ASSESSMENT OF THE COURSE OF THE GESTATIONAL PROCESS USING SURVEY METHOD AND DEPENDING ON THE LABORATORY CONFIRMED PRENATAL ALCOHOL USE (CROSS-SECTION STUDY)

Marianian A.Yu. [1, 2],
Kalkova A.N. [1],
Rashidova M.A. [1],
Semenova N.V. [1],
Belskikh A.V. [1],
Belyaeva E.V. [1],
Sambyalova A.Yu. [1],
Atalyan A.V. [1],
Tiumentceva D.P. [1],
Ilyina A.B. [1],
Kolesnikova L.I. [1]

[1] Scientific Centre for Family Health and Human Reproduction Problems (Timiryazeva str. 16, Irkutsk 664003, Russian Federation)
[2] Irkutsk State Medical Academy of Postgraduate Education – Branch Campus of the Russian Medical Academy of Continuing Professional Education (Yubileyniy 100, Irkutsk 664049, Russian Federation)

Corresponding author:
Anastasia N. Kalkova,
e-mail: Kalkova_Nastya@mail.ru

Received: 14.07.2023
Accepted: 29.08.2023
Published: 28.09.2023

ABSTRACT

Background. *Studying the problem of alcohol consumption by pregnant women using modern laboratory research methods has valuable theoretical and practical significance.*
The aim of the study. *To determine the characteristics of the pregnancy course in women consuming alcohol in the prenatal period confirmed by survey and laboratory tests, depending on the phosphatidylethanol levels.*
Materials and methods. *We examined 863 women under observation at the Irkutsk Regional Perinatal Center for the period from 2014 to 2021 To confirm the fact of alcohol consumption in the prenatal period, 545 women were surveyed, 318 women were examined using laboratory analysis. The diagnostic biomarker for alcohol was PEth:16:0/18:1. To assign pregnant women to the control group, a PEth concentration of ≤ 8 ng/ml was taken. If the PEth concentration was> 8 ng/ml, pregnant women were classified as heavy drinkers. Clinical and laboratory indicators of the course of pregnancy and childbirth were carried out in comparative groups.*
Results. *It has been established that every second woman of reproductive age took alcohol before pregnancy. 24.2 % of women did not stop consuming alcohol in the prenatal period. At the same time, the risk of congenital malformations was high, since 20.4 % of women consumed alcohol in the first trimester of pregnancy. Based on the results of the survey, it was revealed that in women who consumed alcohol in the prenatal period, the following pathological conditions are statistically significantly more common: anemia, congenital heart defects in fetuses, prematurity of gestational age, labor anomalies, uterus subinvolution. Based on the results of laboratory confirmation of alcohol consumption, it was established that parity of birth, intrauterine growth retardation, and premature birth were statistically significantly more often in pregnant women who drink.*
Conclusion. *Thus, in order to obtain the most meaningful and high-quality results, it is necessary to conduct larger studies. In addition, maternal blood biomarkers should be used to confirm levels of alcohol consumption throughout all trimesters of pregnancy.*

Key words: *alcohol, pregnancy, phosphatidylethanol (PEth), fetus*

For citation: Marianian A.Yu., Kalkova A.N., Rashidova M.A., Semenova N.V., Belskikh A.V., Belyaeva E.V., Sambyalova A.Yu., Atalyan A.V., Tiumentceva D.P., Ilyina A.B., Kolesnikova L.I. Assessment of the course of the gestational process using survey method and depending on the laboratory confirmed prenatal alcohol use (cross-section study). *Acta biomedica scientifica*. 2023; 8(4): 49-58. doi: 10.29413/ABS.2023-8.4.6

ОЦЕНКА ТЕЧЕНИЯ ГЕСТАЦИОННОГО ПРОЦЕССА У ЖЕНЩИН МЕТОДОМ ОПРОСА И В ЗАВИСИМОСТИ ОТ ЛАБОРАТОРНО ПОДТВЕРЖДЁННОГО ФАКТА УПОТРЕБЛЕНИЯ АЛКОГОЛЯ В ПРЕНАТАЛЬНОМ ПЕРИОДЕ (КРОСС-СЕКЦИОННОЕ ИССЛЕДОВАНИЕ)

Марянян А.Ю. [1, 2],
Калькова А.Н. [1],
Рашидова М.А. [1],
Семёнова Н.В. [1],
Бельских А.В. [1],
Беляева Е.В. [1],
Самбялова А.Ю. [1],
Аталян А.В. [1],
Тюменцева Д.П. [1],
Ильина А.Б. [1],
Колесникова Л.И. [1]

[1] ФГБНУ «Научный центр проблем здоровья семьи и репродукции человека» (664003, г. Иркутск, ул. Тимирязева, 16, Россия)
[2] Иркутская государственная медицинская академия последипломного образования – филиал ФГБОУ ДПО «Российская медицинская академия непрерывного профессионального образования» Минздрава России (664049, г. Иркутск, Юбилейный, 100, Россия)

Автор, ответственный за переписку:
Калькова Анастасия Николаевна,
e-mail: Kalkova_Nastya@mail.ru

Статья поступила: 14.07.2023
Статья принята: 29.08.2023
Статья опубликована: 28.09.2023

РЕЗЮМЕ

Обоснование. *Изучение проблемы употребление алкоголя беременными посредством современных лабораторных методов исследования несёт в себе ценное теоретическое и практическое значение.*
Цель исследования. *Определение особенностей течения беременности у женщин, принимающих алкогольные напитки в пренатальном периоде, подтверждённое методом опроса и лабораторно, в зависимости от уровней фосфатидилэтанола.*
Материалы и методы. *Обследовано 863 женщины, находящиеся под наблюдением в Областном перинатальном центре г. Иркутска за период с 2014 по 2021 г. Для подтверждения факта употребления алкоголя в пренатальном периоде методом опроса обследованы 545 женщин, методом лабораторно подтверждённого анализа – 318. Диагностическим биомаркером алкоголя был PEth:16:0/18:1. Для отнесения беременных в группу контролям была взята концентрация PEth ≤ 8 нг/мл. В случае значения PEth > 8 нг/мл беременные были отнесены к группе пьющих женщин. Клинико-лабораторные показатели течения беременности и родов проводилась в сравнительных группах.*
Результаты. *Установлено, что каждая вторая женщина репродуктивного возраста принимала алкоголь до беременности. 24,2 % не прекращали потреблять алкогольные напитки в пренатальном периоде. При этом риск возникновения врождённых пороков развития был высоким, так как в первом триместре беременности 20,4 % женщин употребляли спиртные напитки. По результатам анкетирования выявлено, что у женщин, употребивших алкоголь в пренатальном периоде, статистически значимо чаще встречаются следующие патологические состояния: анемия, врождённые пороки сердца у плодов, недоношенность гестационного возраста, аномалии родовой деятельности, субинволюция матки. По результатам лабораторного подтверждения употребления алкоголя установлено, что паритет родов, задержка внутриутробного развития плода, преждевременные роды статистически значимо чаще определялись у пьющих беременных.*
Заключение. *Таким образом, с целью получения наиболее содержательного и качественного результата необходимо провести более масштабные исследования. Кроме того, для подтверждения уровня потребления алкоголя на протяжении всех триместров беременности следует применить биомаркеры материнской крови.*

Ключевые слова: *алкоголь, беременность, фосфатидилэтанол (PEth), плод*

Для цитирования: Марянян А.Ю., Калькова А.Н., Рашидова М.А., Семёнова Н.В., Бельских А.В., Беляева Е.В., Самбялова А.Ю., Аталян А.В., Тюменцева Д.П., Ильина А.Б., Колесникова Л.И. Оценка течения гестационного процесса у женщин методом опроса и в зависимости от лабораторно подтверждённого факта употребления алкоголя в пренатальном периоде (кросс-секционное исследование). *Acta biomedica scientifica*. 2023; 8(4): 49-58. doi: 10.29413/ABS.2023-8.4.6

INTRODUCTION

All over the world, including Russia, one of the ancient destructive habits in world history is excessive alcohol abuse and related consequences [1].

Throughout the nine months of pregnancy, every woman should know that alcohol is toxic to the growing fetus. An expectant mother who resorts to drinking alcohol in anticipation of the birth of a child does not even imagine how easily ethanol enters directly to the fetus, through the entire circulatory system. According to the results of numerous studies, most women continue to drink alcohol during the first month of pregnancy, not knowing that they are pregnant. It should be noted that it is in the first trimester of pregnancy that there are critical periods of development, during which a continuous epithelial cover of the villi is formed – the future placental barrier, which at this stage does not protect the embryo from any external influences [2–5]. At the same time, there is a high risk of complications of pregnancy and the birth of children with fetal alcohol spectrum disorders (FASD). This condition includes disorders that will affect children's health for life and are characterized by a combination of congenital physical and mental defects [6–8]. The diagnosis of FASD requires accurate knowledge of the amount and frequency of alcohol consumed. For this purpose, a survey of women is conducted using various questionnaires [9–11]: T-ACE, TWEAK, AUDIT. The information obtained through the survey is prone to subjectivism, and a person can often indicate deliberately false data. Consequently, biomarkers such as phosphatidylethanol are used to obtain an objective picture of a woman's alcohol consumption [12], the definition of which allows us to establish both the fact and the amount of alcohol consumed.

Based on the results of numerous studies and as practice demonstrates, after the fact of pregnancy is established, the percentage of women who drink alcohol decreases, but does not reach the required level. According to T.N. Balashova et al. [13], after pregnancy diagnosis, about 20 % of women report continued alcohol consumption, which leads to adverse pregnancy outcomes. It has been shown that there is no safe dose of alcohol during pregnancy. The pathophysiological effects of both moderate and low doses of alcohol on the gestational process and the fetus have been proven [14-19].

In order to determine the level of alcohol consumption during pregnancy for the purpose of earlier diagnosis and treatment of fetal lesions, as well as prevention, in addition to existing questionnaires, it is also necessary to pay attention to the study of maternal blood markers. As is known, there are direct and indirect groups of blood biomarkers, which are determined by the laboratory method.

In practice, direct markers of alcohol consumption are practically not used today, since the period of their content in biological fluids varies from 8-12 hours to no more than 7 days, and it is also impossible to differentiate a single alcohol intake from chronic alcoholism. Direct markers include ethyl esters of fatty acids, ethylglucuronide, and ethyl sulfate. On the contrary, the group of indirect biomarkers, such as aspartate aminotransferases, alanine aminotransferases, and gamma-glutamyltransferases, can vary quite widely [20, 21].

To date, there are many studies devoted to the study of another direct biomarker of ethanol, phosphatidylethanol (PEth), in order to obtain an objective picture of alcohol consumption. Due to the long elimination half-life of alcohol, it accumulates in the blood. In this case, it becomes possible to detect it within 28 days after the last alcohol intake [21].

Thus, as a result of the analysis of domestic and foreign literature, it was found that the problem of alcohol consumption by women in the prenatal period is relevant and promising. Therefore, the study of this problem and the conduct of research through modern laboratory research methods will be of great theoretical and practical importance.

In this regard, **the aim of our study** was to determine the characteristics of the course of the gestational process in women who consumed alcoholic beverages in the prenatal period, confirmed by a survey and laboratory, depending on the levels of phosphatidylethanol.

MATERIALS AND METHODS

A total of 863 women who were under observation at the Irkutsk Regional Perinatal Center for the period from 2014 to 2021 were interviewed.

For the purpose of a more convenient perception, the groups in which the survey was conducted are indicated by Arabic numerals (1st and 2nd), and the groups with laboratory confirmation of blood alcohol are indicated by Roman numerals (I and II).

545 women were examined by the survey method, using validated questionnaires, to identify the fact of alcohol consumption in the prenatal period.

Group 1 (n = 261) included women who had never consumed alcoholic beverages during pregnancy (control group).

The 2nd group (n = 284) included women who consumed alcoholic beverages in the prenatal period.

The average age of pregnant women in group 1 was 29.64 ± 5.9 years, and group 2 was 28.75 ± 6.1 years. No statistically significant differences were found when comparing the age indicators ($p > 0.05$).

To determine the PEth biomarker in the blood, that is, for laboratory confirmation of alcohol consumption, only 318 women were examined. Out of 318 pregnant women, 194 women never consumed alcoholic beverages throughout pregnancy (group I – control), 121 women consumed alcoholic beverages in the prenatal period (group II). Clinical and laboratory parameters of the gestational process and childbirth were evaluated in comparative groups.

The main group includes women who meet the following criteria: alcohol consumption during gestation;

belonging to the European race; absence of severe somatic pathology; signing of informed consent; accessibility throughout the duration of the study; current pregnancy; willingness of the participant to comply with all research procedures.

The control group included women with the following criteria: non-use of alcohol and nicotine during pregnancy; belonging to the European race; absence of severe somatic pathology; willingness of the participant to comply with all research procedures; signing informed consent; current pregnancy; accessibility throughout the duration of the study.

Excluded from the study were women who had severe somatic pathology; exacerbation of chronic diseases; presence of exacerbations of infectious diseases (bacterial and viral); presence of sexually transmitted infections, including HIV infection; woman's use of nicotine and narcotic drugs; chronic alcohol dependence, as well as the studied women who changed their place residents and those who refused further supervision.

In working with pregnant women, the ethical principles set forth in the World Medical Association Declaration of Helsinki (1964; last revised in October 2013) were observed. All pregnant women have received informed consent to conduct the study. The conduct of this study was approved by the Ethics Committee of the Scientific Centre for Family Health and Human Reproduction Problems (Protocol No. 2 dated March 4, 2021).

So, in the study groups, which were formed on the basis of the fact of alcohol consumption during pregnancy, diagnosed by the survey method, questionnaires (screening tools) [8-10] T-ACE, TWEAK, AUDIT were used. At the same time, the information is subject to subjectivity, since patients can often make deliberately false data. As described above, biomarkers are used to obtain an objective picture.

In this regard, for laboratory confirmation of alcohol consumption, the presence of such ethanol biomarkers in the blood of pregnant women as PEth:16:0/16:0, PEth:16:0/18:1, PEth:18:1/18:1 was determined. Moreover, the presence of each of the three PEth and their combinations was determined separately in the blood (Fig. 1).

Blood sampling in pregnant women was performed in fasting state from the ulnar vein at 38–40 weeks of gestation. The determination of phosphatidylethanol biomarkers was carried out on the basis of the Laboratory of Personalized Medicine of the Scientific Centre for Family Health and Human Reproduction Problems on a mass spectrometer. The analytical complex is based on an ultra-high-performance liquid chromatograph Shimadzu Nexera X2 (Kyoto, Japan) with an auto-injector and a pumping unit for creating a gradient on the high-pressure side and a tandem three-quadrupole mass-selective detector Shimadzu LCMS 060 (Kyoto, Japan) with a hybrid ion source DUIS.

During the observation of the course of the gestational process and the development of the fetus, a gravidogram was filled in, which indicated the initial body weight, the height of the woman, an increase in the circumference of the abdomen and the height of the uterine fundus. Blood pressure and basic biochemical and hemodynamic parameters were determined in dynamics. According to the generally accepted standard, all pregnant women were examined by a therapist,

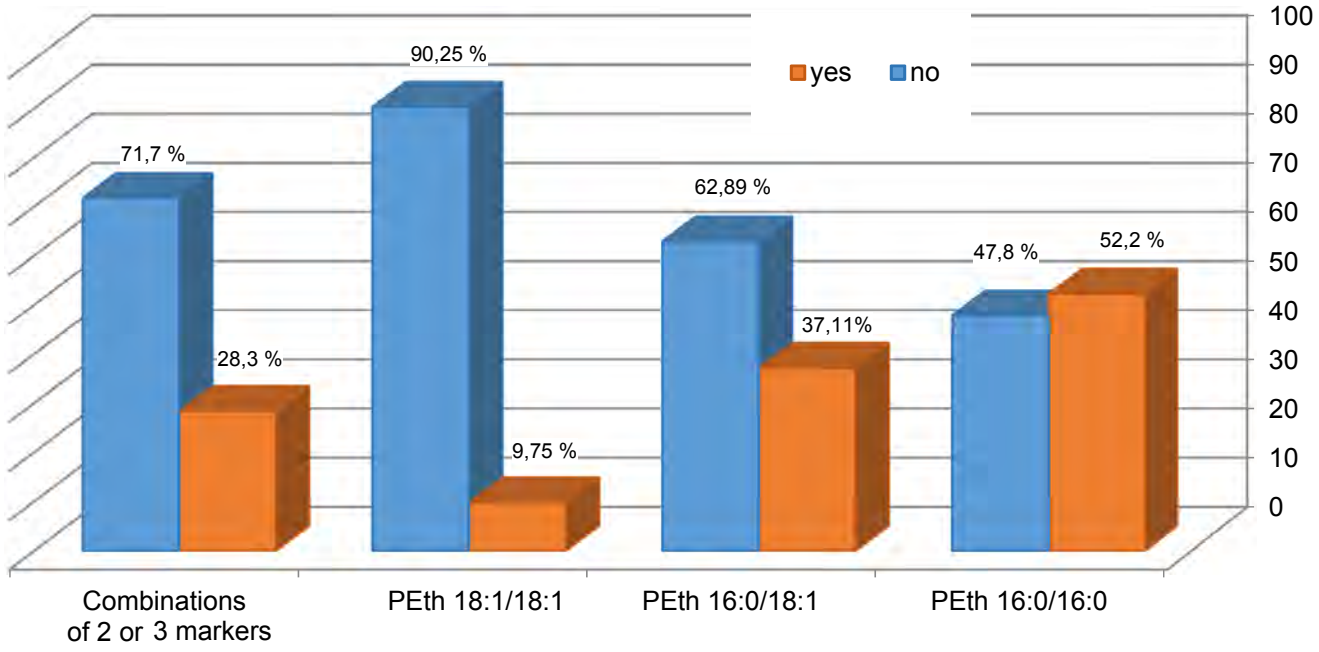

FIG. 1.
Laboratory confirmed fact of alcohol consumption in the prenatal period

neurologist and electrocardiography. The examination of other narrow specialists was carried out only according to indications.

According to the generally accepted standard, ultrasound with measurement of uteroplacental and fetal blood flow was used on Voluson E8 (GE Healthcare, USA), Philips 22, 11 (Philips, Netherlands) devices operating in real time to assess the fetal condition of the fetus. Using cardiotocography on Sonicaid Team devices (Oxford Medical, UK), Advanced Fetal Monitoring System BFM-800 (BIONICS Co. Ltd., South Korea), fetal cardiac activity in the antenatal period was determined.

We also analyzed the available medical documentation (exchange cards and birth histories).

A frequency analysis was performed, comparing the results of PEth:16:0/16:0, PEth:18:1/18:1 with a diagnostic biomarker of alcohol consumption (PEth:16:0/18:1). In the process of analyzing the literature and obtained data, it was found that PEth:16:0/18:1 was the most informative marker in comparison with PEth:16:0/16:0 and PEth:18:1/18:1 [22].

According to the literature [23], a limit of ≤ 8 ng/ml was taken for PEth:16:0/18:1 in order to classify pregnant women into the control group (the group of non-drinking women). The group of pregnant women who drink alcoholic beverages, depending on the concentration of PEth:16:0/18:1 (> 8 ng/ml), was divided into categories, and the dose of alcohol consumed was determined (Table 1).

The statistical analysis of the obtained data was carried out using the Statistica 10 statistical and application software package (StatSoft Inc., USA; the license holder is the Scientific Centre for Family Health and Human Reproduction Problems). Depending on the type of data distribution, various statistical analysis algorithms were used. Descriptive statistics were used to represent quantitative data. In the statistical analysis of the data, the differences in the compared indicators were considered significant at $p < 0.05$.

THE RESULTS OF A STUDY OF WOMEN BEFORE AND DURING PREGNANCY BASED ON A SURVEY

According to the analysis of the data obtained, no statistically significant differences in family status, education, and socio-demographic indicators were revealed ($p > 0.05$). In both groups of pregnant women, extragenital pathology (kidney, liver, bronchial asthma, diabetes mellitus, including gestational, thyroid diseases, heart defects, hypertension, epilepsy, etc.) occurred with the same frequency ($p > 0.05$).

The study revealed that every second woman of reproductive age consumed alcohol before pregnancy, and 24.2 % of them continued to drink alcoholic beverages during the present pregnancy ($p < 0.05$) (Fig. 2).

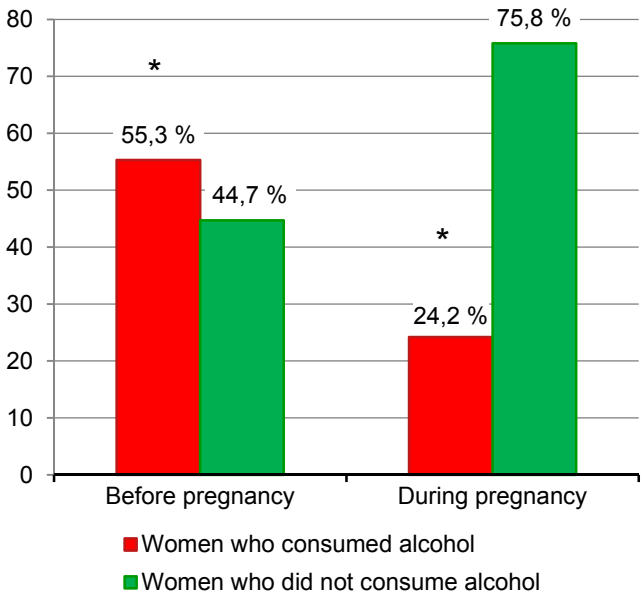

FIG. 2.
*Alcohol consumption before and during pregnancy based on a survey data: * – p < 0.05*

TABLE 1

GROUP OF PREGNANT WOMEN WHO HAD LABORATORY CONFIRMED BLOOD LEVELS OF PETH:16:0/18:1

PEth concentration:16:0/18:1 in the blood of pregnant women, ng/ml	Number of pregnant women ($N = 121$)	Doses of alcohol consumed
8 < PEth:16:0/18:1 < 45	52 % ($n = 63$)	< 1
45 ≤ PEth:16:0/18:1 < 127	31 % ($n = 38$)	≥ 1
PEth:16:0/18:1 ≥ 127	17 % ($n = 20$)	≥ 1

The data obtained show that of all women who consumed alcohol during pregnancy, 20.4 % did not stop drinking alcoholic beverages in the first trimester of pregnancy, which leads to a high risk of congenital malformations, including fetal alcohol syndrome and fetal alcohol spectrum disorders. As a result of studying the qualitative characteristics of alcohol consumption by women before and during pregnancy, it was found that before pregnancy 35.5 % of women consumed beer, 40.6 % – wine, 3.8 % – vodka. In the prenatal period, 20.7 % of pregnant women preferred wine, 13.4 % beer, and 1.2 % vodka from alcoholic beverages.

The results of the study show that almost every second pregnant woman was diagnosed with anemia, but statistically significantly more in the group of pregnant drinkers. So, in the control group, this indicator was 40.23 %, and in the group of women who consumed alcoholic beverages during pregnancy – 48.24 % ($p < 0.05$).

Of the congenital malformations in the fetus, it was found that congenital heart disease (CHD) of the fetus turned out to be significant. In the third trimester of pregnancy, according to the results of screening ultrasound examination, the diagnosis of fetal CHD was diagnosed in 9.96 % of pregnant women of the 2nd group. In the control group, this figure was 1.41 %. Thus, in fetuses of pregnant women who consumed alcoholic beverages in the prenatal period, CHD was diagnosed more often than in the control group ($p < 0.05$).

It was found that of the complications of labor, labor anomalies (LA) (discoordinated contractions of the myometrial muscle) They were statistically significantly more common ($p < 0.05$) in the group of women drinkers: in the group of non–drinkers, the frequency of LA was 3.07 %, in the group of drinkers – 6.34 %.

It was revealed that, according to the results of the analysis of the indicators of complications of the postpartum period, a statistically significant sign was uterine subinvolution. In the control group, its frequency was 11.6 %, and in the 2nd group – 19.54 % ($p < 0.05$).

It was determined that prematurity of gestational age was noted in 4.78 % of newborns in the control group and in 10.95 % of children born to drinking women ($p < 0.05$). The influence of alcohol on the degree of maturity and development of the fetus has been proven, as statistically significant differences were obtained when comparing the indicators of the 1st and 2nd groups.

THE RESULTS OF A STUDY OF WOMEN DURING PREGNANCY BASED ON LABORATORY-CONFIRMED ALCOHOL CONSUMPTION IN THE PRENATAL PERIOD

As a result of the analysis of the obstetric history, it was revealed that the parity of childbirth (the presence of childbirth in the anamnesis) it was statistically significantly more common in pregnant drinkers ($p < 0.05$). There were no statistically significant differences in other indicators ($p > 0.05$) (Table 2).

Table 3 shows the parameters characterizing the course of a real pregnancy in the study groups. As shown in the ta-

TABLE 2

OBSTETRIC HISTORY OF PREGNANT WOMEN WITH LABORATORY CONFIRMED ALCOHOL CONSUMPTION IN THE PRENATAL PERIOD

Parameters (M ± SD)	The entire sample (*N* = 318)	Group I (control): PEth:16:0/18:1 ≤ 8ng/ml (*N* = 194)	Group II (comparison): PEth:16:0/18:1 > 8 ng/ml (*N* = 121)	*p*
Delivery parity	–	2.83 ± 1.96	3.42 ± 2.35	**0.024***
	Outcome of previous pregnancies (M ± SD)			
The birth of a living child	1.21 ± 1.30	1.14 ± 1.27	1.34 ± 1.35	0.175
The birth of a stillborn child	0.02 ± 0.14	0.01 ± 0.12	0.02 ± 0.16	0.890
Spontaneous miscarriage	0.26 ± 0.55	0.22 ± 0.53	0.34 ± 0.58	0.141
Medical abortion	0.51 ± 1.08	0.42 ± 0.85	0.68 ± 1.37	0.196
Ectopic pregnancy	0.02 ± 0.18	0.01 ± 0.14	0.03 ± 0.22	0.771

Note. * – $p < 0,05$.

TABLE 3

CHARACTERISTICS OF THE PARAMETERS OF THE PRESENT PREGNANCY COURSE IN THE STUDY GROUPS

Parameters	The total number of women in the study groups, *n*/*N* (%)	Group I (control): PEth:16:0/18:1 ≤ 8ng/ml (*n* = 194), *n*/*N* (%)	Group II (comparison): PEth:16:0/18:1 > 8 ng/ml (*n* = 121), *n*/*N* (%)	*p*
Nausea, vomiting, early toxicosis	173/315 (54.92)	107/194 (55.15)	66/121 (54.55)	0.447
Anemia	177/315 (56.19)	116/194 (59.79)	61/121 (50.41)	0.103
Vaginal bleeding	32/315 (10.16)	21/194 (10.82)	11/121 (9.09)	0.642
UTS diseases	55/314 (17.52)	34/193 (17.62)	21/121 (17.36)	0.728
Increased BP	43/315 (13.65)	32/194 (16.49)	11/121 (9.09)	0.063
Fever or t > 37.8 °C	40/314 (12.74)	29/194 (14.95)	11/120 (9.17)	0.234
Diabetes mellitus	52/315 (16.51)	30/194 (15.46)	22/121 (18.18)	0.606
Swelling of the lower extremities	94/313 (30.03)	57/193 (29.53)	37/120 (30.83)	0.912
Swelling of the upper extremities	74/315 (23.49)	42/194 (21.65)	32/121 (26.45)	0.347
Candidiasis vaginitis	70/313 (22.36)	39/193 (20.21)	31/120 (25.83)	0.245

ble, in the studied groups, when comparing the indicators of pregnancy (early toxicosis, anemia, vaginal bleeding, diseases of the urinary track system (UTS), increased blood pressure (BP), fever or t > 37.8 °C, diabetes mellitus, edema of the upper and lower extremities, candidiasis vaginitis). There were no statistically significant differences ($p > 0.05$).

When analyzing the state of fetal intrauterine development, it was found that fetal intrauterine growth retardation (IUGR) was statistically significantly more common in women who drank compared with non-drinkers, which amounted to 2.6 % and 0.6 %, respectively ($p < 0.05$).

Among the complications of labor, it was revealed that preterm delivery was statistically significantly more common in the group of women who consumed alcoholic beverages in the prenatal period, which was confirmed by laboratory method, compared with the control group – 8.0 % and 4.8 %, respectively ($p < 0.05$).

Summing up the results of this study, it can be concluded that every second woman of reproductive age took alcohol before pregnancy, and 24.2 % of them continued to drink alcoholic beverages during the present pregnancy ($p < 0.05$). It was found that in the first trimester, 20.4 % of pregnant women consumed alcoholic beverages, which increases the risk of congenital malformations, including fetal alcohol syndrome and fetal alcohol spectrum disorders.

The results of the study obtained on the basis of the survey show that the following pathological conditions are statistically significantly more common in women who consumed alcohol in the prenatal period: anemia, fetal CHD, prematurity of gestational age, labor anomalies, uterine subinvolution ($p < 0.05$).

In our study, the diagnostic biomarker of alcohol consumption was PEth:16:0/18:1, which was determined in 37.11 % of pregnant women. The results of the study, based on laboratory confirmation of alcohol consumption, indicate that the parity of childbirth (the presence of childbirth in the anamnesis), fetal sound, premature birth, were statistically significantly more often determined in pregnant women with confirmed alcohol consumption in the prenatal period ($p < 0.05$).

ADVANTAGES AND LIMITATIONS OF THE STUDY

The advantage of the study is that for the first time in the Irkutsk region, a laboratory analysis method was used, in particular, the determination of alcohol bio-

markers (PEth:16:0/16:0, PEth:18:1/18:1, PEth:16:0/18:1), to confirm the fact of alcohol consumption in the prenatal period.

This study also had a number of limitations. Firstly, the study was partially based on the results of the survey, which reduces the diagnostic value of the data obtained. As mentioned above, information obtained in this way is subject to subjectivity. Based on this, biomarkers (PEth) are used to obtain an objective picture, which determine both the fact and the amount of alcohol consumed.

Secondly, for laboratory confirmation of alcohol, only a single blood sample was taken throughout pregnancy – at 38–40 weeks of gestation, which also reduces the diagnostic value of the data obtained. Due to the long half-life of alcohol consumption, PEth accumulates in the blood and can only be detected within 28 days after the last intake. Therefore, it is necessary that further studies be based on the determination of PEth at the screening time of the examination of pregnant women (in each trimester and at the end of pregnancy).

Despite the above, the conducted research has great theoretical and practical significance and will allow the use of a laboratory method to confirm the fact and amount of alcohol consumption in the practice of doctors. This will help in determining one of the most important risk factors (alcohol) during pregnancy and reduce the risk of complications of the gestational process and fetal complications.

CONCLUSION

An analysis of domestic and foreign literature, as well as the results of our study, show that the problem of alcohol consumption by women at reproductive age and during pregnancy is relevant and promising. There is a need for pregravid training, abstinence from alcohol consumption by women. It is extremely important to conduct the most extensive studies using biomarkers of maternal blood to determine the level of alcohol consumption during pregnancy throughout the gestation period, which will allow us to obtain more informative and high-quality results and further introduce this method into the practical activities of doctors, in particular obstetricians and gynecologists. From the point of view of the medical and social significance of the current problem, further studies of the mechanisms of alcohol's effect on the fetus and effective preventive measures should be developed.

Every pregnant woman should realize that alcohol is toxic to a growing fetus throughout the entire 40 weeks of pregnancy and that there is no safe dose of alcohol during pregnancy!

Conflict of interest

The authors of this article declare the absence of a conflict of interest.

REFERENCES

1. World Health Organization. *Global status report on alcohol and health.* 2018. URL: https://www.who.int/publications/i/item/9789241565639 [date of access: 11.10.2023].

2. Popova S, Lange S, Shield K, Mihic A, Chudley AE, Mukherjee RAS, et al. Comorbidity of fetal alcohol spectrum disorder: A systematic review and meta-analysis. *Lancet.* 2016; (10022): 978-987. doi: 10.1016/S0140-6736(15)01345-8

3. Marianian A, Atalyan A, Bohora S, Darenskaya M, Grebenkina L, Kolesnikova L, et al. The effect of low alcohol consumption during pregnancy on the lipid peroxidation-antioxidant defense system of women, their alcohol-exposed infants, and growth, health, and developmental outcomes. *Birth Defects Res*. 2019; 1: 40-53. doi: 10.1002/bdr2.1582

4. O'Leary C, Lawrence D, Hafekost K, Zubrick SR, Bower C. Maternal alcohol-use disorder and child outcomes. *Pediatrics.* 2020; 145(3): e20191574. doi: 10.1542/peds.2019-1574

5. Protopopova NV, Kolesnikova LI, Ilyin VP. *Metabolism and hemodynamics in pregnant women with arterial hypertension.* Novosibirsk: Nauka; 2000. (In Russ.). [Протопопова Н.В., Колесникова Л.И., Ильин В.П. *Метаболизм и гемодинамика у беременных с артериальной гипертензией*. Новосибирск: Наука; 2000].

6. Balachova TN, Isurina GL, Skitnevskaya LV, Bard D, Tsvetkova LA, Volkova EN, et al. Alcohol consumption among pregnant and non-pregnant women in Russia: Evidence for prevention. *Acta biomedica scientifica.* 2018; 3(3): 59-68. (In Russ.). [Балашова Т.Н., Исурина Г.Л., Скитневская Л.В., Бард Д., Цветкова Л.А., Волкова Е.Н., и др. Изучение употребления алкоголя беременными и небеременными женщинами в России. *Acta biomedica scientifica.* 2018; 3(3): 59-67]. doi: 10.29413/ABS.2018-3.3.9

7. Ikehara S, Kimura T, Kakigano A, Sato T, Iso H, Japan Environment Children's Study Group. Association between maternal alcohol consumption during pregnancy and risk of preterm delivery: The Japan Environment and Children's Study. *BJOG.* 2019; 126(12): 1448-1455. doi: 10.1111/1471-0528.15899

8. Senkevich OA, Tsyganova IV, Sirotina ZV. Causes of premature birth and physical development of premature newborns in Khabarovsk. *Clinical Practice in Pediatrics*. 2006; 1(2): 70-72. (In Russ.). [Сенькевич О.А., Цыганова И.В., Сиротина З.В. Причины преждевременных родов и физическое развитие недоношенных новорожденных, родившихся в Хабаровске. *Вопросы практической педиатрии.* 2006; 1(2): 70-72].

9. Chang G. Alcohol-screening instruments for pregnant women. *Alcohol Res Health*. 2001; 25(3): 204-209.

10. Sampson PD, Streissguth AP, Bookstein FL, Little RE, Clarren SK, Dehaene P, et al. Incidence of fetal alcohol syndrome and prevalence of alcohol-related neurodevelopmental disorder. *Teratology.* 1997; 56(5): 317-326. doi: 10.1002/(SICI)1096-9926(199711)56:5<317::AID-TERA5>3.0.CO;2-U

11. Balachova T, Bonner B, Chaffin M, Bard D, Isurina G, Tsvetkova L, et al. Women's alcohol consumption and risk for alcohol-exposed pregnancies in Russia. *Addiction.* 2012; 107(1): 109-117. doi: 10.1111/j.1360-0443.2011.03569.x

12. Petukhov AE, Nadezhdina AV, Bogstrand ST, Bryun EA, Ramenskaia GV, Koshkina EA, et al. Phosphatidylethanol as the new alcohol abuse biomarker. *Narcology.* 2017; 2: 42-47. (In Russ.). [Петухов А.Е., Надеждина А.В., Богстранд С.Т., Брюн Е.А., Рамен-

ская Г.В., Кошкина Е.А., и др. Фосфатидилэтанол как биомаркер злоупотребления алкоголем. *Наркология*. 2017; 2: 42-47].

13. Balashova TN, Volkova EN, Skitnevskaya LV, Kosykh EA. Peculiarities of alcohol consumption by women of childbearing age in modern Russia. *Tambov University Review. Series: Humanities.* 2012; 1(105): 118-123. (In Russ.). [Балашова Т.Н., Волкова Е.Н., Скитневская Л.В., Косых Е.А. Особенности употребления алкоголя женщинами детородного возраста в Современной России. *Вестник Тамбовского университета. Серия: Гуманитарные науки*. 2012; 1(105): 118-123].

14. Marianian AYu, Kalkova AN. A current view on the alcohol-related teratogenic effects during pregnancy. Potential preventive measures. *Obstetrics, Gynecology and Reproduction.* 2022; 16(1): 48-57. (In Russ.). [Марянян А.Ю., Калькова А.Н. Современный взгляд на тератогенное влияние алкоголя при беременности. Возможные меры профилактики. *Акушерство, гинекология и репродукция*. 2022; 16(1): 48-57]. doi: 10.17749/2313-7347/ob.gyn.rep.2021.254

15. Marianian AYu, Kalkova AN, Akudovich NV. Influence of alcohol consumption on the bioelement status of pregnant women in the prenatal period. *Obstetrics and Gynecology.* 2021; 10: 21-30. (In Russ.). [Марянян А.Ю., Калькова А.Н., Акудович Н.В. Влияние алкоголя на биоэлементный статус беременных женщин, употребляющих алкоголь в пренатальном периоде. *Акушерство и гинекология*. 2021; 10: 21-30]. doi: 10.18565/aig.2021.10.21-30

16. Kolesnikova LI, Darenskaya MA, Kolesnikov SI. Free radical oxidation: A pathophysiologist's view. *Bulletin of Siberian Medicine.* 2017; 16(4): 16-29. (In Russ.). [Колесникова Л.И., Даренская М.А., Колесников С.И. Свободнорадикальное окисление: взгляд патофизиолога. *Бюллетень сибирской медицины.* 2017; 16(4): 16-29]. doi: 10.20538/1682-0363-2017-4-16-29

17. Burina EA, Marianian AY. Psychological aspects of fetal alcohol syndrome prevention in pregnant women of childbearing age. *Acta biomedica scientifica.* 2018; 3(3): 149-154. (In Russ.). [Бурина Е.А., Марянян А.Ю. Психологические аспекты профилактики фетального алкогольного синдрома у беременных женщин репродуктивного возраста. *Acta biomedica scientifica.* 2018; 3(3): 149-154]. doi: 10.29413/ABS.2018-3.3.23

18. Bandoli G, Coles CD, Kable JA, Wertelecki W, Yevtushok L, Zymak-Zakutnya N, et al. Patterns of prenatal alcohol use that predict infant growth and development. *Pediatrics*. 2019; 143(2): e20182399. doi: 10.1542/peds.2018-2399

19. Moore EM, Glass L, Infante MA, Coles CD, Kable JA, Jones KL, et al. Cross-sectional analysis of spatial working memory development in children with histories of heavy prenatal alcohol exposure. *Alcohol Clin Exp Res*. 2021; 45(1): 215-223. doi: 10.1111/acer.14506

20. Myagkova MA, Pushkina VV, Petrochenko SN. Determination of markers of chronic alcohol abuse using capillary electrophoresis. *International Journal of Applied and Basic Research.* 2015; 12(9): 1640-1643. (In Russ.). [Мягкова М.А., Пушкина В.В., Петроченко С.Н. Определение маркеров хронического злоупотребления алкоголем методом капилярного электрофореза. *Международный журнал прикладных и фундаментальных исследований.* 2015; 12(9): 1640-1643].

21. Khapkina AV, Mikhailov AV, Ilyukhin DM, Zheltkova LA. Use of laboratory biomarkers in the diagnostics of chronic abuse of alcohol. *Proceedings of the Tula State University. Natural Sciences.* 2019; 4: 45-55. (In Russ.). [Хапкина А.В., Михайлова А.В., Илюхина Д.М., Желткова Л.А. Использование лабораторных биомаркеров в диагностике хронического злоупотребления алкоголя. *Известия Тульского государственного университета. Естественные науки.* 2019; 4: 45-55].

22. Hahn JA, Murnane PM, Vittinghoff E, Muyindike WR, Emenyonu NI, Fatch R, et al. Factors associated with phosphatidylethanol (PEth) sensitivity for detecting unhealthy alcohol use: An individual patient data meta-analysis. *Alcohol Clin Exp Res.* 2021; 45(6): 1166-1187. doi: 10.1111/acer.14611

23. Bakhireva LN, Leeman L, Savich RD, Cano S, Gutierrez H, Savage DD, et al. The validity of phosphatidylethanol in dried blood spots of newborns for the identification of prenatal alcohol exposure. *Alcohol Clin Exp Res*. 2014; 38(4): 1078-1085. doi: 10.1111/acer.12349

Information about the authors

Anait Yu. Marianian – Dr. Sc. (Med.), Leading Research Officer at the Laboratory of Socially Significant Problems of Reproductive Medicine, Scientific Centre for Family Health and Human Reproduction Problems; Associate Professor at the Department of Obstetrics and Gynecology, Irkutsk State Medical Academy of Postgraduate Education – Branch Campus of the Russian Medical Academy of Continuing Professional Education, e-mail: anait_24@mail.ru, iphr@sbamsr.irk.ru, https://orcid.org/0000-0002-9544-2172

Anastasia N. Kalkova – Postgraduate, Clinical Research Assistant at the Laboratory of Socially Significant Problems of Reproductive Medicine, Scientific Centre for Family Health and Human Reproduction Problems, e-mail: Kalkova_Nastya@mail.ru, https://orcid.org/0000-0002-7626-020X

Maria A. Rashidova – Cand. Sc. (Biol.), Research Officer at the Laboratory of Physiology and Pathology of the Endocrine System, Scientific Centre for Family Health and Human Reproduction Problems, e-mail: rashidovama@mail.ru, https://orcid.org/0000-0003-4730-5154

Natalya V. Semenova – Dr. Sc. (Biol.), Leading Research Officer at the Laboratory of Pathophysiology, Scientific Centre for Family Health and Human Reproduction Problems, e-mail: natkor_84@mail.ru, https://orcid.org/0000-0002-6512-1335

Alexey V. Belskikh – Cand. Sc. (Chem.), Engineer at the Laboratory of Personalized Medicine, Scientific Centre for Family Health and Human Reproduction Problems, e-mail: alex590750@yandex.ru, https://orcid.org/0000-0003-3678-7274

Elena V. Belyaeva – Cand. Sc. (Biol.), Research Officer at the Laboratory of Personalized Medicine, Scientific Centre for Family Health and Human Reproduction Problems, e-mail: belyeva_irk@mail.ru, https://orcid.org/0000-0001-6050-5287

Alexandra Yu. Sambyalova – Junior Research Officer at the Laboratory of Personalized Medicine, Scientific Centre for Family Health and Human Reproduction Problems, e-mail: sambialova95@mail.ru, https://orcid.org/0000-0001-5790-6282

Alina V. Atalyan – Cand. Sc. (Biol.), Senior Research Officer at the Laboratory of Socially Significant Problems of Reproductive Medicine, Scientific Centre for Family Health and Human Reproduction Problems, e-mail: alinaa@mail.ru, https://orcid.org/0000-0002-3407-9365

Daria P. Tiumentceva – Master of Psychology, Clinical Research Assistant at the Laboratory of Socially Significant Problems of Reproductive Medicine, Scientific Center for Family Health and Human Reproduction, e-mail: markova-darya@inbox.ru, https://orcid.org/0000-0002-7926-5241

Alena B. Ilyina – Neurologist, Volunteer at the Laboratory of Socially Significant Problems of Reproductive Medicine, Scientific Centre for Family Health and Human Reproduction Problems, e-mail: alenaiiilina_24@gmail.com, https://orcid.org/0000-0002-5444-5086

Lyubov I. Kolesnikova – Dr. Sc. (Med.), Professor, Member of the RAS, Scientific Advisor, Scientific Centre for Family Health and Human Reproduction Problems, e-mail: iphr@sbamsr.irk.ru, https://orcid.org/0000-0003-3354-2992