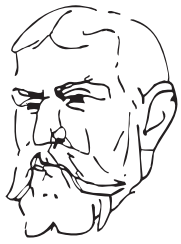
Wiadomości Lekarskie

Official journal of the Polish Medical Association



Memory of
dr Władysław
Biegański

VOLUME LXXIV, ISSUE 10 PART 1, OCTOBER 2021

Since 1928

ALUNA Publishing House

Wiadomości Lekarskie is abstracted and indexed in: PUBMED/MEDLINE, SCOPUS, EMBASE, INDEX COPERNICUS, POLISH MINISTRY OF EDUCATION AND SCIENCE, POLISH MEDICAL BIBLIOGRAPHY

Wiadomości Lekarskie
monthly journal

You can order the subscription for the journal from Wydawnictwo Aluna by:
prenumerata@wydawnictwo-aluna.pl
Wydawnictwo Aluna
Z.M. Przesmyckiego 29
05-510 Konstancin-Jeziorna
Poland

Place a written order first.

If you need, ask for an invoice.
Payment should be done to the following account of the Publisher:
account number for Polish customers (PLN):
82 1940 1076 3010 7407 0000 0000
Credit Agricole Bank Polska S. A., SWIFT: AGRIPLPR

account number for foreign customers (EURO):
57 2490 0005 0000 4600 7604 3035
Alior Bank S. A.: SWIFT: ALBPPLPW

Subscription of twelve consecutive issues (1-12):
Customers in Poland: 480 PLN/year
Customers from other countries: 420 EURO/year

Wiadomości Lekarskie

Distribution and Subscriptions:
Bartosz Guterman prenumerata@wydawnictwo-aluna.pl
Graphic design / production:
Grzegorz Sztank www.red-studio.eu

Publisher:
ALUNA Publishing House
ul. Przesmyckiego 29,
05-510 Konstancin – Jeziorna
www.wydawnictwo-aluna.pl
www.wiadomoscilekarskie.pl
www.wiadlek.pl

FOR AUTHORS

1. The monthly "Wiadomości Lekarskie" Journal is the official journal of the Polish Medical Association. Original studies, review papers as well as case reports are published.
2. The publication of the manuscript in "Wiadomości Lekarskie" is paid. The cost of publishing the manuscript is PLN 1,000 plus 23% VAT (for foreign authors 250 Euro). If the first author of the manuscript is a member of the Editorial Board, we do not charge a fee for printing the manuscript, and if she or he is the next co-author – the fee is PLN 500 plus 23% VAT. The publisher issues invoices. The fee should be paid after receiving positive reviews, and before publishing the manuscript. Membership of the Polish Medical Association with documented paid membership fees for the last 3 years is also the exempt from publication fee.
3. Only papers in English are accepted for publication. The editors can help in finding the right person for translation or proofreading.
4. Papers should be sent to the editor via the editorial panel (Editorial System), available on the journal's website at https://www.wiadlek.pl. In order to submit an article, free registration in the system is necessary. After registration, the author should follow the instructions on the computer screen.
5. All editorial work is under control and using the editorial panel. This applies in particular to sending manuscripts, correspondence between the editor and author and the review process. In special cases, the editor may agree to contact outside the panel, especially in case of technical problems.
6. Acceptable formats for individual elements of the article are as follows:
   A) Content of the article – doc, docx, rtf, odt.
   B) Tables – doc, docx, rtf, odt
   C) Figures – JPG, GIF, TIF, PNG with a resolution of at least 300 dpi
   D) Captions for figures and tables.
   These elements are sent to the editor separately using the editorial panel. References and article metadata such as titles, keywords, abstracts etc. are supplemented by the author manually in the editorial panel in appropriate places.
7. The volume of original papers – including figures and references – must not exceed 21,600 characters (12 pages of typescript), and review papers – up to 28,800 characters (16 pages).
8. The original manuscript should have the following structure: Introduction, Aims, Material and methods, Results, Discussion and Conclusions which cannot be a summary of the manuscript.
9. When using abbreviations, it is necessary to provide the full wording at the first time they are used.
10. In experimental manuscripts in which studies on humans or animals have been carried out, as well as in clinical studies, information about obtaining the consent of the Ethics Committee should be included.
11. The Editorial Board follow the principles contained in the Helsinki Declaration as well as in the Interdisciplinary Principles and Guidelines for the Use of Animals in Research, Testing and Education, published by the New York Academy of Sciences Ad Hoc Committee on Animal Research. All papers relating to animals or humans must comply with ethical principles set out by the Ethics Committee.
12. The abstract should contain 150-250 words. Abstracts of original, both clinical and experimental, papers should have the following structure: Aims, Material and methods, Results, Conclusions. Do not use abbreviations in the title or the abstract. The abstract is pasted or rewritten by the authors into the appropriate field in the application form in the editorial panel.
13. Keywords (3-5) should be given according to MeSH (Medical Subject Headings Index Medicus catalogs – http://www.nim.nih.gov.mesh/MBrower.html). Keywords cannot be a repetition of the title of the manuscript.
14. Illustrative material may be black and white or color photographs, clearly contrasting or drawings carefully made on a white background. With the exception of selected issues, the Journal is printed in shades of gray (black and white illustrations).
15. The content of the figures, if present (e.g. on the charts), should also be in English
16. Links to all tables and figures (round brackets) as well as references (square brackets) the author must place in the text of the article.
17. Only references to which the author refers in the text should be included in the list of references ordered by citation. There should be no more than 30 items in original papers and no more than 40 items in review papers. Each item should contain: last names of all authors, first letters of first names, the title of the manuscript, the abbreviation of the journal title (according to Index Medicus), year, number, start and end page. For book items, please provide: author's (authors') last name, first letter of the first name, chapter title, book title, publisher, place and year of publication. It is allowed to cite websites with the URL and date of use of the article, and if possible the last names of the authors. Each literature item should have a reference in the text of the manuscript placed in square brackets, e.g. [1], [3-6]. Items should be organized as presented in Annex 1 to these Regulations.
18. When submitting the article to the editor, the authors encloses a statement that the work was not published or submitted for publication in another journal and that they take full responsibility for its content, and the information that may indicate a conflict of interest, such as:
    1. financial dependencies (employment, paid expertise, consulting, ownership of shares, fees),
    2. personal dependencies,
    3. academic and other competition that may affect the substantive side of the work,
    4. sponsorship of all or part of the research at the stage of design, collection, analysis and interpretation of data, or report writing.
19. The authors in the editorial panel define their contribution to the formation of scientific work according to the following key:
    A – Work concept and design
    B – Data collection and analysis
    C – Responsibility for statistical analysis
    D – Writing the article
    E – Critical review
    F – Final approval of the article.
20. In the editorial panel along with the affiliation, the author also gives her or his ORCID number.
21. The Journal is reviewed in double, blind review mode. The submitted papers are evaluated by two independent reviewers and then qualified for publishing by the Editor-in-Chief. Reviews are anonymous. The authors receive critical reviews with a request to correct the manuscript or with a decision not to qualify it for publishing. The procedure for reviewing articles is in line with the recommendations of the Ministry of Science and Higher Education contained in the paper "Good practices in review procedures in science" (Warsaw 2011). Detailed rules for dealing with improper publishing practices are in line with COPE guidelines. The publishing review rules are in the Review Rules section.
22. Each manuscript is subject to verification in the anti-plagiarism system.
23. Manuscripts are sent for the author's approval. The author's corrections should be sent within the time limit indicated in the system. No response within the given deadline is tantamount to the author's acceptance of the submitted material. In special cases, it is possible to set dates individually.
24. Acceptance of the manuscript for publishing means the transfer of copyright to the Aluna Publishing House (Aluna Anna Łuczyńska, NIP 5251624918).
25. Articles published on-line and available in open access are published under Creative Common Attribution-Non Commercial-No Derivatives 4.0 International (CC BY-NC-ND 4.0) allowing to download articles and share them with others as long as they credit the authors and the publisher, but without permission to change them in any way or use them commercially.
26. The authors receive a free PDF of the issue in which their mansucript is enclosed, and on request – a printed copy. The printed copy is sent to the address indicated by the authors as the correspondence address.
27. Manuscripts not concordant with the above instructions will be returned to be corrected.
28. The editors do not return papers which have not been commissioned.
29. The editors take no responsibility for the contents of the advertisements.

CONTENTS

ORIGINAL ARTICLES

ORIGINAL ARTICLE

EVALUATION OF HORMONAL FUNCTION IN WOMEN WITH CERVICAL INSUFFICIENCY AND INFERTILITY IN THE HISTORY

DOI: 10.36740/WLek202110109

Oksana M. Perkhulyn[1], Lyudmyla V. Pakharenko[1], Vladyslav S. Sukhin[2], Oleksiy V. Saltovskiy[3], Viktoriia M. Kovalchuk[4], Hanna I. Hranovska[2], Olha V. Kravchenko[5]

[1]IVANO-FRANKIVSK NATIONAL MEDICAL UNIVERSITY, IVANO-FRANKIVSK, UKRAINE
[2]INSTITUTE OF MEDICAL RADIOLOGY OF S. P. GRIGORIEV NATIONAL ACADEMY OF MEDICAL SCIENCES OF UKRAINE, UKRAINE
[3]KHARKIV NATIONAL MEDICAL UNIVERSITY, UKRAINE
[4]MEDICAL CENTER "EVVIVA", UKRAINE
[5]POLTAVA REGIONAL CLINICAL ONCOLOGICAL DISPENSARY OF POLTAVA REGIONAL COUNCIL, UKRAINE

ABSTRACT

The aim: To assess the levels of hormones in women with cervical insufficiency and infertility in the history in the II trimester of gestation.

Materials and methods: 120 pregnant women with cervical insufficiency and anovulatory infertility in the history were examined in the II trimester of gestation: in the I group (60 persons) pregnancy occurred after hormonal treatment of infertility, in the II group (60 individuals) – after in vitro fertilization. 30 pregnant women without cervical insufficiency and a history of infertility were controls. The levels of estradiol, progesterone, placental lactogen, prolactin and cortisol were determined in the blood serum.

Results: The concentration of maternal progesterone was lower in the persons in the I group on 12.36 %, in the II group – on the 15.37 % ($p=0.03$) compared to the healthy women. Cortisol and prolactin amounts were statistically higher in I and II groups ($p<0.001$) than in controls. While the levels of estradiol and placental lactogen were slightly less in the subjects with cervical insufficiency and a history of anovulatory infertility compared to the healthy women.

Conclusions: In pregnant women with cervical insufficiency and a history of anovulatory infertility in the II trimester of gestation there are decrease progesterone level and high prolactin and cortisol concentrations in blood serum. The changes in estradiol and placental lactogen amounts are not significant compared to healthy women.

KEY WORDS: cervical insufficiency, anovulatory infertility, hormones

Wiad Lek. 2021;74(10 p.I):2412-2416

INTRODUCTION

Physiological pregnancy and labor are one of the main priority aspects of modern obstetrics. Nowadays the percent of the complications during pregnancy growths up that leads to the negative obstetrical and perinatal outcomes. According to the data of the World Health Organization 15 million newborns are born before 37 completed weeks of gestation, and the frequency of preterm birth varieties from 5 % to 18 % of babies born [1]. There are different risk factors of prematurity – gestational complications such as placental disorders, diabetes, hypertension, cervical insufficiency (CI), treatment of infertility with additional reproductive technology (ART), such as in vitro fertilization (IVF), donor oocytes and/or thawed embryos [2]. Thus, especially difficulties with the gestational period have the women with a history of infertility. In Ukraine, more than 15 % of married couples are infertile [3]. Such women usually need specific and complex medical treatment for pregnancy occurs. So, the correction of these hormonal problems can lead to pregnancy, but such gestation is usually complicated. Pregnancy loss, missed abortion, miscarriage, premature labor, CI, negative perinatal outcomes are closely related to pregnancies after ART [4, 5].

Cervical insufficiency is one of the reasons for preterm labor and its rate is approximately 1 % [6] but its frequency is much higher in the patients after IVF – up to 9.7-14.4 % [7]. Generally, most of the cases of CI development are connected with organic pathology – cervical trauma during previous labor, gynecological manipulations on the cervix. But also hormonal dysbalance, which is present in the women with anovulatory infertility, can play an important role in the genesis of functional CI.

THE AIM

The aim of the study was to assess the levels of hormones in women with cervical insufficiency and infertility in the history in the II trimester of gestation.

MATERIALS AND METHODS

We examined 120 pregnant women with cervical insufficiency in the term of 19-22 weeks of gestation. The diagnosis of CI was based according to the transvaginal ultrasound criteria: the length of the cervix is 25 mm and less, V-shaped transformation of the cervical canal

Table I. Reproductive characteristics of observed groups (abs., (%))

Parameter	I group (n=60)	II group (n=60)	Control group (n=30)
Age:			
till 19 years	-	-	1 (3.33)
19-34 years	55 (91.67)	50 (83.33)	26 (86.67)
35 and more years	5 (8.33)	10 (16.67)	3 (10.00)
Pregnancy:			
the first	29 (48.33)	39 (65.00)	17 (56.67)
the second	26 (43.34)	10 (16.67)	8 (26.67)
the third and more	5 (8.33)	11 (18.33)	5 (16.66)
Labor:			
null	41 (68.33)	55 (91.67)	19 (63.33)
one	17 (28.34)	5 (8.33)	8 (26.67)
two and more	2 (3.33)	-	3 (10.00)
Miscarriage	7 (11.67)	9 (15.00) •	2 (6.67)
Missed abortion	3 (5.00)	3 (5.00)	-
Molar pregnancy	1 (1.67)	1 (1.67)	-
Induced abortion	3 (5.00)	5 (8.33) °	2 (6.67)
Ectopic pregnancy	1 (1.67)	5 (8.33)	-

Notes: • - three of nine persons had two miscarriages; ° - one from five women had two induced abortions.

Table II. The levels of hormones in the blood serum in examined patients

Hormone	I group (n=60)	II group (n=60)	Control group (n=30)
Estradiol, pg/ml	9414.18±182.39	9243.12±199.64	9826.43±286.38
Progesterone, ng/ml	46.29±1.38	44.70±1.93*	52.82±3.18
Placental lactogen, mg/l	2.64±0.09	2.53±0.11	2.86±0.19
Prolactin, ng/ml	231.02±7.91*	269.07±10.39*	162.33±10.76
Cortisol, nmol/L	534.57±18.22*	583.56±17.59*	409.04±25.09

Note: * – the statistical significance of differences of indicator relative to the control group ($p<0.05$).

on 40 % and more [8]. All these persons in anamnesis had infertility associated with anovulation. According to the type of the treatment of infertility the women with CI were divided into two groups. Thus, the I group consisted of 60 patients with CI and infertility in whom the pregnancy occurred after hormonal treatment (ovarian stimulation with clomiphene citrate, gonadotropin-releasing hormone agonists). 60 women with CI and infertility who became pregnant after the use of ART – in vitro fertilization – formed the II group. In the I trimester of pregnancy persons in the I group received vaginal micronized progesterone 200 mg ones a day, in the II group – 400 mg. Infertility was diagnosed according to the recommendations of the World Health Organization [9]. The control group involved 30 women with physiological pregnancy and without a history of infertility. Inclusion criteria: singleton pregnancy, CI, infertility associated with anovulation, written consent of the patient. Exclusion criteria: multiple pregnancy, antiphospholipid syndrome, thrombophilia, pregnancy complicated with ovarian hyperstimulation syndrome, cytogenetic causes of pregnancy loss induced by IVF, male infertility, connective tissue dysplasia, increased risk of chromosomal fetal abnormalities according to first or second genetic screening. The study was carried in City Clinical Perinatal Centre (Ivano-Frankivsk, Ukraine) and approved by the Ethics Commission at Ivano-Frankivsk National Medical University (protocol 97/17, 19.10.2017).

ELISA method was used to determine hormones in the serum blood in pregnant women. The levels of hormones were studied in the term of the 19-22 weeks of pregnancy after a confirmed diagnosis of CI. The concentrations of estradiol, progesterone, placental lactogen, prolactin, and cortisol were determined with reagents "IMMULITE 2000 Estradiol", "IMMULITE 2000 Progesterone", "IMMULITE 2000 Placental lactogen", "IMMULITE 2000 Prolactin" and "IMMULITE 2000 Cortisol" respectively.

Statistical data were analyzed by the program Statistica 6.0. We calculated arithmetic mean value, average standard error, criterion χ^2 (Yates corrected Chi-square), the nonparametric Mann-Whitney test was used to compare two independent groups by a single feature. The difference between the values was considered significant by $p\leq0.05$.

RESULTS

Our data demonstrated that the average age of women with the history of infertility after IVF (31.42±0.56 years,

p<0.001) was significantly higher compared to control persons (27.30±0.92 years). While in the II group there was no considerable difference in average age of examined patients (29.07±0.59 years) compared to controls. Also, there was no distinction in the age structure between individuals of all groups (table I). Persons of active reproductive age (20-34 years old) predominated in all groups. The number of primigravida subjects over multigravida ones was more in the II and control groups, multigravida women were in majority in the I group, but the difference between individuals with the first pregnancy and the second or more pregnancies was not significant. At the same time, 55 (91.67 %) pregnant women with CI after IVF were going to deliver at the first time, that was in 1.45 and 1.34 times more than in control group (63.33 %; χ^2=9.13, p=0.003) and in the I group (68.33 %; χ^2=8.80, p=0.003) respectively. In the I group primary infertility was diagnosed in 29 (48.33 %) individuals, secondary one – in 31 (51.67 %), in the II group – 39 (65.00 %) and 21 (35.00 %) women respectively.

Endometriosis was the most spread gynecological pathology among the patients with the history of infertility – 22 (36.67 %) women in the I group and 29 (48.33 %) subjects in the II. In the I group hyperprolactinemia was in the second place among gynecological diseases – 19 (31.67 %) individuals, 10 (16.67 %) women had diminished ovarian reserve, 9 (15.00 %) – thyroid diseases, 3 (5.00 %) – uterine myoma. In the II group besides endometriosis, 23 (38.33 %) patients were diagnosed polycystic ovary syndrome, 16 (26.67 %) – diminished ovarian reserve, 7 (11.67 %) – hyperprolactinemia, 5 (8.33 %) – uterine myoma and 2 (3.33 %) – pathology of the thyroid gland. Only 2 (6.67 %) controls persons had endometriosis.

It was found some variations in the concentrations of hormones between control persons and women in the I and II groups (table II). The level of estrogen and placental lactogen in the blood serum in the patients with CI and infertility in both groups was slightly less than in healthy subjects. The amount of progesterone was lower in individuals in the I group on 12.36 %, in the II – on the 15.37 % (p=0.03) compared to the healthy persons. The most significant changes related to the levels of cortisol and prolactin. So, the concentration of prolactin was higher in the women in the I group on 42.32 % (p<0.001), in the II group – on the 65.75 % (p<0.001) compared to the control persons. A similar trend observed regarding the amount of cortisol. Its level was on the 30.69 % (p<0,001) and 42.67 % (p<0.001) more in the I and II group respectively compared to the control individuals.

DISCUSSION

Numerous researches indicate the hormonal changes in the women after ART in the I trimester of pregnancy compared to spontaneous pregnancy. Thus, Vygivska LM and Nykoniuk TR found that the rate of pregnancy loss in the patients with endocrine infertility was determined in 4.5 and 5.8 times more often compared with the subjects with tubal infertility and male infertility respectively [10]. They estimated that in the women with endocrine infertility and ART the concentration of estradiol in blood serum in the I trimester of gestation was in 2 times higher compared to the women without infertility and use of ART, in individuals with tubal infertility – in 1.6, male infertility – 1.3 times more than in controls. The authors associated such hyperestrogenism with the use of gonadotropin-releasing hormone agonists and human menopause gonadotropins for ovarian stimulation. At the same time, the level of progesterone was slightly less in subjects with infertility that can be explained that the pregnant women with ART take progesterone drugs in the I trimester of gestation [10]. However, individuals after ART have higher cortisol level at the beginning of gestation compared with healthy women with spontaneous conceived [11]. Furthermore, according to the data of Vygivska LM et al. the amount of cortisol was significantly greater in the I, II, III trimester of gestation in the pregnant persons after ART compared to control individuals (p<0.05), as well as prolactin concentration, which was higher in such patients during the whole gestational period (p<0.05). The scientists believe that such changes in the amount of theses hormones are connected with increased level of state and trail anxiety. Grossi E. et al. studied the concentrations of 17β-estradiol and progesterone in venous blood of women with spontaneous singleton pregnancy between 5^{+0} and 13^{+6} weeks of gestation. Their results indicate the presence of specific week variations of 17β-estradiol in the I trimester that can be helpful for assessment of the course of twin gestation and pregnancy after ART [12]. It is known that there is a higher concentrations of β-chorionic gonadotropin and estradiol in maternal blood samples by twin pregnancy compared to singleton pregnancy after the use of ART in the first trimester of gestation [13].

Cervical insufficiency is mostly diagnosed in the II trimester of gestation, so, the results of hormonal variations in patients with CI commonly regard the second part of pregnancy (II or the III trimester). Impairment of the cervix obstructive function is also relative to the variations of estradiol and progesterone in the blood serum in pregnant women [14]. Estradiol level in the persons with CI in the II and III trimesters was correlated to the control indices of the physiological pregnancy. However, the progesterone concentration was almost in 2 times less compared to the individuals with normal cervical obstructive function. Such differences in the concentrations of the hormones lead to relative hypoprogesteronemia [14, 15].

According to the research of Patil AS et al. the maternal amount of progesterone and its metabolites, especially 11-deoxycorticosterone, may have meaning in the development of spontaneous preterm delivery and increases its risk. It was found that the concentration of deoxycorticosterone at the end of the I trimester and the beginning of the II trimester was associated with spontaneous delivery until 32 weeks

of gestation. The ratio of 11-deoxycorticosterone / 16-alpha-hydroxyprogesterone was higher in women with preterm labor until 32 weeks [16].

We did not find scientific publications about estradiol, progesterone, placental lactogen, prolactin and cortisol concentrations in blood serum in pregnant women in the II trimester of gestation, who conceived after anovulatory infertility and were diagnosed cervical insufficiency. So, the results of our research demonstrated that in the II trimester of gestation the there is a lower concentration of progesterone in the pregnant women with CI and infertility in the history, especially in patients conceived after IVF ($p<0.05$), compared to controls, that corresponds to the data of other scientists. But it's worth mentioning that such results of progesterone concentration were obtained despite the fact that patients in the II group received progesterone drugs. Also, we found the tendency to decrease of placental lactogen amount in women with CI and infertility in the history. The higher levels of cortisol and prolactin in blood serum in women with CI and infertility are consistent with other studies that demonstrate the similar increased parameters in patients who have CI, as well in pregnant persons after the use of ART. According to the results of this research it is worth to discuss the possibility to prolong to use vaginal progesterone in the II trimester of gestation in women, who conceived after anovulatory infertility, as well as about additional psychological support for decrease of stress-related hormones such as prolactin and cortisol.

CONCLUSIONS

In the II trimester of gestation the concentration of progesterone in blood serum of pregnant women with cervical insufficiency and anovulatory infertility in the history, expressly in persons after IVF, is significantly lower compared to persons without cervical incompetence and infertility and amounts of prolactin and cortisol are significantly higher. At the same time, there was no pronounced difference between levels of estradiol and placental lactogen in women with cervical insufficiency and anovulatory infertility and controls, but there is a trend to decrease of these hormones in the II trimester.

REFERENCES

1. World Health Organization. Preterm birth. https://www.who.int/news-room/fact-sheets/detail/preterm-birth. [Accessed September 8, 2019].
2. Luke B., Brown M.B., Wantman E. et al. Risk of prematurity and infant morbidity and mortality by maternal fertility status and plurality. J Assist Reprod Genet. 2019;36(1):121-138. doi: 10.1007/s10815-018-1333-z.
3. Vspomogatel'nye reproduktivnye tekhnologii. Opyt ispol'zovaniya VRT v SSHA, Evrope, Izraile i Ukraine [Assisted reproductive technologies. Experience of the use of ART in USA, Europe, Israel and Ukraine]. Slovo o zdorov'e. 2017; 2 (8): 6–10. (In Russian).
4. Luke B. Pregnancy and birth outcomes in couples with infertility with and without assisted reproductive technology: with an emphasis on US population-based studies. Am J Obstet Gynecol. 2017;217(3):270-281. doi: 10.1016/j.ajog.2017.03.012.
5. Stern J.E., Liu C.L., Cabral H.J. et al. Birth outcomes of singleton vaginal deliveries to ART-treated, subfertile, and fertile primiparous women. J Assist Reprod Genet. 2018;35(9):1585-1593. doi: 10.1007/s10815-018-1238-x.
6. Brown R., Gagnon R., Delisle M.F. Cervical insufficiency and cervical cerclage. J Obstet Gynaecol Can. 2019;41(2):248-263. doi: 10.1016/j.jogc.2018.11.028.
7. Trifonova N.S., Zhukova E.V., Grineva A.M. et al. Klinicheskie osobennosti techeniya beremennosti, rodov i perinatal'nye iskhody u zhenshchin posle ekstrakorporal'nogo oplodotvoreniya s primeneniem donorskih ovocitov [Clinical features of the course of pregnancy, labor, delivery, and perinatal outcomes in women after in vitro fertilization using donor oocytes]. Rossijskij vestnik akushera-ginekologa. 2017; 1:46-52. (In Russian).
8. Klinichnyi protokol «Nevynoshuvannia vahitnosti». Nakaz №624 Ministerstva okhorony zdorovia Ukrainy vid 03.11.2008. [Clinical protocol «Miscarriage». Order №624 of the Ministry of Health of Ukraine dated 03.11.2008.]. https://zakon.rada.gov.ua/rada/show/v0624282-08#Text. (In Ukrainian).
9. Zegers-Hochschild F., Adamson G.D., Mouzon de J. et al. on behalf of ICMART and WHO. The International Committee for Monitoring Assisted Reproductive Technology (ICMART) and the World Health Organization (WHO) Revised Glossary on ART Terminology, 2009. Human Reproduction. 2009; 24(11): 2683–2687.
10. Vyhivska L.M., Nykoniuk T.R. Etiopatohenetychni aspekty perebihu I trymestra vahitnosti u zhinok pislia zastosuvannia dopomizhnykh reproduktyvnykh tekhnolohii [Ethiopathogenetic aspects of the I trimester pregnancy course in the women after the use of assisted reproductive technologies]. Zdorov'ia zhinky. 2017; 4 (120): 98-101. (In Ukrainian).
11. Vyhivska L.M., Usevych I.A., Maidannyk I.V. et al. Osoblyvosti psykhoemotsiinoho stanu ta bioprodukuvannia stres-asotsiiovanykh hormoniv u vahitnykh pislia zastosuvannia dopomizhnykh reproduktyvnykh tekhnolohii [Features of psycho-emotional state and bioproduction of stress-associated hormones in the pregnant women after the use of assisted reproductive technologies.]. Zdorov'ia zhinky. 2018; 6 (132): 118-121. (In Ukrainian).
12. Grossi E., Parisi F., Duca P. et al. Maternal Estradiol and Progesterone Concentrations Among Singleton Spontaneous Pregnancies During the First Trimester. J Endocrinol Invest. 2019;42(6):633-638. doi: 10.1007/s40618-018-0961-6.
13. Póvoa A., Xavier P., Matias A. et al. First Trimester β-hCG and Estradiol Levels in Singleton and Twin Pregnancies After Assisted Reproduction. J Perinat Med. 2018;46(8):853-856. doi: 10.1515/jpm-2017-0132.
14. Zhabchenko I.A., Oleshko V.F. Rol hormonalnoho ta obminnoho dysbalansu v rozvytku porushen obturatsiinoi funktsii shyiky matky ta sposoby yoho korektsii [The role of hormonal and metabolic imbalance in the development of disorders of the cervical obstruction function and methods of its correction]. Medychni aspekty zdorov'ia zhinky. 2017; 2 (107): 5-14. (In Ukrainian).
15. Zhabchenko I.A., Oleshko V.F., Bondarenko O.M. et al. Osoblyvosti hormonalnoho homeostazu vahitnykh iz funktsionalnym porushenniam obturatsiinoi funktsii shyiky matky [Features of hormonal homeostasis in pregnant women with functional disorders of the cervix obstructive function]. Reproduktyvna endokrynolohiia. 2016; 5(31): 85-89. (In Ukrainian).
16. Patil A.S., Gaikwad N.W., Grotegut C.A. et al. Alterations in Endogenous Progesterone Metabolism Associated With Spontaneous Very Preterm Delivery. Hum Reprod Open. 2020;2:007. doi: 10.1093/hropen/hoaa007.

ORCID and contributionship:
Oksana M. Perkhulyn: 0000-0002-0033-5156 [B-D]
Lyudmyla V. Pakharenko: 0000-0003-4774-8326 [A, D-F]
Vladyslav S. Sukhin: 0000-0002-4403-3707 [A, F]
Oleksiy V. Saltovskiy: 0000-0002-1597-7493 [A, D, F]
Viktoriia M. Kovalchuk: 0000-0002-6597-5154 [C, E]
Hanna I. Hranovska: 0000-0002-1238-5855 [C, F]
Olha V. Kravchenko: 0000-0002-2562-7497 [C, E]

Conflict of interest:
The Authors declare no conflict of interest

CORRESPONDING AUTHOR
Lyudmyla V. Pakharenko
Ivano-Frankivsk National Medical University
2 Halytska st., 76018 Ivano-Frankivsk, Ukraine
tel: +380974306921
e-mail: ludapak@ukr.net

Received: 16.09.2020
Accepted: 15.08.2021

A – Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article