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ORIGINAL ARTICLE

INFECTIONS ASSOCIATED WITH OBSTETRIC AND GYNECOLOGICAL SURGERIES AS A CAUSE OF FEMALE INFERTILITY IN UKRAINE

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Aidyn G. Salmanov[1,2], Volodymyr A. Terekhov[3], Serhiy M. Baksheev[1,4], Alla D. Vitiuk[1], Svitlana M. Korniyenko[5], Svitlana Nagirniak[1,6], Mykola Hafiichuk[1,7]

[1]SHUPYK NATIONAL HEALTHCARE UNIVERSITY OF UKRAINE, KYIV, UKRAINE
[2]INSTITUTE OF PEDIATRICS, OBSTETRICS AND GYNECOLOGY OF THE NATIONAL ACADEMY OF MEDICAL SCIENCES OF UKRAINE, KYIV, UKRAINE
[3]MEDICAL INSTITUTE OF SUMY STATE UNIVERSITY, SUMY, UKRAINE
[4]KYIV CITY MATERNITY HOSPITAL, KYIV, UKRAINE
[5]ODESA NATIONAL MEDICAL UNIVERSITY, ODESA, UKRAINE
[6]CLINICAL PERINATAL CENTER OF IVANO-FRANKIVSK CITY, UKRAINE
[7]NADIYA ODESA CLINIC OF REPRODUCTIVE MEDICINE, ODESA, UKRAINE

ABSTRACT

The aim: To assess the role of surgical site infections types associated with obstetric and gynecological surgeries as a cause of infertility among women reproductive age in Ukraine.

Materials and methods: We conducted a retrospective multicentre cohort study was based on reproductive health surveillance data among women reproductive age from 2019 to 2021. Definitions of infertility were used from the WHO and surgical site infections were used CDC/ NHSN.

Results: Among all the 3,825 of infertility women in this study, the prevalence of surgical site infection (SSI) was 67.9%. The prevalence of SSI among primary infertility group and secondary infertility group women was 67.5% and 71.4%, respectively. There were differences among SSI type associated with infertility, primary infertility and secondary infertility. In logistic multivariate regression analyses, infertility was associated history of induced abortion ($p < 0.001$), history of obstetric and gynecological surgeries ($p < 0.001$), Salpingitis ($p < 0.001$), Oophoritis ($p < 0.001$), Endometritis ($p < 0.001$), Adnexa utery ($p=0.009$), and Pelvic abscess or cellulitis ($p=0.043$). The main factors associated with primary infertility were history of Salpingitis (33.6%) and Oophoritis (28.2%) after gynecological surgery. A factors associated with secondary infertility were history of Endometritis (27.2%), Pelvic abscess or cellulitis (11.2%), Salpingitis (10.1%), Adnexa utery (9.4%), Oophoritis (4.8%), and Chorioamnionitis (3.9%).

Conclusions: One of the main causes of infertility in women of reproductive age in Ukraine are SSIs after obstetric and gynecological surgeries, and induced abortion. This applies to both primary and secondary infertility group women's in this cohort study.

KEY WORDS: reproductive health, primary and secondary infertility, obstetric and gynecological surgery, induced abortion, risk factors, surgical site infection, Ukraine

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INTRODUCTION

Infertility is a global socio-demographic, economic and clinical issue worldwide. Its consequences are manifested in many ways in our society, including the monetary costs of its investigation, diagnosis, and treatment as well as the psychosocial stresses it imposes on this portion of the population. Available data suggests that between 48 million couples [1] and 186 million individuals have infertility globally [2]. Infertility is estimated to affect half a million of reproductive age women attempting to conceive in the Ukraine.

One of the causes of female infertility is a history of infections after obstetric and gynecological surgeries [3-7]. The most common infections after these procedures are Endometritis, Pelvic abscess or cellulitis, Episiotomy, Vaginal cuff infection, Adnexa utery, Salpingitis, Oophoritis, Parametritis, Chorioamnionitis, and Bacterial Vaginitis. The prevalence of reproductive tract infection (RTI) after gynecological surgery varies from country to country and ranges from 1.8% [8] to 37.8% [7, 9]. Incidence rate of SSI after obstetric and gynecological surgeries were highest in Ukraine. According to a variety of sources, rates of RTI among women in Ukraine varied from 4.6% to 38.8% [3,7,8,10]. In the United States, 1 million women are diagnosed with RTI each year and the cost of their treatment is estimated at $4.2 billion [11].

Over the past three decades, the problem of infertility in Ukraine has not been given due attention, although increase fertility level has been a priority task for in the country. The decline of fertility level in Ukraine is increasing social interests about infertility as one of priority areas to be addressed not only to respond a potential population aging but also to improve reproductive health. The introduction of family planning programs in the face

of deteriorating economic dynamics in Ukraine did not contribute to a permanent and significant increase in the total fertility rate to the level of among most European countries. Despite the availability of new technologies for diagnosing and treating patients, the number of infertile men and women does not decrease.

Despite of significant socio-demographic, economic and clinical meaning of childlessness, there has been less scientific focuses on causes of infertility in Ukraine. To our knowledge, only a few studies were conducted to study infertility within narrow clinical features, showing that the percentage of infertile women seeking infertility treatment services has grown increasingly in Ukraine. Also, several studies have been conducted to study the prevalence of SSIs after obstetric and gynecological surgeries [3, 7, 12, 13]. The results of studies showed high prevalence and incidence rate of surgical site infections after these surgeries. In addition, there has been no attempt to study focused on female infertility in the context of surgical site infections after obstetric and gynecological surgeries based on surveillance data. Therefore, it is clearly important to understand infertility dynamics for its current level and health-care associated infections as a cause of female infertility, to not only effectively respond to fertility decrease but also ensure reproductive health rights of residents in Ukraine.

THE AIM

The aim of this study was to assess the role of surgical site infections types associated with obstetric and gynecological surgeries as a cause of infertility among women reproductive age in Ukraine.

MATERIALS AND METHODS

DESIGN AND STUDY POPULATION

We conducted a retrospective multicentre cohort study was based on reproductive health surveillance data among women reproductive age from January 1st, 2019 to December 31st, 2021 in Ukraine. We compiled list of the 17 medical centers for family planning and reproductive health. Of these, only 12 medical centers from 8 regions (Lviv, Ivano-Frankivsk, Vinnytsia, Kyiv, Sumy, Kherson, Dnipropetrovsk, and Odessa) of Ukraine agreed to take part in our study. The study population included women who had experienced infertility had sought medical or professional help for the problem. The inclusion criteria in this study for participants were as follows: 20–49 years old; married or cohabitational; local residents. Te exclusion criteria: not a local resident of the selected regions; cancer; Chlamydial infections; positive serological test for syphilis or other sexually transmitted bacterial infections. In addition, local women were excluded from the study if they did not regularly visit doctors and medical records were not properly executed. In total of 17 women were excluded from the study.

DEFINITIONS

In our study infertility is defined as disease of the female reproductive system defined by the failure to achieve a pregnancy after 12 months or more of regular unprotected sexual intercourse [14]. In present study infertility among married women was classified as primary and secondary. In this study primary infertility is defined as a woman who has never been diagnosed with a clinical pregnancy and meets the criteria of being classified as being infertile, while secondary infertility is defined as a woman unable to establish a clinical pregnancy who has previously been diagnosed with a clinical pregnancy [15]. The CDC/NHSN (Centers for Disease Control and Prevention/National Healthcare Safety Network) definition [16] for SSI types after obstetric and gynecological surgeries was used.

DATA COLLECTION

This study includes interviews, questionnaires, and examinations medical records. Information on Infertility was collected at baseline and each follow-up visit. Full text ambulatory medical records and relevant hospital records were reviewed for the all women's. All free-text notes were reviewed, and encounters for which the principal focus was the Infertility were identified. A standard data collection form was created to extract demographic and clinical data, and outcome information from routine patient records. Supervision and quality control were conducted throughout the entire study. In this study adopted double entry mode of paper questionnaire data and were analyzed anonymously. According to their history of pregnancy, child birth and contraception, the infertile women were divided into primary infertility and secondary infertility cohorts.

ETHICS

Our study was performed in line with the principles of the Declaration of Helsinki. Also, the Shupyk National Healthcare University of Ukraine Ethics Committee approved this study. All participants signed an informed consent.

STATISTICAL ANALYSIS

The prevalence of SSIs after obstetric and gynecological surgeries was reported as the percentage of the total number of infertile women's. Cases of SSIs were analysed by type of infection, which were mutually exclusive. The analysis of statistical data was performed using Excel (Microsoft Corp., Redmond, WA, USA). Results are expressed as median (range), mean standard deviation for continuous variables, and number and corresponding percentage for qualitative variables. Comparisons were undertaken using Student's t-test and Fisher's exact test for categorical variables. In this study we used binary logistic multivariate regression analysis, and for variable selection we used forward stepwise regression based on maximum likelihood estimation. Statistical significance was defined as $P<0.05$.

RESULTS

PREVALENCE SURGICAL SITE INFECTION AMONG INFERTILE WOMEN

In during study period (2019-2021) we sampled 3825 infertile women who were 20–49 years old in 12 medical centers of 8 regions in Ukraine. The prevalence of primary infertility and secondary infertility was about 88.6% (3,388/3,825) and 11.4% (437/3,825), respectively. The mean ± SD age was 32.97 ± 0.25 years for the primary infertility group and 34.95 ± 0.39 years for the secondary infertile group. The difference in mean age between these two groups was statistically significant (p< 0.001). As shown in Table I, the difference in the history of obstetric and gynecological surgery, procedure of induced abortion, and history of surgical site infection (SSI) between the two groups were statistically significant (p < 0.001). In total, 95.7% (3,661/3,825) of infertile women had a history of surgical procedures. The prevalence of SSIs in this study cohort of infertility women was 67.9% (2,599/3,825). The prevalence of SSI among primary infertility group and secondary infertility group women was 67.5% and 71.4%, respectively. Characteristics of infertile women who have a history of obstetric and gynecological surgery, procedure of induced abortion, and history of SSI are presented in Table I.

There were differences among SSI type associated with infertility, primary infertility and secondary infertility. The main factors associated with primary infertility were history of salpingitis (33.6%) and oophoritis (28.2%) after gynecological surgery. A factors associated with secondary infertility were history of Endometritis (27.2%), Pelvic abscess or cellulitis (11.2%), Salpingitis (10.1%), Adnexa utery (9.4%), Oophoritis (4.8%), and Chorioamnionitis (3.9%). Comparison of characteristics of primary and secondary infertile groups is shown in Table II.

RISK FACTORS OF SSI ASSOCIATED WITH INFERTILITY

Table III showed the odds ratio (OR) and 95% confidence interval (CI) for the risk factors of SSI associated with infertility in logistic multivariate regression analyses. Unsurprisingly, infertility was associated with SSI after obstetric and gynecological surgery, and surgical procedure for induced abortion as shown in logistic regression analysis. Further, there were differences among risk factors of SSI associated with infertility, primary infertility and secondary infertility.

In Table IV, factors associated with primary infertility were Salpingitis (p< 0.001) and Oophoritis (p< 0.001) after gynecological surgery. In single-factor analysis, history of gynecological surgery (p< 0.001) and pelvic abscess or cellulitis (p = 0.043) might have association to primary infertility but all of them were excluded when binary logistic multivariate regression analyses were carried out.

In Table V, risk factors of SSI associated with secondary infertility were history of induced abortion (p < 0.001), gynecological surgery (p < 0.001), Cesarean section (p < 0.001), Endometritis (p < 0.001), Salpingitis (p < 0.001), Oophoritis (p < 0.001), Adnexa utery (p=0.009), and Pelvic abscess or cellulitis (p=0.043). In single-factor analyses, history of Chorioamnionitis (p < 0.001) might be associated with secondary infertility but it was excluded when binary logistic multivariate regression analyses were carried.

Table I. Characteristics of infertile women who have a history of surgery for delivery or elective gynecological surgery for benign reasons in Ukraine (2019-2021)

Variables	Infertile women (n=3825)		*p*-value	95%CI[a]
	n	%		
History of surgical procedure				
Cesarean section	335	8.8	< 0.001	8.3 – 9.3
Surgery for benign gynecological disease	2971	77.7	< 0.001	77.0 – 78.4
Induced abortion	355	9.3	< 0.001	8.8 –9.8
History of SSI[b] type				
A pelvic abscess or cellulitis	127	3.3	< 0.001	3.0 – 3.6
Adnexa utery	70	1.8	< 0.001	1.6 – 2.0
Salpingitis	1000	26.1	< 0.001	25.9 – 28.8
Oophoritis	1160	30.3	< 0.001	29.6 – 31.0
Endometritis	170	4.4	< 0.001	4.1 – 4.7
Chorioamnionitis	17	0.4	0.043	0.3 – 0.5
Vaginal cuff infection	48	1.2	0.074	1.0 – 1.4
Episiotomy	7	0.2	0.087	0.13 – 0.3

[a]CI, confidence interval
[b]SSI, surgicai site infection

Table II. Characteristics of primary and secondary infertile groups among women's (n=3825) in Ukraine (2019-2021)

Characteristics	Primary infertility (n = 3,388)		Secondary infertility (n = 437)		p-value
	n	%	n	%	
History of surgical procedure					
Cesarean section	0	0.0	335	76.7	< 0.001
Surgery for benign gynecological disease	2909	85.9	62	14.2	
Induced abortion	0	0.0	355	81.2	
History of pelvic abscess or cellulitis					
No					
Yes	78	2.3	49	11.2	< 0.001
History of Adnexa utery					
No					< 0.001
Yes	29	0.9	41	9.4	
History of Salpingitis					
No					< 0.001
Yes	1139	33.6	44	10.1	
History of Oophoritis					
No					< 0.001
Yes	956	28.2	21	4.8	
History of Endometritis					
No					< 0.001
Yes	48	1.4	122	27.9	
History of Chorioamnionitis					
No					< 0.001
Yes	0	0.0	17	3.9	
History of Vaginal cuff infection					
No					< 0.001
Yes	37	1.1	11	2.5	
History of Episiotomy					
No					< 0.001
Yes	0	0.0	7	1,6	

DISCUSSION

To the best of our knowledge, this is the first study examining surgical site infections associated with obstetric and gynecological surgeries as a cause of infertility among women reproductive age in Ukraine. We found that the prevalence of surgical site infection (SSI) among women with infertility was 67.9%. The prevalence of SSI among primary infertility group and secondary infertility group women was 67.5% and 71.4%, respectively. There were differences among SSI type associated with infertility, primary infertility and secondary infertility. In logistic multivariate regression analyses, infertility was associated history of induced abortion ($p < 0.001$), history of obstetric and gynecological surgeries ($p < 0.001$), Salpingitis ($p < 0.001$), Oophoritis ($p < 0.001$), Endometritis ($p < 0.001$), Adnexa utery ($p=0.009$), and Pelvic abscess or cellulitis ($p=0.043$). The main factors associated with primary infertility were history of Salpingitis (33.6%) and Oophoritis (28.2%) after gynecological surgery. A factors associated with secondary infertility were history of Endometritis (27.2%), Pelvic abscess or cellulitis (11.2%), Salpingitis (10.1%), Adnexa utery (9.4%), Oophoritis (4.8%), and Chorioamnionitis (3.9%).

The prevalence of SSIs after induced abortion, obstetric and gynecological surgeries varies greatly in different countries and regions, and change all the times. The SSI cases estimates use different definitions considering different periods, which make direct comparisons difficult between various studies. SSIs in Ukraine are among the most common healthcare-associated infections (HAIs) after, obstetric and gynecological surgeries, and induced abortion.

Over the past two decades, along with significant improvements in clinical obstetric care in many countries,

Table III. Logistic multivariate regression analyses of risk factors associated with infertility women in Ukraine (2019-2021)

Characteristics	*p*-value	Unadjusted OR[a] (95% CI[b])	*p*-value	Adjusted OR (95% CI)
History of Cesarean section				
No		Ref		Ref
Yes	< 0.001	0.557 (0.344–0.902)	0.008	0.494 (0.294–0.830)
History of gynecological surgery				
No		Ref		Ref
Yes	< 0.001	3.611 (2.235–5.832)	< 0.001	3.063 (1.819–5.159)
History of induced abortion				
No		Ref		Ref
Yes	< 0.001	6.618(1.549–28.274)	0.031	5.031 (1.163–21.830)
History of pelvic abscess or cellulitis				
No		Ref		Ref
Yes	0.043	0.563 (0.386–0.822)	0.012	0.517 (0.342–0.781)
History of Adnexa utery				
No		Ref		Ref
Yes	0.009	0.557 (0.344–0.902)	0.008	0.494 (0.294–0.830)
Histiry of Salpingitis				
No		Ref		Ref
Yes	< 0.001	5.131 (2.662–9.889)	< 0.001	3.835 (1.908–7.711)
History of Oophoritis				
No		Ref		Ref
Yes	< 0.001	9.379 (2.165–40.622)	0.011	6.862 (1.557–30.248)
History of Endometritis				
No		Ref		Ref
Yes	< 0.001	6.618(1.549–28.274)	0.031	5.031 (1.163–21.830)
Constant			0.003	0.109

[a]OR, Odd Ratio
[b]CI, confidence interval

the incidence rate of SSI after CSEC remains an important issue. According to literature data, the incidence of SSI after CSEC was 7-10% [17, 18]. Previous studies have shown that prevalence of SSI after Cesarean section (CSEC) in Ukraine was 14.2% [12]. In European Union Member States for CSEC operations, the percentage of SSIs was 2.2%, with an inter-country range from 0.6% to 7.7% [19]. The percentages of SSIs for CSEC operations in the Ukraine were significantly higher than those reported from EU for 2014–2016 [19] and other countries [17, 18].

Healthcare-associated reproductive tract infections (RTIs) after gynecological surgery include Endometritis, Episiotomy, Vaginal cuff infections and other infections of the female reproductive tract. Other infection of the female reproductive tract involves the Deep pelvic tissue infection or other infection of the female reproductive tract (for example, vagina, ovaries, uterus) including chorioamnionitis. The prevalence of healthcare-associated deep pelvic tissue infection and other infections of the female reproductive tract after gynecologic surgery in Ukraine was 26.3%. Incidence of infection was: 13.3% Pelvic abscess or cellulitis, 14.6% Adnexa utery, 9.5% Salpingitis, 7.1% Oophoritis, 12.2% Parametritis, 4.6% Chorioamnionitis, and 38.8% Bacterial Vaginitis [7]. The prevalence of RTIs varies from country to country and ranges from 1.8% [8] to 48% [20, 21]. In the United States, 1 million women are diagnosed with RTI each year [11]. Available literatures there are no epidemiologic studies (prevalence or incidence) of different types of healthcare-associated deep pelvic tissue infection and other infections of the female reproductive tract. Therefore, we were unable to compare our results with other studies in other countries.

Induced abortion is one of the most common surgical procedures in the world. In Ukraine, USA, most European and other countries, the law allows abortion on request or on broad social grounds. One of the major complications resulting from the unsafe abortions is RTIs. The reported of SSI rate following first trimester induced abortion ranges widely due to various clinical practices and degrees of ascertainment and diagnostic biases. According to literature, SSI after induced abortion, the rates were very variable between studies (from 0.7% to 3.6% with

Table IV. Logistic multivariate regression analyses of factors associated with primary infertility among women in Ukraine (2019-2021)

Characteristics	*p*-value	Unadjusted OR[a] (95% CI[b])	p-value	Adjusted OR (95% CI)
History of gynecological surgery				
No		Ref		Ref
Yes	< 0.001	2.937 (1.772–4.870)	< 0.001	2.695 (1.548–4.695)
Histiry of Salpingitis				
No		Ref		Ref
Yes	< 0.001	4.175(2.357–7.394)	< 0.001	3.359 (1.827–6.174)
History of Oophoritis				
No		Ref		Ref
Yes	< 0.001	7.117 (2.651–19.107)	0.002	6.258 (1.962–19.956)
Constant			< 0.001	0.095

[a]OR, Odd Ratio
[b]CI, confidence interval

Table V. Logistic multivariate regression analyses of factors associated with secondary infertility among women in Ukraine (2019-2021)

Characteristics	*p*-value	Unadjusted OR[a] (95% CI[b])	*p*-value	Adjusted OR (95% CI)
History of Cesarean section				
No		Ref		Ref
Yes	< 0.001	0.637(0.428–0.950)	0.043	0.650 (0.428–0.987)
History of Induced abortion				
No		Ref		Ref
Yes	< 0.001	4.175(2.357–7.394)	< 0.001	3.359 (1.827–6.174)
History of gynecological surgery				
No		Ref		Ref
Yes	< 0.001	3.611 (2.23–5.83)	< 0.001	3.063 (1.819–5.159)
History of pelvic abscess or cellulitis				
No		Ref		Ref
Yes	0.043	0.637(0.428–0.950)	0.049	0.650 (0.428–0.987)
Histiry of Adnexa utery				
No		Ref		Ref
Yes	0.009	2.924(1.481–5.773	0.036	2.170 (1.052–4.479)
Histiry of Salpingitis				
No		Ref		Ref
Yes	< 0.001	3.690 (1.913–7.114)	< 0.002	3.145 (1.532–6.455)
History of Oophoritis				
No		Ref		Ref
Yes	< 0.001	2.937 (1.772–4.870)	< 0.001	2.695 (1.548–4.695)
History of Endometritis				
No		Ref		Ref
Yes	< 0.001	2.924(1.481–5.773	0.036	2.170 (1.052–4.479)
Constant			< 0.001	0.039

[a]OR, Odd Ratio
[b]CI, confidence interval

one study reporting 8%) [22-24]. This rate in Ukraine was significantly higher than the rate observed in other country after terminated pregnancy but probably is a reflection of the variable abortion practices and definition

of SSIs used in these different countries. The prevalence of SSI after induced abortion in Ukraine was 25.9%. Of these SSIs, 25.9 were Endometritis, 21.8% Bacterial Vaginitis, 14.3% Parametritis, 13.1% Cervicitis, 9.9% Adnexa utery, 7.8% Salpingitis, 6.3% Chorioamnionitis, and 0.9% other reproductive tract infections [3].

According to literature data, the role of reproductive surgery is declining due to the widespread availability of assisted reproductive technology, but an evidence-based fundament for this decline is lacking. Worldwide assisted reproductive technology (ART) has replaced reproductive surgery for tubal factor infertility, limiting its role as first-line treatment [25]. However, it is not clear whether this change in clinical practice is due to the higher cost-effectiveness of ART compared to reproductive surgery or caused by other factors such as a lack of surgical expertise, patient's desires to achieve results rapidly or the concern to protect patients from procedure-related complications. In addition, the shift away from reproductive laparoscopic surgery favoring ART is not supported by solid evidence. The position of hysteroscopy in current fertility practice is similarly unclear.

Finally, our study showed that SSI remains the most common complication of gynecologic procedures. Despite the introduction into medical practice of new diagnostic technologies and treatment, as well as broad-spectrum antibiotics, the number of SSI after induced abortion, obstetric and gynecological surgeries is not decreasing. Implementing programs to reduce SSI requires a collaborative approach that involves clinicians, nurses, and staff.

STRENGTH AND LIMITATION

The main advantage of this study is that we conducted a multicentre cohort study was based on women reproductive health surveillance data. This investigation provides valuable data as a first study for national surveillance of SSI associated with induced abortion, obstetric and gynecological surgeries as a cause of infertility among women reproductive age in Ukraine and potential comparison with data from other countries. In addition, this study included all types of SSIs after operations in the reproductive tract of women according to the CDC/NHSN definition. A limitation of this study is its retrospective design.

CONCLUSIONS

One of the main causes of infertility in women of reproductive age is surgical site infections (SSIs) after obstetric and gynecological surgeries, and induced abortion. The results of this study revealed high level the prevalence rate of SSI among infertile women of reproductive age in Ukraine is high. This applies to both primary and secondary infertility group women's in this cohort study. This study provides the newest data of SSIs after obstetric and gynecological surgeries, and induced abortion in Ukraine and finds some predictors of SSI. The data presented in our study can be a tool to develop optimal preventive measures and improve surgical quality in Ukraine. The most of the risk factors identified are amendable through interventions of infection control. Surveillance is a key component in the prevention of healthcare-associated infections and an important tool for monitoring the effectiveness of prevention and control measures. Optimizing the management and empirical antimicrobial therapy may reduce the burden of SSIs, but prevention is the key element.

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ORCID and contributionship:
Aidyn G. Salmanov: 0000-0002-4673-1154 [A, C- F]
Volodymyr A. Terekhov: 0000-0002-9837-5374 [B-D, F]
Serhiy M. Baksheev: 0000-0003-4144-5965 [B- D, F]
Alla D. Vitiuk: 0000-0003-0550-1076 [B-D, F]
Svitlana M. Korniyenko: 0000-0003-3743-426X [B- D, F]
Svitlana Nagirniak: 0000-0001-5552-2031 [B- D, F]
Mykola Hafiichuk: 0000-0003-0383-4337 [B- D, F]

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The Authors declare no conflict of interest

CORRESPONDING AUTHOR
Aidyn G. Salmanov
Shupyk National Healthcare University of Ukraine,
9 Dorohozhytska St., 04112, Kyiv, Ukraine
tel: +380667997631
e-mail: mozsago@gmail.com

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