

Particular qualities of the microelement status in women with reproductive losses

Ph.D. Ashurova N. G., resident magistrates Shodiev B.V.

Bukhara State Medical Institute, Department of Obstetrics and Gynecology, Uzbekistan

Abstract. *Today, at the fast developing century, multivitamin and mineral deficiency - is obstetric and perinatal problem, because it is registered in the world at 40-70% of pregnant women, depending on the region. Micronutrient demand increases significantly and during pregnancy. High demand for vitamins and minerals in these periods of life is associated with the activation of the functions of the endocrine glands, acceleration of metabolism, increasing the loss of vitamins and minerals in the urine, and during childbirth - with the placenta and amniotic fluid, lactation - with milk. In addition, a pregnant woman transmits the vitamins and minerals to the fetus - to meet its needs. Essential trace elements and minerals that should be considered as an integral part of the diet of pregnant women (and nursing) are iron, folic acid, iodine, calcium, magnesium, copper, manganese. In this publication stated dates of latest years. Also discovered certain etiopathogenetic aspects of reproductive losses. However, among them unnoticed the status of microelement deficiency as a possible etiological factor of pathology.*

Keywords: *reproductive losses, vitamins and minerals, spontaneous abortion, hormonal status, mineral deficiency*

Аннотация. *В эти дни, поливитаминный и минеральный дефицит организма - это акушерская и перинатальная проблема, потому что она зарегистрирована в мире на 40-70% беременных женщин, в зависимости от региона. Микронутриентов спрос значительно возрастает и во время беременности. Высокий спрос на витамины и минералы в эти периоды жизни связано с активацией функции эндокринных желез, ускорение обмена веществ, увеличивая потери витаминов и минералов в моче, а также во время родов - с плацентой и амниотической жидкости, период лактации - с молоком. Кроме того, беременная женщина передает витамины и минералы для плода - для удовлетворения своих потребностей. Эссенциальных микроэлементов и минералов, которые следует рассматривать в качестве составной части рациона питания беременных женщин и кормящих являются железо, фолиевая кислота, йод, кальций, магний, медь, марганец. В этой статье изложены данные литературы за последние годы. Также выявлены определенные этиопатогенетические аспекты репродуктивных потерь. Однако, среди них незамечено дефицитное состояние микроэлементов, как возможный этиологический фактор патологии.*

Ключевые слова: репродуктивная потеря, витамины и минералы, спонтанный аборт, гормональный статус, минеральная недостаточность

Introduction

The results of population of surveys conducted by the World Institute of Nutrition, suggest a very alarming situation in recent years in particular areas. There have been extremely inadequate intake and increasingly growing shortage of vitamins (A, group B, C, E). For example, vitamin B deficiency is detected in 30-40% (deficiency of vitamin B6 in pregnant approaching 90-100%), b-carotene - more than 40%, and vitamin C - 70-90% in the subjects. (World Health Organisation, 2001)

This lack of vitamins is combined nature and is found not only in winter and spring, but in summer and autumn. Pregnant women often detected multi-component malnutrition. Most often they are deficient in iron, iodine, calcium, zinc, chromium, folic acid, biotin, vitamin A, D, B1, B6, a-linolenic acid. At the same time we should not think that the balance of minerals is always negative, scarce. The prevalence of excess chemical elements ranging from 1/6 to 1/10 part of all dismicroelementoses, and in industrial areas and in some regions this figure is even higher - up to 50%. (Royal College of Obstetricians and Gynaecologists SAC: Guideline No. 17. 2011)

It is estimated that 70% of conceptions are lost prior to live birth. The majority of these losses occur prior to implantation or before the missed menstrual period, and since they are not revealed to the woman they are termed preclinical. In the pregnancy loss 'iceberg', they are therefore below the 'waterline'. Figure reproduced with permission from Oxford University Press (Wang X, Chen C, 2003).

The Russians often found not only an excess of toxic lead, cadmium and aluminum, but also above normal concentrations of iron, vanadium, nickel, chromium, molybdenum, boron. In some areas there is often an excess of copper, zinc, fluorine, selenium, i.e. those elements which come in many vitamins and minerals. In fact, these essential, i.e. vital trace elements must be ingested in

minute quantities. The metabolic processes and metabolism of matters not separately taken a trace element and a set of trace elements and their balance, as between themselves in the body there is a ME interaction. Thus, there is synergy, magnesium, copper, cobalt and zinc in their effect on the growth and development. Cobalt effectively acts on the blood only when there are sufficient quantities of iron and copper, and magnesium improves absorption of copper. At the same time it is known that iron, calcium, magnesium and zinc compete with each other while receiving. In addition, calcium and inhibit absorption of iron, manganese and zinc - copper. When iron deficiency rate of absorption of nickel increases significantly. While miscarriage is a term for early pregnancy loss, it is also frequently known in medical literature as "spontaneous abortion". Those fetuses born before 24 weeks of gestation rarely survive. However, the designation "[fetal death](#)" applies variably in different countries and contexts, sometimes incorporating weight, and gestational age from 16 weeks in Norway, 20 weeks in the US and Australia, 24 weeks in the UK to 26 weeks in Italy and Spain. A fetus that died before birth after this gestational age may be referred to as a [stillbirth](#). Under UK law, all stillbirths should be registered, although this does not apply to miscarriages.

Among those who know they are pregnant, the miscarriage rate is roughly 10% to 20%, while rates among all [fertilized zygotes](#) is around 30% to 50%.

Determining the precise rate is not possible as a large number of miscarriages occur before pregnancies become established and before the person is aware they are pregnant. In addition, those with bleeding in early pregnancy may seek medical care more often than those not experiencing bleeding. Some studies have attempted to account for this by recruiting people who are planning pregnancies and testing for very early pregnancy, although these would also not be representative of the wider population. A systematic review found that the cumulative risk of miscarriage between 5 and 20 weeks of gestation varied from 11% to 22% in studies assessing miscarriage rates. Up to the 13th week of pregnancy, the risk of miscarriage each week was around 2%, dropping to 1% in week 14 and reducing slowly between 14 and 20 weeks.*(Jauniaux E, Farquharson RG, 2006)*

The prevalence of miscarriage increases with the age of both parents. In a Danish register-based study where the prevalence of miscarriage was 11%, the prevalence rose from 9% at 22 years of age to 84% by 48 years of age. Another study found that when either parent was over the age of 40, the rate of known miscarriages doubled.

Autoimmune disease in a woman may be the cause of miscarriage according to new research. Study authors are encouraging doctors to test women who experience recurrent pregnancy losses for autoimmune diseases as a way to better prevent miscarriages.

The study, conducted by researchers at the Center for Human Reproduction, reviewed available published literature on autoimmune disease and its relationship to infertility. What they discovered was that the autoimmune disease in itself can cause genetic abnormalities of the embryo. These abnormalities are then what lead to miscarriage. So, if the disease is left untreated, the woman would continue to have recurrent pregnancy losses. “Indeed, it is precisely when a chromosomal problem is detected in embryos that we need to look into maternal autoimmunity,” says Dr. David Barad, a study author and Clinical Director of ART at the Center for Human Reproduction. “Especially when a woman experiences repeated miscarriages, her autoimmunity needs to be investigated as a cause.” “Identifying the root cause is the crucial starting point in miscarriage prevention,” said Dr. Norbert Gleicher, the study's lead author and Medical Director of the Center for Human Reproduction. “If we know that autoimmunity is causing a woman to miscarry, there are preventive measures we can take.” “When you consider that a woman’s body views sperm as a foreign object, it’s a wonder that pregnancy happens at all,” says Dr. Scher. “But most of the time, a fertilized egg sends a message to the mother that says ‘don’t treat me like a germ,’ and pregnancy proceeds without incident.” In some cases, though, the embryo isn’t accepted by the woman’s body. “Antiphospholipid antibodies—antibodies that attack one’s own tissue, including embryos—account for many miscarriages that physicians used to think were unexplainable,” **Dr. Scher says. (Holers VM, Dr. Scher, 2002)**

If you have a uterus that is “abnormally” shaped or divided--called uterine septum--miscarriage occurs because the embryo either can't implant or once it does implant, can't get the nourishment it needs to survive. “Uterine anomalies account for about 10 percent of miscarriages,” says Dr. Cowan.

An accepted cause of recurrent pregnancy loss is uterine malformations that may be acquired or congenital. The latter include didelphic, bicornuate, arcuate, and septate uteri. In a recent systematic review including 89,861 women, the prevalence of all congenital uterine malformations was 5.5% (95% CI 3.5 to 8.5) in an unselected population and 15.4% (95% CI 10.3 to 23) among women with ≥ 3 miscarriages (*Weimar CH, Kavelaars A, 2012*).

A weakened or incompetent cervix is another problem that can lead to miscarriage, because toward the end of the first trimester the fetus has grown large enough that the cervix starts to bulge. If the cervix is weakened, it can't hold the fetus in.

“Mismatched chromosomes account for at least 60 percent of miscarriages,” says Bryan Cowan, MD, chair of the department of obstetrics and gynecology at the University of Mississippi Medical Center in Jackson, and a spokesperson for the American College of Obstetricians and Gynecologists. Chromosomes are the tiny structures in each cell that carry our genes; we each have 23 pairs of them, one set from our mother and one set from our father. Sometimes, when the egg and sperm meet, one or the other is faulty and then the chromosomes can't line up properly. In that case, the resulting embryo has a chromosomal abnormality and the pregnancy usually results in a miscarriage. Couples who experience two or more miscarriages in a row sometimes learn, through medical testing, that they have chromosomal anomalies that don't affect them, but do prevent a pregnancy from taking hold. (*Christiansen OB, Kolte AM, 2012*)

Although fetal chromosomal aberrations may be identified in 29% to 60% of cases in women with RM, the incidence decreases as the number of miscarriages

increases suggesting other mechanisms as a cause of the miscarriage in RM couples with multiple losses .(*Morris JK, Wald NJ,1999*)

The case against offering routine karyotyping for couples with RM rests primarily on the findings of a large index-control study with a mean follow-up period of 5.8 years. This study showed that carrier couples with at least two previous miscarriages had the same chance of having a healthy child as non-carrier couples with at least two miscarriages (83% and 84%, respectively), and more importantly a low risk (0.8%) of pregnancies with an unbalanced karyotype surviving into the second trimester(*Branch DW, Gibson M, 2010*).

Thyroid conditions and uncontrolled diabetes are both associated with “unfavorable” uterine environments. The effects of these conditions make it difficult for the embryo to survive, explains *Twig G.*(*Twig G, Shina A,2012*)

Polycystic ovarian syndrome (PCOS) is a common endocrine disorder of reproductive-age women. PCOS may be associated with ovulatory disorder and miscarriage when fertility is desired. Using strict criteria the prevalence of PCOS among women with RM is estimated to be 8.3% to 10%(*Negro R, Schwartz A, 2010*)

“This is now an emerging cause of recurrent miscarriage,” says Dr. Scher. Women with PCOS have too-high levels of the male hormone testosterone which, among other things, causes irregular ovulation and menstruation. “Even in women who don’t have diabetes, PCOS causes insulin resistance, which prevents the endometrial lining from maturing properly,” explains Dr. Scher. He estimates that between 5 and 10 percent of reproductive-age women have PCOS.(*Cocksedge KA, Saravelos SH,Dr. Scher, 2009*)

Many micro-organisms live harmlessly—even helpfully—in the male and female reproductive tracts. But certain bacteria can cause problems, including an increased risk of miscarriage. Two in particular—*mycoplasma hominis* and *ureaplasmaurealyticum*—live in the genital tracts of healthy men and women, but can raise the risk of miscarriage. In women, infection with these bacteria can inflame the endometrium (the lining of the uterus), making it impossible for an

embryo to develop. “There are no symptoms, however, so the only way you know if you or your partner is carrying the organism is to be tested,” says Dr. Scher.

“Nicotine crosses the placenta and interferes with blood supply and fetal growth,” says Dr. Scher. Smokers have twice the rate of miscarriage as nonsmokers. Drinking more than two alcoholic beverages a day is also associated with miscarriage, he says, and it goes without saying—but he says it anyway—that using recreational drugs when you’re attempting to get pregnant (or during pregnancy) is foolish. Finally, women who work in certain environments—including farms, operating rooms, dental offices and hospital laboratories—have a higher rate of miscarriage for unknown reasons.

Although pregnant women are advised to refrain from alcohol a national Danish birth cohort study including nearly 100,000 pregnant women showed that 45% had some level of alcohol intake (*Andersen AM, Andersen PK and others, 2012*).

In contrast to alcohol consumption, coffee drinking in pregnancy is fully acceptable in many countries. Another Danish study has looked into the association between miscarriage and coffee intake (*Chin JR, Heuser CC*).

Only in cases where mothers were drinking more than seven cups of coffee a day could the authors demonstrate an increased risk of miscarriage (adjusted hazard ratio 1.48 (95% CI 1.01 to 2.17)).

There are many pregnancy-related complications associated with obesity, including miscarriage. A meta-analysis from 2008 including primarily studies on infertile populations showed significantly increased miscarriage rates when women with a body mass index (BMI) ≥ 25 kg/m² were compared to women with a BMI < 25 kg/m² (*Wisborg K, Kesmodel U, 2003*).

Even though, the new studies shine a brighter light on the elusive causes of reproductive losses, the reasons behind the majority of cases are still mysterious. The biggest component to the risk for miscarriages is something else—some factors that we haven't analyzed yet or some factors we don't know. Thus, the study of these literatures of recent years has revealed some etiopathogenic aspects of

reproductive losses. However, among them unnoticed micronutrient deficiency states, as a possible etiological factor of disease. On this basis, further scientific study will examine the role of trace elements in the body of women with reproductive losses and will be installed the risk factors for this disease. Also, the tactics of the patients will be recommended to the various kinds of micronutrient deficiencies.

References:

1. *Jauniaux E, Farquharson RG, Christiansen OB, Exalto N: Evidence-based guidelines for the investigation and medical treatment of recurrent miscarriage. Hum Reprod. 2006, 21: 2216-2222. [PubMedView Article](#)*
2. *Royal College of Obstetricians and Gynaecologists SAC: Guideline No. 17. The investigation and treatment of couples with first and second trimester recurrent miscarriage. 2011, London, UK: RoyalCollegeofObstetriciansandGynaecologists, 1-18.*
3. *Holers VM, Dr. Scher, Girardi G, Mo L, Guthridge JM, Molina H, Pierangeli SS, Espinola R, Xiaowei LE, Mao D, Vialpando CG, Salmon JE: Complement C3 activation is required for antiphospholipid antibody-induced fetal loss. J Exp Med. 2002, 195: 211-220. [PubMedPubMed CentralView Article](#)*
4. *Christiansen OB, Kolte AM, Dahl M, Larsen EC, Steffensen R, Nielsen HS, Hviid TV: Maternal homozygosity for a 14 base pair insertion in exon 8 of the HLA-G gene and carriage of HLA class II alleles restricting HY immunity predispose to unexplained secondary recurrent miscarriage and low birth weight in children born to these patients. Hum Immunol. 2012, 73: 699-705. [PubMedView Article](#)*
5. *Twig G, Shina A, Amital H, Shoenfeld Y: Pathogenesis of infertility and recurrent pregnancy loss in thyroid autoimmunity. J Autoimmun. 2012, 38: J275-J281. [PubMedView Article](#)*
6. *Andersen AM, Andersen PK, Olsen J, Gronbaek M, Strandberg-Larsen K: Moderate alcohol intake during pregnancy and risk of fetal death. Int J Epidemiol. 2012, 41: 405-413. [PubMedView Article](#)*
7. *Weimar CH, Kavelaars A, Brosens JJ, Gellersen B, de Vreeden-Elbertse JM, Heijnen CJ, Macklon NS: Endometrial stromal cells of women with recurrent miscarriage fail to discriminate between high- and low-quality human embryos. PLoSOne. 2012, 7: e41424. [PubMedPubMed CentralView Article](#)*
8. *Cocksedge KA, Saravelos SH, Dr. ScherMetwally M, Li TC: How common is polycystic ovary syndrome in recurrent miscarriage?. Reprod Biomed Online. 2009, 19: 572-576. [PubMedView Article](#)*

9. Negro R, Schwartz A, Gismondi R, Tinelli A, Mangieri T, Stagnaro-Green A: Increased pregnancy loss rate in thyroid antibody negative women with TSH levels between 2.5 and 5.0 in the first trimester of pregnancy. *J ClinEndocrinolMetabol.* 2010, 95: E44-E48.[View Article](#)
10. Wisborg K, Kesmodel U, Henriksen TB, Hedegaard M, Secher NJ: A prospective study of maternal smoking and spontaneous abortion. *ActaObstetGynecolScand.* 2003, 82: 936-941.[PubMedView Article](#)
11. Chin JR, Heuser CC, Eller AG, Branch DW, Nelson LT, Silver RM: Leptin and leptin receptor polymorphisms and recurrent pregnancy loss. *J Perinatol.* Inpress
12. Wang X, Chen C, Wang L, Chen D, Guang W, French J: Conception, early pregnancy loss, and time to clinical pregnancy: a population-based prospective study. *FertilSteril.* 2003, 79: 577-584.[PubMedView Article](#)
13. Branch DW, Gibson M, Silver RM: Clinical practice. Recurrent miscarriage. *N Engl J Med.* 2010, 363: 1740-1747.[PubMedViewArticle](#)
14. Morris JK, Wald NJ, Watt HC: Fetal loss in Down syndrome pregnancies. *PrenatDiagn.* 1999, 19: 142-145.[PubMedView Article](#)

