Review Article

Neurology of Preeclampsia and Related Diseases: A Literary Review

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Abstract

Preeclampsia is a pregnancy complication characterized by the presence of hypertension and renal dysfunction. Preeclampsia leads to heterogeneous disorders, which ultimately has an adverse effect on the health of the mother and fetus. The most common cause of illness and death among mothers and perinatals, preeclampsia affects 7–18% of pregnancies. Furthermore, problems resulting from preeclampsia accounted for almost one-third of all maternal fatalities connected to pregnancy. Preeclampsia's elevated arterial pressure can cause placental abruption, miscarriage, early delivery, low birth weight, and even the mother's or fetus's death. The relative risk of fetal death in early Preeclampsia is 5.8%, in late Preeclampsia - 2.0%. After delivery, patients with Preeclampsia noted hypertension (39% for 3 months), proteinuria (20% for a year). At the same time, there is an increased risk of diabetes mellitus. The most severe clinical variants of the course of Preeclampsia are associated with maladaptation of the immune system and impaired placentation. They are characterized by such manifestations as early activation of the sympathoadrenal system, an increase in the level of markers of endothelial dysfunction, insufficient invasion of the trophoblast and incomplete transformation of the spiral uterine arteries. This article examines the scientific information about Preeclampsia in order to clarify the facts.

Keywords: Preeclampsia, Neuroacoustic disorder, Headache, Acute cerebral circulation disorder, Maternal mortality

Introduction

Currently, a classification of gestational hypertension and Preeclampsia has been developed depending on the duration of pregnancy at the time of diagnosis. The period of 34 weeks is most often considered as a reference period. Early Preeclampsia is associated with a higher incidence of neonatal morbidity and mortality; late Preeclampsia is 4 times more common, leading to premature birth, maternal mortality and severe morbidity.

The pathogenesis of Preeclampsia is not obvious, prediction, prevention and treatment are difficult. It is believed that the nature of the diseases differs in cases of early and late Preeclampsia [1].

Because of the body's damage from systemic oxidants, preeclampsia is considered a significant cause of the development of chronic arterial hypertension, diabetes mellitus, severe renal failure, and cardiomyopathy.

Over thirty well-reasoned etiopathogenetic ideas explaining the disease's development have been put forth by obstetrics specialists, the most prominent of which are:

- Hereditary
- Immune system
- Placental
- Cortico-visceral [1].

Preeclampsia is responsible for approximately 14 % of all maternal deaths worldwide **(Figure 1)** [2]. Unfortunately, neurological complications in pregnant women, especially in the postpartum period, are often ignored. It is believed that 50% of the maternal deaths due to preeclampsia could have been avoided if the conditionwas detected, diagnosed, and treated earlier [3].

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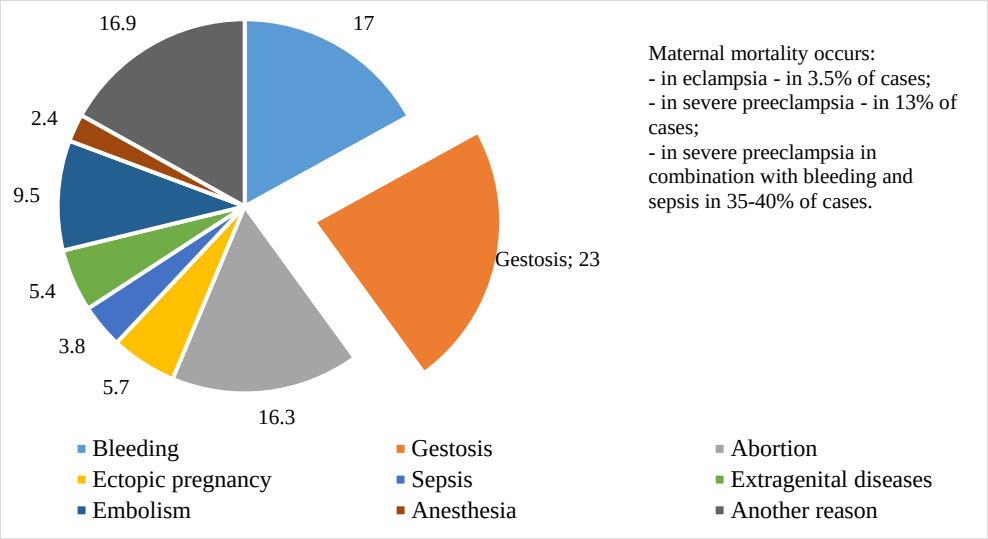

Figure 1. Statistics of preeclampsia as a cause of maternal mortality in Russia

Autopsy data and a series of cases indicate that neurological complications are the direct cause of 30 to 70 percent of deaths among women suffering from preeclampsia (high blood pressure during pregnancy). These complications are most often caused by intracerebral hemorrhage (cerebral hemorrhage) or cerebral edema. Neurologists are often asked for help in the diagnostic examination of women who are suspected of having "excluded preeclampsia. The diagnosis affects delivery timing, technique, and blood pressure regulation. Because of this, it is critical that neurologists possess a thorough grasp of the etiology, clinical manifestation, and neurological implications of preeclampsia and associated disorders [4]. In this review, we discuss definitions, epidemiology, complex pathophysiology, and recent translational and clinical data on preeclampsia and related conditions; the relationship between preeclampsia and migraine; and overlapping features between preeclampsia, reversible cerebral vasoconstriction syndrome (RCVS) and posterior reversible encephalopathy syndrome (PRES).

The essential function of trophoblast cells is to feed, remove waste from, and deliver oxygen to the developing embryo. Week 10 sees the establishment of a vascular bed with lower intravascular pressure as a result of trophoblast invasion, causing the muscle layer of the spiral arteries to undergo apoptosis. Right now, it's thought that uterine (decidual) natural killers (uNK), a unique subset of lymphocytes, interact with trophoblast cells.

Additionally, a predisposition for hypercoagulation is developed as a result of various physiological and physical changes that are associated with pregnancy. The lower extremities experience a reduction in blood flow due to the stagnation of blood in the pelvic veins brought on by pregnancy. The placenta's physiological and hormonal alterations, in addition to a variety of other physical aspects of pregnancy, are important to the pathogenesis of the pregnancy's numerous unfavorable consequences.

With its low-resistance arteries, the placenta is an organ with a high vascularization density. Reduced fetal development rates, functional inadequacy of the placenta, and other unfavorable prenatal problems can result from thrombosis in the placental vascular network.

Since maternal blood passes through the interstitial space after implantation, placental circulation changes to a procoagulant state, which appears to balance the risk of bleeding. Trophoblasts, which are endothelial cells, are less able to lyse fibrin than other cells that line the spiral arteries of the uterus and eventually migrate into the placenta. The reason for this is thought to be large concentrations of plasminogen activator inhibitors (PAI-1 and PAI-2), which help to build fibrin at the placental location and prevent the anticoagulant tissue plasminogen activator from acting. Additionally, phosphatidylserine and tissue factor are secreted in significant quantities by trophoblasts, which further tips the scales in favor of increased coagulation potential [5].

Materials and Methods

A search was conducted for scientific articles in various scientometric databases. The following keywords were used: "preeclampsia", "neuroacoushery", "headache", "acute cerebral circulation disorder", "maternal mortality". Such resources as PubMed, CyberLeninka, Hindawi, Google Scholar were used as sources of information, while access to the materials of interest was not limited. In addition, a manual literature search was also conducted.

Results and Discussion

Preeclampsia is a complex syndrome that has been defined in different ways over time. However, headaches and other neurological symptoms have long been recognized as signs of high risk and may indicate the development of eclamptic seizures. Hippocrates in 400 BC noted that "drowsiness and

headaches of varying degrees occur during pregnancy. In such cases, seizures can also occur simultaneously"[6]. This is a reasonable description of eclampsia, which occasionally has prodromal neurological symptoms. For instance, Dr. J. Robert Jones of Dublin Hospital described the prodromal phase in 1843 and included the following symptoms: "headache, heaviness or dizziness, tinnitus, or temporary loss of vision." These warning signs existed before birth in the majority of instances, if not all of them. My contention is that if they had been given the appropriate care at that point, further seizures may have been prevented" [7]. 383 pregnant women with eclampsia (preterm seizures) reported headaches before their seizures in 1994; 19% had visual impairments [8]. These findings were made by researchers Douglas and Redman. Frequently, these signs manifest prior to an individual realizing they have high blood pressure.

2013 saw a revision to the preeclampsia definition by the American College of Obstetricians and Gynecologists (ACOG). As per these guidelines, women who first suffered hypertension during pregnancy can be diagnosed with preeclampsia after 20 weeks, even if they do not have proteinuria. The symptoms of this illness include neurological symptoms such as a strong headache, which are indicative of organ malfunction [9]. Neurological characteristics are thought to be important in the development of preeclampsia in addition to first-time hypertension, according to the International Society for the Study of Arterial Hypertension during Pregnancy (6). Prolonged headaches, delusions like eclampsia, strokes, dark patches in eyesight permanently, or blindness in the brain's visual cortex are some of the symptoms that may accompany these conditions. In **Figure 2** below, the neurological abnormalities that are indicated are part of the widely recognized diagnostic criteria for preeclampsia.

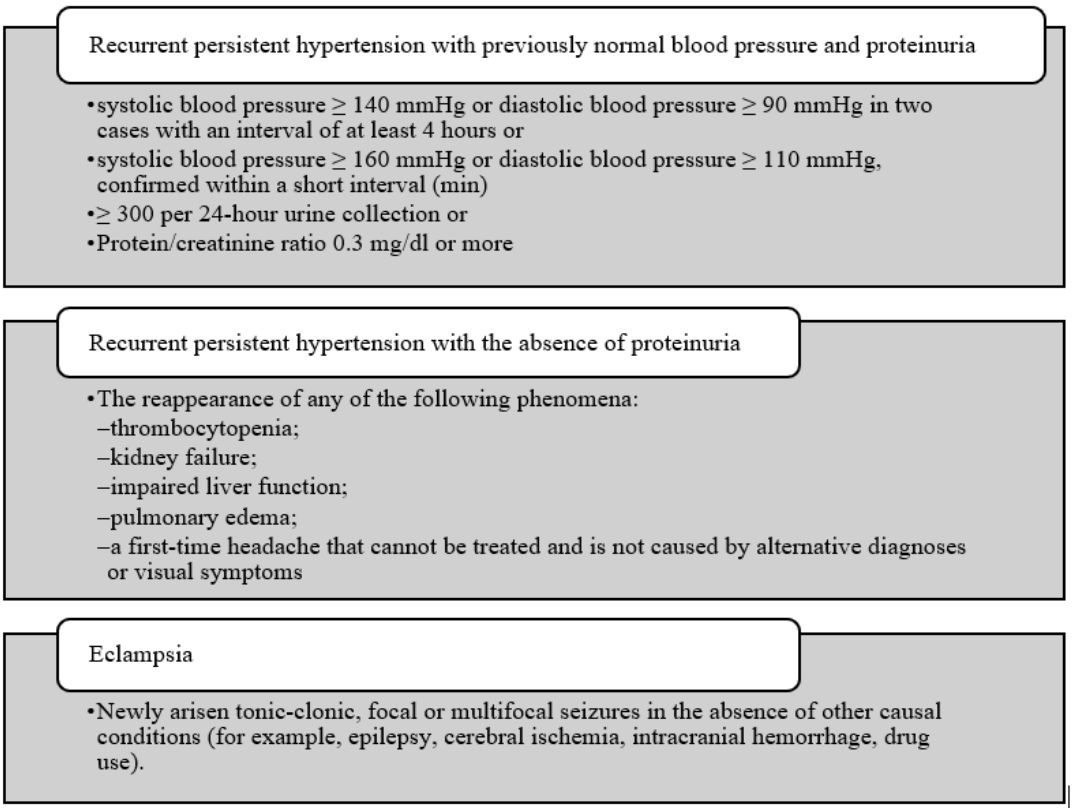

Figure 2. Diagnostic criteria for preeclampsia

Preeclampsia affects from 7 (in developed countries) to 18 (in developing countries) pregnant women [6].

The probability of Preeclampsia is significantly higher in countries with low and below-average economic levels of the population. This is primarily due to the inability to receive timely and correct prenatal medical care. Chronic pre-pregnancy hypertension leads to Preeclampsia in half of the cases. Preeclampsia is thought to be mostly caused by the spread of acute endotheliosis and vasoconstriction, which started off locally in the placenta and included brain tissues in the pathological procedure. Damage to cell membranes, a decrease in neuronal metabolism, and a rise in nerve cell excitability are all results of vascular dysfunction. In parallel, pyramidal insufficiency develops, which is manifested by tendon-periosteal hyperreflexia, anisoreflexia, increased convulsive readiness. Destructive processes occur in the stem parts of the brain, liver, kidneys, and lung tissue [10].

The main symptoms of Preeclampsia are swelling, high blood pressure, dizziness, weakness, tearfulness, increased intracranial pressure, accompanied by severe headache in the back of the head. There are failures in the work of the central nervous system: lethargy, lethargy, fatigue, apathy, hand trembling, drowsiness or insomnia. Photophobia, blurred vision, nausea, and hallucinations are less common.

It is generally believed that eclampsia is a logical consequence of the development of moderate and severe Preeclampsia, being the most severe form of Preeclampsia. However, the occurrence of eclampsia does not always clearly correlate with the degree of proteinuria or the magnitude of arterial hypertension. With eclampsia, cerebrovascular lesions occur, seizures are of a special "non-traditional" nature. This, apparently, explains the low effectiveness of traditional anticonvulsants, which usually affect the function of neurons, in comparison with magnesium sulfate, which affects vascular tone.

Epilepsy (eclampsia), subarachnoid hemorrhage, ischemic stroke (arterial stroke), and cerebral venous sinus thrombosis are among the neurological consequences linked to preeclampsia. Intracerebral hemorrhage and cervical artery dissection are less prevalent but nonetheless possible. Intracerebral hemorrhage, in particular, is the most serious complication, directly leading to 70% of deaths due to preeclampsia [11]. Acute cerebrovascular accident in a pregnant woman associated with preeclampsia has a high incidence and fatal outcome. In the general population, ischemic reasons account for 87% of strokes, whereas hemorrhagic causes account for 50% of stroke-related hypertensive pregnancy problems [12, 13]. For women experiencing hypertensive pregnancy problems, stroke is linked to a 100-fold increased risk of mortality. In fact, 13% of these women die as a result of a stroke [14]. That is why it is important to collect a complete obstetric history in women with cerebrovascular symptoms, regardless of their age. Furthermore, women with a history of preeclampsia are more likely to experience a stroke and develop cardiovascular disease and to experience clinical symptoms of the disease earlier, particularly in the first two weeks following childbirth. However, the risk increases to 12 weeks during the postpartum period [15]. In fact, the period of greatest risk of stroke in a mother is the postpartum period. In addition, prenatal detection of gestational hypertension or preeclampsia diagnosed before childbirth may worsen after childbirth and lead to the development of neurological complications, including eclamptic seizures [14]. In 68% of instances, headaches were the most prevalent symptom in the research, including 121 women with delayed postpartum preeclampsia (DPOPE) [15].

Initially, it was believed that preeclampsia was caused by toxic or inflammatory conditions during pregnancy [16]. As a result, the role of placental insufficiency and ischemia in the development of preeclampsia was recognized. There are a few possible explanations for this, including inadequate trophoblast cell implantation, insufficient remodeling of spiral arteries in the decidual layer of the placenta, or the mother's cardiovascular system not being able to appropriately adapt to the increased demands on cardiac output during pregnancy. An imbalance in angiogenic factors causes the maternal endothelium to malfunction systemically, which in turn contributes to the development of this illness [16, 17]. It has recently been recognized that the role of inflammation in the mother, expressed in maternal inflammation, has been recognized as the main cause of the pathophysiology of preeclampsia. Proinflammatory caspases and pattern recognition receptors (PRRs) make up the signaling multi-protein complexes known as inflammasomes, which are triggered by stress, infection, and other stimuli, as well as hazard-related molecular patterns (DAMPs) [18]. The discovery of these innate immune pathways as an important component of the pathophysiology of preeclampsia indicates that the long-standing debate about this condition has returned to the original hypothesis of "toxicosis".

The capacity of the cerebral arteries to dynamically modify their diameter in response to variations in the body's blood pressure in order to provide a steady supply of blood to the brain is known as cerebral autoregulation. This helps prevent damage to brain cells due to excessive blood flow or hyperperfusion. Impaired cerebral autoregulation in preeclampsia syndrome has been demonstrated both in animals and in clinical studies [18]. Investigation of the intricate connection between these disorders and brain autoregulation is ongoing. In human research, prolonged autoregulatory failure following preeclampsia has not yet been reported [19]. Nevertheless, the latest research revealed that in a rat model of preeclampsia, brain autoregulation strangely improved [20]. Subsequently, the same team discovered that modifications to the renin-angiotensin system were linked to this impact. A study using the precampsia method in Chris RUPP revealed serious violations of autoregulation compared with the control group [17]. Another study showed a paradoxical increase in the brain's ability to self-regulate in women with preeclampsia [14].

Seizures are linked to eclampsia, hyperreflexia—which is no longer regarded as a distinguishing characteristic—and elevated sympathetic nervous system activity in preeclampsia. Preeclampsia is a condition marked by high blood pressure during pregnancy. The word "preeclampsia" suggests that it may be a forerunner to eclampsia, meaning a highly intense and abrupt attack that develops at any time. However, not all cases of preeclampsia lead to eclampsia, and seizures can occur without the prodromal symptoms of preeclampsia. Studies have shown that pregnancy alone can increase a woman's risk of seizures [19]. In the context of elevated cerebral blood flow resulting from compromised cerebrovascular autoregulation and heightened blood-brain barrier permeability, this might potentially exacerbate the onset of eclampsia.

A vasoconstrictor that induces RCVS is thought to be the postpartum state and the use of sympathomimetic medications [17]. For pregnant patients with preeclampsia, a magnesium infusion may lower their chance of seizures. Many mechanisms, including NMDA receptor antagonistic action, blood-brain barrier stability, systemic vasodilation (which causes a sharp drop in blood pressure), and prevention or reversal of cerebral vasospasm, are thought to be responsible for this. Fascinatingly, independent of pregnancy status, intravenous magnesium delivery has been suggested as a successful treatment for individuals with both PRES and RCV. Clinical trials have not yet been conducted to test this tactic, albeit [21].

The risk factors for Preeclampsia are well known:

- A history of Preeclampsia;
- age over 40 years;
- chronic autoimmune diseases;
- type 1 diabetes mellitus;
- multiple pregnancies;
- first birth;
- obesity;
- chronic pre-pregnancy hypertension;
- kidney disease.

Preeclampsia-complicated pregnancies account for the majority of cases; these women are primarily primiparous (73.1%), over 34 (37.2%), and overweight or obese (44.7%). The most frequently hypothesized triggering causes of preeclampsia in 34.6% of respondents were stress (45.5%), lack of sleep (10.1%), anxiety connected to delivery (16.2%), and family history of PE (17.2%) [6].

Migraine sufferers are 1.5-3.5 times more likely to develop Preeclampsia [22].

Not much research has been done on the relationship between migraine and preeclampsia. The exact mechanisms that cause migraines are still unclear and are probably complex and multifactorial. The relationship between migraine and preeclampsia may be explained by the existence of neuroinflammation, vascular endothelial and smooth muscle cell dysfunction, platelet dysfunction, and alterations in vascular reactivity [23].

It is believed that the migraine phase includes sterile neurogenic inflammation, leading to extravasation of proteins from the dura mater and increased permeability of cerebral vessels. The dilatation of arterial arteries and the activation of local immune cells come next. Substance P, a peptide linked to the calcitonin gene, and other molecules close to meningeal blood vessels are among the vasoactive neurotransmitters released upon operation of the trigeminal nerve. These neurotransmitters result in extravasation of dura mater proteins and vasodilation of the meningeal arteries [24]. Moreover, mast cells degranulate and become triggered. Animal models demonstrated neurogenically mediated extravasation of dura mater proteins after stimulation of the trigeminal ganglion. During migraine attacks, the levels of TNF-α (tumor necrosis factor alpha), IL-1β (interleukin 1 beta), IL-10 (interleukin 10) and histamine in the proinflammatory components of mast cells increase, which further confirms this hypothesis [25].

Conclusion

Neurological complications are recognized as the main cause of maternal morbidity and mortality during pregnancy and in the postpartum period. Pregnant women and those who are directly in the postpartum period experience headaches, and any alarm signals during the collection of anamnesis or examination should prompt urgent neuroimaging (brain tomography) and laboratory tests. To identify those at elevated risk of developing preeclampsia (high blood pressure during pregnancy) and other associated hypertension diseases, pregnant women should get information regarding a history of headaches as part of regular obstetric treatment.

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