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ANALYSIS OF PERINATAL LOSSES

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РЕЗЮМЕ

С демографической точки зрения перинатальные потери принципиально отличаются от смертей в других возрастных группах, поскольку каждый нерожденный ребёнок и умерший младенец – это потеря биологического потенциала и человеческого капитала. В статье представлены данные обследования 500 женщин группы риска перинатальных потерь, 528 женщин репродуктивного возраста с отягощённым акушерским анамнезом и 87 случаев неонатальной смерти.

Perinatal losses are one of the most painful and complex issues in reproductive medicine, as their etiology often remains unknown and evidence-based strategies for diagnosis and treatment are few.

Perinatal loss is defined as fetal and infant loss due to spontaneous early termination of pregnancy, spontaneous abortion and premature birth, intrauterine fetal death, non-developing pregnancy, fetuses with malformations incompatible with life requiring early termination of pregnancy, as well as neonatal deaths. Perinatal loss therefore includes all pregnancy losses from conception to the 28th day of the neonatal period inclusive [2].

Clinically confirmed pregnancy loss (documented by ultrasound or histopathological examination) occurs in about 15-25% of pregnancies. The study of the structure of perinatal losses is an important medico-demographic issue and at the same time expresses the quality of obstetric and neonatal care [1].

The study of the structure of perinatal losses showed that ectopic pregnancy was found in 13 (2.5%) of 500 pregnant women admitted with threat of loss, 65 (13%) had birth defects incompatible with life, 85 (17%) had intrauterine fetal loss. death, non-developing pregnancy in 65 (13%), premature birth in 45 (9%), spontaneous abortion in 25 (5%), i.e., every fourth examined had a miscarriage.

Analysis of data from a study of 528 women with a history of perinatal loss showed that only 2% of these women had a term delivery with a stillbirth.

Every 7th woman examined (15%) had a non-developing pregnancy, and 12% had a spontaneous abortion, 24% had a premature birth, that is, 51% had an early termination of pregnancy, 22% of women had intrauterine fetal death, congenital malformations were noted in every fifth case.

Spontaneous abortions account for the majority of perinatal losses. It is noteworthy that the prevalence of spontaneous abortions has an increasing trend. Based on our data, we identified the most frequently important risk factors of spontaneous habitual miscarriages in the world professional literature, such as: epidemiological risk factors, among which the age of parents, reproductive anamnesis, environmental factors were considered [3,8].

A woman's age and number of previous miscarriages are two independent risk factors for subsequent miscarriage. The increase in the age of a woman is accompanied by a decrease in both the number and quality of oocytes. According to the research data, the risk of miscarriage due to the age of the woman in confirmed pregnancies is: among 20-24 years old - 11%, 25-29 years old - 12%, 30-34 years old - 15%, 35-39 years old - 25%, 40-44 years old - 51%, 45 and older age group - 93%. A man's age is also

considered a risk factor for miscarriage. The risk is highest when a woman is \ge 35 years old and a man is \ge 40 years old.

Reproductive history is an independent predictor of future pregnancy outcomes. Our research has shown that the risk of subsequent miscarriage increases after each consecutive pregnancy loss, reaching approximately 45% after three consecutive pregnancy losses and approximately 40% after each miscarriage [7].

As for environmental risk factors, they affect at a sporadic level and do not lead to habitual miscarriages. Smoking continues to be a risk factor, which was not reported by any of the women surveyed, but the percentage of passive smoking is very high [6].

Endocrine, immune, infectious factors, anatomical irregularities and birth defects of the uterus, hereditary and acquired thrombophilia are among the most common risk factors [9].

Among the endocrine risk factors, obesity, thyroid diseases, and diabetes were considered, which undoubtedly increase the probability of both sporadic and habitual miscarriages and perinatal losses.

The majority of examined pregnant women - about 70% - were overweight, and every fourth one was obese. In addition, hyperandrogenemia, hyperinsulinemia, and hyperprolactinemia prevail among women, unlike the control group. It should be taken into account that an increase in the index of free androgens is a prognostic factor in women with vaginal bleeding.

Over time, immune factors become even more relevant than risk factors. Over the years, data on the role of antigenic overload have been increasing. It follows that even conditional pathogens can lead to further deepening of congestion, complicating the entire course of reproductive activity. Our research showed that women with an obstetric anamnesis complicated by perinatal losses predominately have inflammatory diseases such as appendicitis, ulcer disease, cholecystitis, enterocolitis, pyelonephritis, thyroiditis, which is a possible stimulus for the activation of the immune system and the connection of the autoimmune process, resulting from with consequences. This is evidenced by the chained activation of unique elimination processes. inflammation, immune response, hemostatic reactions with subsequent local thrombosis.

The study looked at infection risk factors. According to the world professional literature, any viremia and bacteremia can lead to miscarriage.

According to the data we received, it becomes clear that women with a complicated obstetric anamnesis are carriers of pathogenic and conditional pathogens in the vaginal flora, such as candidiasis (25%), Staph. epidermitis (32%), E.coli (56%), alpha hemolytic streptococcus (52%), group B streptococcus (31%), Staph. aureus (5.9%), Gardnerella vaginalis (41.6%). That's why it is important to find the foci of chronic infection in the prenatal preparation, to regulate the biocenosis of the vagina. Bacterial vaginosis has been assessed as a risk factor for miscarriage and preterm delivery in the second trimester, but this association has not been established in the first trimester [5].

An important feature of the structure of perinatal losses is the steady increase of intrauterine death in the structure of stillbirth (about 60%), and in the structure of all perinatal losses (45%). It is important to note that the majority of women with a history of antenatal fetal mortality are women in a disadvantaged socio-economic situation, from this point of view, an increase in the proportion of prenatal fetal mortality is an indicator of the unfavorable socio-economic status of the population.

According to the analysis of the obtained pathoanatomical examination data, the main causes of perinatal losses (antenatal death, stillbirth, early neonatal death) are intrauterine hypoxia (about 40%), intrauterine infections (18%), congenital malformations (16%), bilateral intraventricular hemorrhages of the brain (10%). In the case of fetal death comorbidity, the probability of obstetric pathological bleeding reaches 21%, therefore the problem of reducing antenatal mortality is currently gaining importance as a pledge to reduce not only perinatal, but also maternal mortality.

Women with a history of perinatal losses in the intergenerational (interval between pregnancies) period should be examined to identify and eliminate the causes of perinatal loss. From the above it becomes clear that in terms of etiology, perinatal losses are diverse and for each of them it is necessary to develop special management tactics and procedures [4].

However, in addition to routine investigations, which often miss the true cause of loss, other etiological factors should be considered. We believe that antiphospholipid syndrome should be emphasized as one of the main predictors of perinatal loss syndrome, whose adequate treatment reduces the number of perinatal losses by 54%. Plasmapheresis should be considered as a method of antigen handling, an additional mechanism of elimination, parallel to the natural elimination mechanisms.

Medical-genetic consultation with cytogenetic study of miscarriage products, karyotyping of the married couple's peripheral blood cells and fetal egg should also be emphasized.

The folate-reductase system also deserves special attention, the various mutations of which and the hyperhomocysteinemia that follow them undoubtedly contribute to the occurrence of birth defects (especially the neural tube) in the first trimester of pregnancy. Adequate and targeted administration of folic acid in early pregnancy management should be considered.

References:

- Abalovich M., Amino N., Barbour L.A., Cobin R. H. De Groot, L. J. et all, Management of thyroid dysfunction during pregnancy and postpartum: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2017, 92:S1-S47.
- 2. Bricker L., Farquharson R.G. Types of pregnancy loss in recurrent miscarriage. Implication for research and clinical practice. Hum Reprod 2015; 17:1345.
- 3. Chrisiansen O.B., Andersen A-M.N., Borsch E., Daya S., Delves P.J., et al, Evidence-based investigations and treatments of recurrent pregnancy loss. Fert Steril.2005; 83:821-839.
- 4. Field K. Murphy DJ. Perinatal outcomes in a subsequent pregnancy among women who have experienced recurrent miscarriage: a retrospective cohort study. Hum. Reprod. 2019; 30:1239.
- 5. Goldenberg RL, Myberry SK, Copper RL, et al Pregnancy outcome following a second-trimester loss. Obstet. Gynecol 2019; 81:444.
- Jacobs P.A. Hassold T., Chromosome abnormalities: origin and etiology in abortions and livebirths. in: F. Vogel, K. Sperling (Eds.) Human genetics. Springer-Verlag, Berlin; 2010; 93:1234-1243.
- 7. Togas Tulandi, Haya M Al-Fozan. Defination and etiology of recurrent pregnancy loss. 2020. http://www.uptodate.com/contents/definition-and-etiology-of-recurrent-pregnancy-loss
- Van Niekerk, Elzaan C; SIEBERT, Igno; KRUGER, Theunis Frans. An evidence-based approach to recurrent pregnancy loss. South African Journal of Obstetrics and Gynecology, [S.I.] 19(3):61-65, jul 2013. ISSN 2305-8862. Available at: http://www.sajog.org.za/index.php/SAJOG/article/view/670. Date accessed: 05 Nov. 2016. doi:10.7196/sajog.670
- 9. Werlin L., Rodi I, DeCherney A, et al Preimplantation genetic diagnosis as both a therapeutic and diagnostic tool in assisted reproductive technology. Fertil Steril 2020; 80:467.

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SUMMARY

From a demographic point of view, perinatal losses are fundamentally different from deaths in other age groups, because each unborn child and dead infant is a loss of biological potential and human capital. This article presents data from a study of 500 women at risk of perinatal loss, 528 women of reproductive age with a complicated obstetric anamnesis, and 87 cases of neonatal death.

Keywords: perinatal loss, reproductive anamnesis, antigenic overload

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რეზიუმე

დემოგრაფიული თვალსაზრისით, პერინატალური დანაკარგები ფუნდამენტურად განსხვავდება სხვა ასაკობრივ ჯგუფებში სიკვდილისგან, რადგან ყოველი არდაბადებული ბავშვი და გარდაცვლილი ჩვილი არის ბიოლოგიური პოტენციალისა და ადამიანური კაპიტალის დაკარგვა. ამ სტატიაში წარმოდგენილია 500 ქალის კვლევის მონაცემები პერინატალური დაკარგვის რისკის ქვეშ, 528 რეპროდუქციული ასაკის ქალი გართულებული სამეანო ანამნეზით და ახალშობილთა სიკვდილის 87 შემთხვევა.

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