have been extensively studied as possible risk factors for the onset of preterm birth include social, medical, environmental and genetic factors or infections.²⁴

There are many elements that support the involvement of genetic factors in the etiology of preterm birth. Often it occurs in members of the same family and women born prematurely, themselves have a higher risk of premature labor. Also, the risk of preterm delivery increases up to 80% in women whose sisters have experienced preterm birth.²⁵ Premature birth is a complex phenotype that is influenced by both the maternal and the embryonic genome. There have been several studies on SNPs (single nucleotide polymorphisms) and their connection to preterm labor although strong correlations with specific genetic polymorphisms have not been identified.²⁶

Six genetic sites that have been identified and associated with the duration of pregnancy are: EBF1, EEFSEC, AGTR2, WNT4, ADCY5, RAP2C.²⁵

EBF1 encodes the early B-cell factor 1 (early B-cell factor 1), which is necessary for the development of normal B-cells and there are studies that correlate it with the regulation of blood pressure, the thickening of the middle-inner tunic of carotids, hypospadias and risk of metabolic syndrome.²⁷ It remains to be determined whether its effect during pregnancy is due to mechanisms related to pregnancy itself or to general cardiovascular and metabolic characteristics that affect pregnancy. Singh A et al.²⁸ confirmed that this genetic site also affects the birth weight, probably indirectly through to its effect on gestation.

The EEFSEC gene encodes the selenocysteine tRNA-specific eukaryotic elongation factor and participates in the integration of selenocysteine into selenoproteins. These proteins regulate the cellular homeostasis via maintaining the acid-base balance and the antioxidants defensive mechanisms, as well as the regulation of the inflammatory response. These physiological functions have been linked to the birthing process and the appearance of prematurity.²⁸ The study of selenocysteine pathway²⁹ may be beneficial for investigators who try to correlate reduced selenium with preterm delivery. Malawi, the country with the world's highest risk of premature labors, has a high incidence of selenium deficiency.³⁰

It has also been suggested that AGTR2, which encodes the angiotensin II receptor type 2, plays a critical role in regulating uterine circulation and displays polymorphisms

that contribute to preeclampsia risk.³¹

Mutations of WNT4 which encodes the wingless-type MMTV integration site family member 4 have been found in women with Muller's pore abnormalities, primary amenorrhea and hyperandrogenemia.³² WNT4's rs3820282 polymorphism-variant is associated with an increase in pregnancy duration and is protective against preterm delivery. Additionally, the same genetic area is associated with endometriosis and ovarian cancer, conditions also due to hormonal imbalance. The population incidence of endometriosis in Asian, European and African women corresponds to the frequencies of rs3820282 T allele.³³

ADCY5 Coding for Type 5 adenylate cyclase and RAP2C encoding a family member of RAS oncogenes have been studied in relation to pregnancy complications. Mononucleotide polymorphisms (SNPs) in ADCY5 have been associated with birth weight and type 2 diabetes, but not with gestation. The polymorphism rs2747022 in the RAP2C region (in the gene FRMD7) has been associated with preterm birth in studies in Denmark and Norway.³³

Newer genome wide association studies²⁷, showed that variants at the EBF1, EEFSEC, AGTR2, WNT4, ADCY5, and RAP2C genetic loci were associated with gestational duration and variants at the EBF1, EEFSEC, and AGTR2 genetic loci were associated with preterm birth.

Efforts to address preterm labor (<37 weeks of gestation) and its consequences as a major public health problem (increased mortality and disability in children under 5 years of age) include the administration of 17-alpha hydroxyprogesterone caproate (17 OP-C), which has reduced the onset of preterm birth to 33% in women with a previous history of preterm delivery. The plasma concentration of 17-alpha hydroxyprogesterone caproate (17 OHP-C) varies among pregnant women and has been found- from newer studies³⁴ - that in females with a concentration in the lower quadrant the preterm birth rate was 40% versus 25% in women with higher concentrations.

Progesterone is a hormone with a decisive role in implantation and preservation of the cyst. Progesterone replacement therapy with vaginal and intramuscular drugs helps to reduce the rate of preterm birth. The role of maternal or embryonic polymorphisms of the progesterone receptor gene on prematurity remains controversial.³⁵

Some studies report a possible correlation of progesterone receptor gene polymorphisms with premature childbirth³⁵ while, other studies³¹ have shown that polymorphisms in the progesterone receptor gene, rs578029, rs471767, rs666553, rs503362, rs500760 are not related to premature birth and they don't have an effect on the efficacy of 17 OHP-C.

Plasma concentration of progesterone is an important factor determining its efficacy, but the reasons leading to a large variation in its concentration have not been fully clarified. Although 17 OHP-C is mainly metabolised by enzymes CYP3A4 and CYP3A5, polymorphisms in enzymes CYP3A4 and CYP3A5 cannot explain the wide range of 17 OHP-C plasma concentration.^{35,36} Factors such as the

maternal weight, drug interactions, in particular drugs competing with the metabolism of 17 OHP-C, such as omeprazole, nelfinavir, fluconazole and sertraline seem to be determinants of progesterone plasma concentration.^{37,38}

Oxytocin and its receptor (OXTR) is another important hormonal system involved in childbirth. Oxytocin is produced in the hypothalamus and is secreted from the pituitary gland. It causes contractions of the myometrium and plays a dominant role in the development of childbirth. The oxytocin receptor gene is expressed in the myometrium, in the endometrial tissue, but also in other tissues of the body including the nervous system. Several studies have been conducted in order to investigate the correlation between polymorphisms in the OXTR gene and preterm delivery.³⁶

Two SNPs of OXTR (rs4686302, rs237902) were found to be related to preterm labor. Also in a study of four polymorphisms of OXTR (rs53576, rs2254298, rs237911, rs2228485), although no correlation was revealed for each of the four individual polymorphisms with premature birth, however the combination of simplistic of the allele rs2228485 C, rs2254298 A, rs237911 G was found to be strongly related to preterm labor.³⁹⁻⁴¹

Relaxine is an important hormone produced in the macular luteum of the ovary, in the breast and during pregnancy in the placenta and dermis. During the first trimester of pregnancy the levels increase and the maximum is achieved in the 14 weeks of the first trimester and during childbirth. Relaxine mediates in the hemodynamic changes occurring during pregnancy, such as increasing cardiac output, increasing renal blood flow, while relaxing the pelvic ligaments and softening the pubic symphysis. Increased expression of intrauterine relaxine occurs in women with premature rupture of the hymen. The risk of preterm delivery is high in women who have in homozygosity a rare allele (rs10115467 and rs4742076) in the Relaxine 2 gene (RLN2).⁴²

Polymorphisms in other endocrine system's genes have also been associated with premature childbirth. SNPs in the receptor gene of follicle stimulating hormone (follicle stimulating hormone receptor, FSHR) have been associated with premature childbirth.⁴³

Ryckman KK et al.⁴⁴ confirmed that polymorphism in the prostaglandin receptor gene E (PTGER3-prostaglandin E receptor 3, rs977214) appears to have a protective action against preterm delivery. PTGER3 is a gene associated with the inflammatory response and plays a role in the onset of childbirth. Grisaru-Granovsky S et al.⁴⁵ showed that polymorphisms in the prostaglandin receptor gene D (PTGDR) also increase the risk of preterm delivery. Polymorphisms in the gene IGF1R-type 1 insulin-like growth factor receptor in the fetus and IGFBP3-insulin-like growth factor binding protein 3 in the mother also increase the risk of preterm delivery.⁴⁶

Pre-eclampsia and HELLP syndrome

Chromosomes 2q, 5q, 13q have been associated with pre-

eclampsia and chromosome 12q with HELLP syndrome. There is evidence of correlation with pre-eclampsia of ERAP1 and ERAP2 (endoplasmic reticulum aminopeptidases) genes. ERAP 1 and 2 genes encode endoplasmic network enzymes that play a role in regulating blood pressure through the renin-angiotensin system, but also play a role in the immune response, particularly with pro-inflammatory activity. Immune regulation, inflammatory response, and vascular disorders are clearly implicated in the pathophysiology of preeclampsia. Correlation with pre-eclampsia has been found for the ACVR2A (ACE receptor type 2) gene encoding the Type 2 activin A receptor. Activin A stimulates the proliferation and differentiation of trophoblast and appears to play a key role in implantation, and also contributes to placental hormone genesis. Placenta is the primary source of activin A in motherhood. Increased levels of activin A have been found in women with preeclampsia. Disruption of ACVR2A gene expression may affect the concentration of activin with effects on the implantation and outcome of pregnancy. Correlation with preeclampsia has been found for the COL1A1 genes (collagen type1 alpha1) and PLAUR (plasminogen activator urokinase receptor).⁴⁷

In conclusion, the genes that are correlated with pre-eclampsia early-onset and HELLP syndrome are the following: STOX1: Storkhead box-1, Syncytin envelope decrease, MBL: Mannose Binding Lectin 2 (Maternal heterozygote at codon 54 of MBL B allele protects against pre-eclampsia and HELLP syndrome), V Leiden factor (increased risk of both pre-eclampsia and HELLP syndrome), MTHFR C677T: methylene tetrahydrofolate reductase (development of HELLP syndrome), Factor II G20210A (development of pre-eclampsia), VEGF TT-460: vascular endothelial growth factor (increased risk of HELLP syndrome), ACE I/I/D: angiotensin-converting enzyme, Bcll GR-gene polymorphism (development of HELLP syndrome), EPHX: Epoxide hydrolase 1 (development of pre-eclampsia), NFRSF6-670: Fas cell surface death receptor (homozygous people for the AG or GG genotype are more likely to develop HELLP syndrome than homozygous for the wild-type Fas receptor-TNFRSF6-670A / A), TLR4: Toll Like Receptor 4 (early onset of pre-eclampsia and HELLP syndrome) and finally LEPR: Leptin Receptor (increased risk of pre-eclampsia).

Gestational diabetes mellitus (GDM)

Gestational diabetes mellitus (GDM) and its associated complications have significant prevalence during pregnancy. Silverman BL et al.⁴⁸ showed that diabetes during pregnancy is not only associated with the later risk of diabetes in mothers but also with metabolic changes that may lead to the development of diabetes in their offspring.

Also, another study⁴⁹ noticed that it is quite remarkable that women with a diabetic sibling had an 8.4-fold higher risk of GDM than women with no diabetic siblings. Furthermore, genetic studies of type 2 diabetes mellitus have

concluded that it is a multigenic disease in which common variants in multiple genes interact with environmental factors to cause the disease.⁵⁰

The possible contribution of genetic predisposition for Gestational Diabetes Mellitus has been analyzed. Genes that have been implicated are: GLUT1 (Glucose transporter 1), TCF7L2 (Transcription factor 7-like 2), PPARGC (Peroxisome proliferative activated receptor gamma) and PPARG-C1A (Peroxisome proliferative activated receptor-gamma coactivator 1-alpha). These genes have produced similar findings when studied in different populations⁵¹; nevertheless, additional studies are needed.

On the other hand, genetic associations have been found between GDM and some other genes like: IGF2 (insulin-like growth factor 2), INS (insulin), IRS1 (insulin receptor substrate 1), ADRB3 (β -3 adrenergic receptor), and INSR (insulin receptor). Though, these associations were across different populations due to several factors like: differences in genetic background, differences in environment and lifestyle factors, and differences in the selection criteria for subjects in each of these specific studies.⁵¹

Association with type 2 diabetes mellitus, as well as on their physiological role in the pathogenesis of diabetes, have variants within genes like: CAPN10 (Calpain 10), MBL2 (Mannose-binding lectin (protein C) 2), KCNJ11 (β -Cell KATP channel subfamily J, member 11, ND1: Mitochondrially encoded NADH dehydrogenase 1), TCF7L2 (Transcription factor 7-like 2), ADIPOQ (Adiponectin), and PAI-1 (Plasminogen activator inhibitor type 1). These genes are considered the most promising markers for genetic predisposition in GDM as well, although large sample studies in different populations are needed in order to lead to specific conclusions about their genetic coherence with diabetes in pregnancy.⁵¹

CONCLUSION

The genetic background of pregnancy complications is the subject of several studies investigating genetic polymorphisms affecting pregnancy outcome. Pregnancy has many short and long-term effects on the woman and the fetus; that is the reason why a better prenatal care is mandatory in order to prevent any adverse pregnancy outcomes. The genetic basis of pregnancy complications can also contribute to achieving this medical goal. For most of the polymorphisms studied so far, data refer to small studies size but research is on-going. The identification of genetic polymorphisms with strong correlations with certain pregnancy complications could provide us useful tools which could be incorporated in diagnostic algorithms that could facilitate early detection and treatment of major pregnancy complications.

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Conflict of Interest

Authors have no conflict of interest to declare.

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Генетические полиморфизмы, связанные с серьёзными осложнениями во время беременности - обзор

Георгиос Дрилис, Панайота Лиаку, Марианна Политу

Гематологическая лаборатория - банк крови, Больница Аретаеион, Афинский национальный университет имени Каподистрии, Афины, Греция

Адрес для корреспонденции: Марианна Политу, Гематологическая лаборатория - банк крови, Больница Аретаеион, Афинский национальный университет имени Каподистрии, бул. „Василис Софиас“ 76, 11528 Афины, Греция E-mail: mariannapolitou@gmail.com; Тел.: +30 210-7286238

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Абстракт

Краткосрочные или долгосрочные осложнения беременности могут повлиять на здоровье матери, плода или обоих. Был проведён систематический обзор литературы, который включал исследования с октября 2018 года из Medline (PubMed), Science Direct, Web of Science и Google Scholar. Применялись следующие критерии включения: опубликованные до 2018 года исследования, касающиеся генетического происхождения осложнений беременности, таких как высокое кровяное давление, гестационный диабет, преэклампсия, потеря плода, смерть от рака эндометрии, отслойка плаценты, преждевременные роды и задержка внутриутробного развития, которые могут причислить беременность к состояниям высокого риска.

Мы нашли 164 статьи, которые соответствовали критериям включения, рассмотрели и проанализировали их. Результаты противоречивы, и патогенетическая природа этих осложнений беременности остается неясной. В большинстве изученных полиморфизмов данные относятся к небольшим исследованиям, но исследования продолжаются.

Выявление генетических полиморфизмов с сильной корреляцией с некоторыми осложнениями беременности может обеспечить нас соответствующими инструментами для внедрения их в диагностические алгоритмы, которые могут помочь в раннем выявлении и лечении серьёзных осложнений беременности.

Ключевые слова

генетические полиморфизмы, гестационный диабет, задержка внутриутробного развития, осложнения в акушерстве и гинекологии, отслойка плаценты, преэклампсия, преждевременные роды
