

CLINICAL ARTICLE

Gynecology

The impact of the war in Ukraine on the reproductive health of female military personnel

Anastasia Serbeniuk^{1,2}  | Viacheslav Kaminskiy¹  | Yana Kumpanenko¹  |
Alla Vash-Margita³ | Iryna Malysheva²

¹Department of Obstetrics, Gynecology, and Reproduction, Shupyk National Healthcare University of Ukraine, Kyiv, Ukraine

²Clinic of Reproductive Technologies, Shupyk National Healthcare University of Ukraine, Kyiv, Ukraine

³Department of Obstetrics, Gynecology and Reproductive Sciences, Yale University School of Medicine, New Haven, Connecticut, USA

Correspondence

Anastasia Serbeniuk, Department of Obstetrics, Gynecology, and Reproduction, Shupyk National Healthcare University of Ukraine, Dorogozhitska 9, Kyiv, Ukraine. Email: anastasia.serbenyk@gmail.com

Abstract

Objective: To explore the link between mental health, physical well-being, and reproductive system pathology in females who suffered war-related concussions.

Methods: A study was conducted at the Kyiv Center of Reproductive and Perinatal Medicine with 715 participants. The group included 457 female military personnel with concussions (211 with post-concussive syndrome (PCS), 246 without), 208 women from occupied/deoccupied areas (103 with PCS, 105 without), and 50 civilians from safe zones. Average deployment time (mean \pm standard deviation) was 60.26 ± 42.21 months, and trauma occurred 18.81 ± 9.221 months ago. Medical history and physical examinations were performed.

Results: Female soldiers with PCS had a 1.3 times higher likelihood ($P < 0.015$) of experiencing longer menstrual periods. Painful menstruation was 1.47 times more frequent ($P < 0.001$), and heavy periods were 1.64 times more common ($P < 0.003$). Infertility duration in concussed women was 5.36 ± 0.13 years, whereas those with PCS experienced 1.29 times longer duration (6.02 ± 0.21 years) ($P < 0.001$) compared with women without PCS (4.69 ± 0.13 years). Among concussed soldiers, 69.27% had endometrial structural pathology, with PCS occurring 1.64 times more often ($P < 0.001$).

Conclusions: The health decline in female veterans and active-duty personnel extends beyond medical implications and has social significance. The well-being of these Ukrainian women affects the country's defense, demographic patterns, socio-political landscape, and social stability.

KEYWORDS

combat operations, concussion, female military, Postconcussion syndrome: Posttraumatic stress disorder, reproductive health, Ukraine war

1 | INTRODUCTION

A traumatic brain injury (TBI) can be caused by a forceful bump, blow, or jolt to the head, or from an object that pierces the skull and enters the brain.¹

Concussion, as part of a mild TBI, is defined as a traumatically induced transient disturbance of brain function and involves a complex pathophysiologic process.² It is estimated that around 70 million individuals experience concussion from all causes each year.³ The most prevailing and consistent indicators of it are observed

and documented disorientation or confusion immediately after the event, impaired balance within 1 day after the injury, slower reaction time within 2 days after injury, and/or impaired verbal learning and memory within 2 days after injury.⁴

It is a frequent consequence of blast weaponry exposure, especially during war.

Due to the Russian aggression on Ukraine in February 2014 with a full-scale invasion in February 2022, according to the United Nations, more than 17 million people were directly affected by the invasion and needed humanitarian aid and protection. More than 8 million refugees escaped Ukraine.⁵ As of March 2023, the office of the High Commissioner for Human Rights recorded 21 965 civilian casualties in the country: 8231 killed and 13 734 injured.⁶ It is important to state that not all cases are reported, military personnel and missing civilians are currently not included. The numbers are likely to rise significantly. It is impossible to accurately comprehend the consequences the war had, has, and will have on the Ukrainian population at this time.

According to Hanna Malyar, the Deputy Minister of Defense of Ukraine, more than 50 000 women serve in the Ukrainian armed forces, including around 5000 on the front lines.⁷ Among women, who participated in combat operations, some have suffered a concussion, but continue military service, or, after being released from it, are active in society. At the same time, it is accompanied by mental aberrations of the “pre-morbid” level (asthenic syndrome, vestibular and autonomic dysfunction, anxiety-depressive inclusions), neurologic, and physical as well.^{8–11} Female individuals are also generally more susceptible to concussion than male individuals.¹²

Despite the name “mild brain injury”, patients can experience secondary continuous behavioral and cognitive impairment, due to brain matter and vasculature damage, inflammation, and abnormal deposits of hyperphosphorylated tau.¹³ These features comprise post-concussive syndrome (PCS). Approximately 90% of concussion symptoms are transient, and symptoms typically resolve within 2 weeks but can persist beyond this.¹⁴

Behavioral symptoms that may occur after mild TBI include irritability, mood and sleep disturbances, rapid fatigue, daytime dizziness, and emotional lability. People with anxiety or depression, posttraumatic stress disorder (PTSD), and people who abuse alcohol or drugs have a much higher risk of developing these symptoms. A recent meta-analysis investigating war-exposed populations noted that 25% of people experienced PTSD.¹⁵

Female gender, non-officer ranks, frequent and prolonged deployments, history of trauma, and/or psychological problems contribute to the development of the disorder in some individuals.¹⁶ It is also important to note that complex PTSD, conforming to International Classification of Diseases 11th revision, involves not only PTSD symptoms but also a broader spectrum of problems: problems in affect regulation, self-worthlessness, accompanied by feelings of shame, guilt, or failure, and difficulties in interpersonal communication.¹⁷ These symptoms cause notable disturbances in all spheres of human life.

Based on the information above, the following objectives were pursued: investigating the impact of mild TBI (concussion) on

reproductive health in female military personnel and civilian women. It assessed postconcussive symptoms, menstrual patterns, hormonal profiles, endometrial pathology, and infertility rates, and highlighted the need for comprehensive support and healthcare for women affected by the ongoing war in Ukraine.

2 | MATERIALS AND METHODS

A single-center, longitudinal, interventional study was held in Kyiv, Ukraine based on the facilities of the Ukrainian State Institute of Reproduction, Department of Obstetrics, Gynecology, and Reproduction of the Shupyk National Healthcare University of Ukraine (NHCU) during January 2021–October 2022. The study was approved by the Ethics Committee of NHCU. Informed consent was obtained from all patients for de-identified data use in scientific research. Exclusion criteria were pregnancy, lactation, active infectious or exacerbation of the chronic disease, perimenopause and menopause, substance addiction, and not being willing to participate in the study.

A prospective study was conducted of 665 patients of reproductive age who suffered concussions of a mild degree (group All), of which 457 were military personnel who took part in combat operations (group M). Consequently, they were subdivided into MO ($n=211$)—female military personnel with a history of concussion with PCS, and MP ($n=246$)—female military personnel with a history of concussion without PCS. The T group consisted of 209 female civilian patients who stayed in occupied/de-occupied territories and suffered mild TBI. In the same manner, they were subdivided into TO with PCS ($n=103$) and TC without PCS ($n=105$). The control group C ($n=50$) consisted of female civilians, who stayed in relatively safe areas of Ukraine.

Complete past medical history was assessed in detail. A thorough physical examination was conducted. Assessment of menstruation was based on FIGO (the International Federation of Gynecology & Obstetrics) systems for nomenclature of symptoms of normal and abnormal uterine bleeding.¹⁸ Blood tests were obtained, and the following hormones were checked: luteinizing hormone (LH), follicle-stimulating hormone (FSH), prolactin, and steroid hormones (free testosterone, estradiol, progesterone).

Hormonal assessment of LH, FSH, prolactin, estradiol, progesterone, and free testosterone was taken on the 5th day of the menstrual cycle, and estradiol and progesterone were measured on the 21st day. Blood serum hormone levels were measured using standard kits for chemiluminescent immunoassays.

Concussion symptoms at the time of examination were determined according to the Standardized Assessment of Concussion, Post-Concussion Scale, and Military Acute Concussion Evaluation.¹⁹ At the same time, the patients performed a self-assessment of their symptoms relating to the present. The checklist for mental disorders (PCL-5) in veterans was used for PTSD screening.²⁰

The two following tools were used to assess anxiety: the State-Trait Anxiety Inventory²¹ and the Beck Anxiety Scale.²² The

questionnaire consists of 21 items. Each item includes one of the typical symptoms of anxiety, either physical or mental. Each item was rated from 0 (the symptom does not disturb) to 3 (disturbs a lot).

Statistical processing of the research results was performed using Statistica 13.4 software package and Microsoft Office software package using standard descriptive statistics methods. Analysis of variance was used for descriptive characteristics of the study for continuous variables and for categorical variables χ^2 tests were used. Independent t tests were performed to compare the groups. An α level of 0.05 was used to determine the statistical significance.

3 | RESULTS

Complete examination and analysis of the clinical and past medical history data of 715 women of reproductive age from 20 to 40 years old were carried out.

The average age of the examinees was 29.6 years. The period of stay in the combat zone was 60.26 ± 42.21 months, and the period since receiving a mild TBI (concussion) was 18.81 ± 9.221 months.

Characteristics of our study populations are shown in Table 1.

The groups of MO, MP, TO, and TP were homogeneous in terms of age, body mass index, menstrual, ovulatory, and reproductive function, and gynecologic, somatic, and infectious past medical history, which allows for comparing the results of further studies.

In patients of group All, the duration of menstrual bleeding exceeded that of group C by 1.09 times ($P < 0.01$) (>8 days). The duration of menstruation in women of group M was 1.3 times longer than in patients of group T ($P < 0.015$).

Analysis of the nature of menstruation showed (Table 2) that in women of groups MO and MP, compared with controls, menstruation was more likely to be painful (1.54 times, $P < 0.001$ and 1.38 times, $P < 0.02$, respectively) and 3.27 times ($P < 0.01$) more likely to be heavy.

The vast majority of menstrual cycles in the examined women involved ovulation, which was confirmed by basal temperature graphs and ovulation tests.

Analysis of the reproductive history revealed that among the examined female military personnel, primary infertility was observed in 221 (48.46%), and secondary infertility in 236 (51.54%).

The main reasons for patients of the All group with a history of childbirth to access infertility treatment were the desire to have a child in a remarriage (242; 33.80%); the desire to have a second child (212; 29.58%); perinatal losses in history (171; 23.94%), and loss of an adult child (91; 12.68%).

In the female military group, the above changes in the hormonal profile of peripheral blood serum were more pronounced than in women of a group of civilians. Hence, in patients of groups M and T, in the follicular phase of the menstrual cycle, the level of FSH was increased by 1.11 times, and LH by 1.32 times compared with the control group ($P < 0.001$). During ovulation, the FSH range in patients of group C was 1.19 times lower than that in controls ($P < 0.001$) (Table 3).

In patients of the M and T groups, deviations of sex hormones were more evident in the mid-luteal phase (Table 4).

In patients of group M, changes in the hormonal profile of peripheral blood serum were more pronounced than in women of group T: in the early follicular phase of the cycle, the FSH level was increased by

TABLE 1 Characteristics of our study populations.^{a,b}

Characteristics	Military personnel		Occupied/ de-occupied		Control (n = 50)
	With PCS (n = 211)	Without PCS (n = 246)	With PCS (n = 103)	Without PCS (n = 105)	
Age group, y	30 (25–36)	28 (24–34)	32 (26–36)	30 (24–35.5)	28 (24–36)
BMI	24 (23–26)	24 (23–26)	25 (23.5–26)	24 (22–25)	24 (23–26)
Menstrual cycle characteristics					
Menarche, y	12.87 ± 0.10	12.71 ± 0.12	12.84 ± 0.09	12.63 ± 0.09	12.72 ± 0.14
Cycle duration, d	28.23 ± 0.18	28.63 ± 0.29	28.50 ± 0.16	28.52 ± 0.14	28.03 ± 0.24
Bleeding duration, d	5.50 ± 0.10	5.61 ± 0.09	5.21 ± 0.09	5.18 ± 0.12	5.07 ± 0.17
Cycles/year	12.99 ± 0.09	12.88 ± 0.13	12.85 ± 0.07	12.83 ± 0.06	13.05 ± 0.11
Reproductive history					
Present pregnancy	74 (35)	86 (35)	48 (46.5)	47 (44.8)	30 (60)
Artificial abortions	47 (22.2)	63 (25.6)	31 (30)	32 (30.5)	7 (23.3)
Miscarriage	36 (17)	37 (15)	6 (5.8)	7 (6.7)	5 (50)
Childbirth	54 (25.6)	60 (24.4)	18 (17.4)	19 (18)	37 (74)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); PCS, Post-concussion scale.

^aData are presented as mean ± standard deviation, median (interquartile range) or as number (percentage).

^bThe groups were homogeneous in terms of age, body mass index, menstrual, ovulatory, and reproductive function, and gynecologic, somatic, and infectious past medical history. Distribution of study participants according medical/medication history, Kyiv Center of Reproductive and Perinatal Medicine.

TABLE 2 Menstrual characteristics.^{a,b}

Group	Menstruation characteristics				
	Not painful	Painful	Light flow	Moderate flow	Heavy flow
All, n=457	214 (50.59±0.34)	243 (49.41±0.34)	18 (4.26±0.10)	294 (69.50±0.40)	145 (26.24±0.25)
MO, n=211	45 (41.28±0.73)	64 (58.72±0.73)	4 (3.67±0.18)	70 (64.22±0.77)	35 (32.11±0.54)
MP, n=246	44 (41.90±0.74)	61 (58.10±0.74)	3 (2.86±0.16)	67 (63.81±0.78)	35 (33.33±0.56)
TO, n=103	65 (61.90±0.60)	39 (38.10±0.60)	5 (4.76±0.21)	79 (76.19±0.85)	20 (19.05±0.43)
TP, n=105	60 (57.69±0.64)	44 (42.31±0.64)	6 (5.77±0.24)	77 (74.04±0.84)	21 (20.19±0.44)
C, n=30	20 (66.67±1.07)	10 (33.33±1.07)	2 (6.67±0.48)	24 (80.00±1.65)	3 (10.00±0.59)

Abbreviations: C, female civilians, who stayed in relatively safe areas of Ukraine; MO, female military personnel with a history of concussion with PCS; MP, female military personnel with a history of concussion without PCS; PCS, post-concussion scale; TC, female civilian patients who stayed in occupied/de-occupied territories without PCS; TO, female civilian patients who stayed in occupied/de-occupied territories with PCS.

^aData are presented as mean±standard deviation.

^bThe analysis of the menstruation showed that in groups MO and MP, compared to controls, menstruation was more likely to be painful and more often abundant. Distribution of study participants according medical/medication history, Kyiv Center of Reproductive and Perinatal Medicine.

TABLE 3 Levels of gonadotropins in examined patients in the dynamics of menstrual cycle.^{a,b}

Group	Cycle day	FSH, mmol/mol	LH, mmol/mol	LH/FSH	PRL, ng/mL
All, n=457	5th	5.41±0.11	6.89±0.16	1.34±0.03	8.76±0.21
	14th	10.66±0.21	36.10±0.54	3.70±0.09	-
	21st	3.70±0.07	6.09±0.17	1.74±0.05	-
MO, n=211	5th	5.49±0.14	6.93±0.25	1.32±0.05	9.14±0.28
	14th	10.48±0.28	35.98±0.87	3.79±0.15	-
	21st	3.82±0.09	6.13±0.25	1.70±0.08	-
MP, n=246	5th	5.32±0.17	6.84±0.2	1.36±0.04	8.37±0.31
	14th	10.84±0.32	36.23±0.63	3.60±0.10	-
	21st	3.57±0.10	6.05±0.21	1.78±0.07	-
TO+TP, n=209	5th	4.87±0.10	5.96±0.21	1.30±0.05	8.67±0.25
	14th	11.69±0.21	38.61±0.56	3.52±0.09	-
	21st	3.51±0.06	6.14±0.22	1.83±0.07	-
TO, n=103	5th	4.94±0.14	5.88±0.32	1.23±0.06	8.52±0.45
	14th	11.51±0.28	38.75±0.84	3.54±0.11	-
	21st	3.53±0.09	6.05±0.33	1.77±0.09	-
TP, n=105	5th	4.80±0.14	6.05±0.28	1.37±0.08	8.82±0.23
	14th	11.87±0.31	38.47±0.75	3.50±0.13	-
	21st	3.50±0.09	6.23±0.28	1.89±0.11	-
C, n=50	5th	4.65±0.15	4.88±0.18	1.08±0.04	8.98±0.47
	14th	12.73±0.42	46.69±1.76	3.76±0.16	-
	21st	3.55±0.12	6.64±0.25	1.92±0.08	-

Abbreviations: C, female civilians, who stayed in relatively safe areas of Ukraine; E₂, estradiol; FSH, follicle-stimulating hormone; LH, luteinizing hormone; MC, menstrual cycle; MO, female military personnel with a history of concussion with PCS; MP, female military personnel with a history of concussion without PCS; P, progesterone; PCS, post-concussion scale; PRL, prolactin; T, free testosterone; TC, female civilian patients who stayed in occupied/de-occupied territories without PCS; TO, female civilian patients who stayed in occupied/de-occupied territories with PCS.

^aData are presented as mean±standard deviation.

^bDistribution of study participants according medical/medication history, Kyiv Center of Reproductive and Perinatal Medicine.

more than 1.05 times compared with the control group, and LH by 1.16 times. During the period of ovulation, FSH was reduced by more than 1.09 times, and LH by 1.11 times. In the mid-luteal phase, estradiol decreased by more than 1.09, and progesterone by 1.15.

During the histologic examination of endometrial samples from 214 women with PCS (109 group M and 105 group T), it was found that 65 (30.37%) did not correspond to the phase and day of menstrual cycle according to the criteria of R.W. Noyes.²³ Thus, in the

TABLE 4 Levels of sex steroids in the examined patients in the dynamics of menstrual cycle.^{a,b}

Group	MC day	E ₂ , pmol/L	P, pmol/L	E ₂ /P
All, n = 457	5th	0.424 ± 0.005	2.14 ± 0.07	0.278 ± 0.02
	21st	0.352 ± 0.005	35.40 ± 0.95	0.011 ± 0.00
MO, n = 211	5th	0.426 ± 0.006	2.11 ± 0.09	0.286 ± 0.022
	21st	0.350 ± 0.008	34.97 ± 1.33	0.012 ± 0.000
MP, n = 246	5th	0.421 ± 0.007	2.18 ± 0.11	0.270 ± 0.020
	21st	0.355 ± 0.008	35.84 ± 1.35	0.011 ± 0.000
TO+TP, n = 209	5th	0.394 ± 0.012	2.36 ± 0.07	0.200 ± 0.008
	21st	0.385 ± 0.006	40.71 ± 0.94	0.010 ± 0.000
TO, n = 103	5th	0.403 ± 0.014	2.34 ± 0.09	0.207 ± 0.013
	21st	0.381 ± 0.010	39.80 ± 1.31	0.010 ± 0.000
TP, n = 105	5th	0.384 ± 0.018	2.38 ± 0.12	0.193 ± 0.010
	21st	0.390 ± 0.008	41.62 ± 1.35	0.011 ± 0.001
C, n = 50	5th	0.326 ± 0.019	2.31 ± 0.22	0.289 ± 0.074
	21st	0.446 ± 0.020	55.01 ± 1.32	0.008 ± 0.000

Abbreviations: C, female civilians, who stayed in relatively safe areas of Ukraine; E₂, estradiol; MC, menstrual cycle; MO, female military personnel with a history of concussion with PCS; MP, female military personnel with a history of concussion without PCS; P, progesterone; PCS, post-concussion scale; TC, female civilian patients who stayed in occupied/de-occupied territories without PCS; TO, female civilian patients who stayed in occupied/de-occupied territories with PCS.

^aData are presented as mean ± standard deviation.

^bIn patients of the M and T groups, deviations of sex hormones were more evident in the middle luteal phase. Distribution of study participants according medical/medication history, Kyiv Center of Reproductive and Perinatal Medicine.

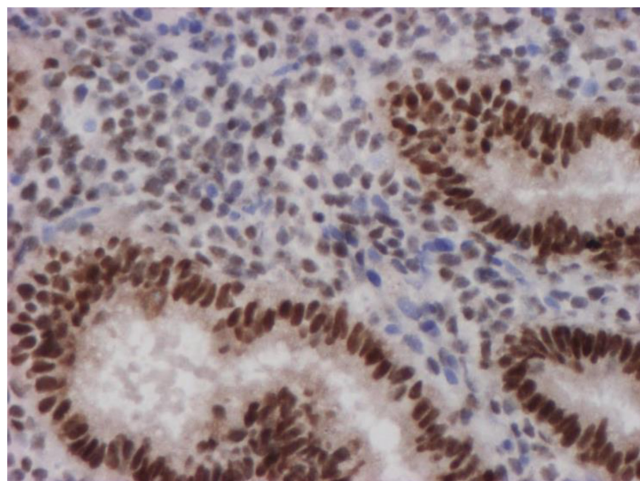


FIGURE 1 Increased expression of receptors for estrogen- α in the endometrial glands on the 21st day of menstrual cycle with the proliferation phase. Immunohistochemistry staining, $\times 150$.

endometrial glands of patients with PCS, an increase in the expression of estrogen receptor- α and a decrease in the production of androgen receptors was observed with a normal number of receptors to progesterone (Figures 1 and 2). Estradiol and progesterone interact with specific receptors that are crucial for gene expression in implantation and early pregnancy.²⁴ Estrogens stimulate epithelial cell proliferation and the development of the secretory apparatus, inducing the synthesis of estrogen and progesterone receptors. Estradiol enhances its own receptors and promotes progesterone

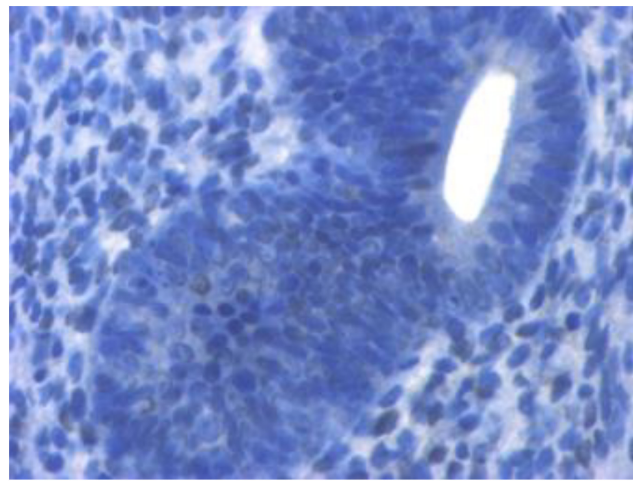


FIGURE 2 The decrease of expression of androgen receptors in the glands in the stroma of the endometrium on the 21st day of menstrual cycle corresponds to the early secretion phase. Immunohistochemistry staining, $\times 300$.

and androgen receptor synthesis, while progesterone suppresses its own receptors, similarly to its effect on estradiol receptors. Receptor abundance depends on hormone concentration and other steroid classes.

Endometrial hyperplasia is commonly attributed to an imbalance between estrogen and progesterone levels. When ovulation fails to take place, progesterone production is hindered, resulting in the failure to shed the endometrial lining. Consequently, the endometrium may continue to proliferate in response to elevated estrogen levels.

4 | DISCUSSION

Female soldiers with PCS are 1.3 times ($P < 0.015$) more likely to experience longer menstrual periods (> 8 days). Painful menstruation is 1.47 times ($P < 0.001$), and heavy periods are 1.64 times ($P < 0.003$) more frequent. The infertility duration in those who suffered a concussion is 5.36 ± 0.13 years, whereas with PCS it is 1.29 times longer (6.02 ± 0.21 years) ($P < 0.001$), compared with women without (4.69 ± 0.13 years). In all, 170 (69.27%) soldiers who suffered a concussion had endometrial structural pathology (hyperplasia without atypia, atypical hyperplasia), with PCS this was 1.64 times ($P < 0.001$) more frequent.

Hormonal imbalances were observed, including increased prolactin, decreased LH, FSH, estradiol, and progesterone. These imbalances led to extended menstrual periods, anovulation, luteal phase defect, and oocyte aging.

The study has multiple limitations that should be addressed. The small sample size of civilians from safe zones may limit generalizability, while the cross-sectional design prevents establishing causality between concussion and reproductive system pathology. These limitations should be acknowledged and discussed in the study's interpretation to ensure a balanced perspective on the findings. Additionally, other limitations include not accounting for potential confounding factors and relying on self-reporting, which could introduce bias and affect data reliability. Consideration of objective measures and independent assessments is recommended to enhance the robustness of the study.

One survey has evaluated the state of the reproductive health of active-duty female service members. It reported, that 21% had urinary tract or vaginal infections during deployment, one in five did not have access to their preferred form of birth control, the unintended pregnancy rate was 5.9%, and 11% were unable to conceive after 12 months of trying.²⁵

Because of the ongoing war in Ukraine, the prevalence of sexual and gender-based violence is difficult to measure.²⁶ Only in one city north of Kyiv, named Bucha, 25 rapes were documented after the occupation of the city. According to experts, the underreporting of the number of Russian sexual crimes in Ukraine is probably massive, and the reported cases are only "the tip of the iceberg". In the Russian-Ukrainian war, sexual violence has been taking place since 2014. The estimated number of raped women in the former Yugoslavia ranged between 14000 and 50000.^{27,28} According to the British historian Anthony Bivory, nearly 130000 women and girls were raped in Berlin between 1941 and 1945, many of them repeatedly. Also, according to the historian, about 10000 rape victims died because of their injuries.²⁹

A lot of Ukrainian service women and citizens from the occupied territories are being kept in captivity, where their physical and psychological health is being violated.²⁶ All this is a method of war. Much of the data will come after liberating the occupied territories. Many women will need proper medical and psychological counseling.

At the same time, millions of women have become refugees inside or outside Ukraine, which has also led to major stress and disruption of the hypothalamic-pituitary-gonadal axis. This leads to

reproductive health disorders. In addition, war-affected populations are at risk for sexually transmitted diseases.

At the same time, the problem of the health of female veterans, active servicewomen, and civilians is not only medical, but also social, because the physical, mental, and social well-being of this portion of the people of Ukraine depends not only on the defense capability of the state but also on the country's demographic, socio-political and social stability.

AUTHOR CONTRIBUTIONS

AS, VK, YK, AV-M, and IM contributed to the design and implementation of the research, to the analysis of the results, and to the writing of the manuscript. VK supervised the project.

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ORCID

Anastasia Serbeniuk  <https://orcid.org/0000-0002-7212-2678>

Viacheslav Kaminskiy  <https://orcid.org/0000-0002-5369-5817>

Yana Kumpanenko  <https://orcid.org/0000-0002-7019-5662>

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