

## ORIGINAL ARTICLE

**PREVALENCE AND RISK FACTORS OF INFERTILITY IN UKRAINE: RESULTS A MULTICENTER STUDY (2019-2021)**

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**INTRODUCTION**

Infertility is a global socio-economic, demographic, reproductive health and clinical issue affecting millions of people of reproductive age worldwide. Infertility also can cause significant financial loss and emotional stress. Furthermore, infertility is associated with increased risk of subsequent chronic health conditions such as cardiovascular disease [1]. Available data suggests that infertility affects an estimated 15% of couples globally, amounting to 48.5 million couples [2,3], and 186 million individuals [4-6]. However, prevalence estimates of lifetime infertility vary widely, in part because there is no agreed or consistent definition of infertility [7] and because study populations vary by age range, unit of measurement and relationship status [8]. Establishing the true magnitude of infertility as a public health problem is challenging, given that it is not categorized as a disability or chronic condition and may be largely unreported [9].

Fertility is one of the primary components of population dynamics. In the last three decades, the population of Ukraine has been rapidly shrinking due to low birth rates [10]. Within 30 years, its population declined by 10.4 million, from a high of 51.9 million in 1991 to 41.5 million in 2020 [11]. One of the reasons for the low birth rate is the infertility among married population [12]. For this reason decline of fertility level 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 in Ukraine. In addition, the declining birth rate could potentially worsen the aging problem in Ukraine.

Infertility is a reproductive healthcare problem which affects not only individuals, families and social populations in Ukraine. Childlessness has still a great social concern which often leads to severe pressure on married couples to have a child. These pressures would more serious each year

of marriage. Despite of significant social meaning of childlessness, there has been less scientific focuses on infertility in sexual and reproductive health field in Ukraine. With a remarkable decline of total fertility rate (TFR), the infertility prevalence rate is considerably high in Ukraine. The introduction of family planning programmers' in Ukraine and other factors derived from socio-economic dynamics did not contributed to a significant increase of the TFR.

Recently, the infertility rate in Ukraine has a trend of increase year by year, and few studies have reported the infertility rate in other regions of Ukraine [13]. However, these data are too old to show the current level in Ukraine, calling for an attempt to measure up-to-date infertility prevalence rate at national level. From our knowledge, only a few studies were conducted to study infertility within narrow clinical features, showing that the percentage of infertile couples seeking infertility treatment services has grown increasingly in Ukraine. Moreover, there has been no attempt to study focused on both of prevalence measurement and investigation of associating risk factors of infertility. In addition, there are did not national data on the prevalence of male and female infertility, as well as primary and secondary infertility among married women in Ukraine.

## THE AIM

The aim of this study was to assess the current prevalence and identify the risk factors for infertility among couples of 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 married populations from January 1st, 2019 to December 31st, 2021 in Ukraine. We compiled list of the 25 medical centers for family planning and reproductive health. Of these, only 19 medical centers from 17 regions (Lviv, Ivano-Frankivsk, Rivne, Vinnytsia, Volyn, Chernivtsi, Cherkasy, Chernihiv, Poltava, Zhytomyr, Kyiv, Kharkiv, Kherson, Dnipropetrovsk, Donetsk, Luhansk, Odessa) of Ukraine agreed to take part in the study. Cities and villages located respectively in the west and east, and north and south, as well as the in central region of Ukraine were used as objects of comparison, since they often resemble opposing views on social, historical and demographic processes up to the present day. The study population included couples living together and married for more than 1 year, of whom the female spouse was 20-49 years old. Multistage stratified random sampling was used. Participants this study were selected using stratified probability sampling from which couples resident in Ukraine was selected at random. The inclusion criteria for participants were as follows: 20–49 years old; married or cohabitational; local residents. Te exclusion criteria for participants were as follows: never had sexual

intercourse; received continuous medical treatment that could affect fertility.

## DEFINITIONS

In our study fertility is defined as the ability of a man and woman to reproduce, while infertility denotes lack of fertility or an involuntary reduction in the ability to produce children. Infertility is a disease of the male or female reproductive system defined by the failure to achieve a pregnancy after 12 months or more of regular unprotected sexual intercourse [14]. In this study infertility among married women was classified as primary and secondary. Primary infertility is the inability to have any pregnancy, while secondary infertility is the inability to have a pregnancy after previously successful conception. In this study 'Thin' means that Body Mass Index (BMI) is less than 18.5 kg/m<sup>2</sup>. 'Normal' means 18.5 kg/m<sup>2</sup> ≤ BMI < 24 kg/m<sup>2</sup>. 'Overweight' means 24 kg/m<sup>2</sup> ≤ BMI < 28 kg/m<sup>2</sup>. 'Obesity' means that BMI is more than 28 kg/m<sup>2</sup>.

## DATA COLLECTION

This study includes interviews and questionnaires of couples, also analyses medical records infertile married women's. We formed a working group to conduct this research, which included obgyne specialists (nurses and physicians) and reproductive medical graduate students. Married women were approached via telephone and face-to-face in medical centers conversation to complete the standardised and structured questionnaire by trained interviewers. The next step was to complete the paper questionnaires, which contained a series of questions, including basic information, marriage and childbirth history, and personal lifestyle habits, under the guidance of this specialist. During the interviews, participants were introduced this research. The next step was to complete the paper questionnaires, which contained a series of questions and divided into three parts, including basic information, marriage and childbirth history, and personal lifestyle habits, under the guidance of this specialist. Participants had access to free reproductive health counseling in the process. Additionally, anthropometric (height and weight) examinations were performed and recorded by other two specialists. In this study adopted double entry mode of paper questionnaire data and were analysed anonymously. We distributed 8920 paper questionnaires and collected 7113 completed paper questionnaires (79.4%). After excluding those who did not meet the inclusion criteria and who met the exclusion criteria, the final number of study participants was 6885. According to their history of pregnancy, child birth and contraception, the infertile women were divided into primary infertility and secondary infertility cohorts.

## ETHICS

This study was performed in line with the principles of the Declaration of Helsinki. The Shupyk National Healthcare

University of Ukraine Ethics Committee approved this study. All participants signed an informed consent and each had a unique identification number assigned to protect their privacy.

## STATISTICAL ANALYSIS

In this study the analysis of statistical data was performed using Excel. Prevalence and identify the risk factors for infertility was reported as the percentage of the total number of married women. We conducted descriptive analyses to determine frequencies for categorical variables and calculated medians (or means) for continuous variables. Comparisons were undertaken using Student's t-test and Fisher's exact test for categorical variables. We used binary logistic multivariate regression analysis, and for variable selection we used forward stepwise regression based on maximum likelihood estimation.  $p < 0.05$  indicated that the difference was statistically significant.

## RESULTS

### PREVALENCE OF INFERTILITY

During the study period (January 1st, 2019 and December 31st, 2021), of the 6885 participants included in the study, infertility was detected in 1746. The prevalence of infertility in this study cohort was 25.4% (95% confidence interval [CI] 24.9%, 25.9%,  $p < 0.012$ ). The mean  $\pm$  SD age was  $32.9 \pm 0.25$  years for the fertile group and  $34.9 \pm 0.39$  years for the infertile group. The difference in mean age between these two groups was statistically significant ( $p < 0.001$ ). The levels of infertility in the regions of Ukraine had significant differences. It was detected the high level couples infertility rate in South and Central regions, and low level in West, East and North regions of Ukraine (Table I). The difference in the age, age of marriage, history of gynecological surgery, long-term stay in air-conditioning environment, ovarian dysfunction, and history of endometriosis between the two groups were statistically significant ( $p < 0.05$ ). The infertility rate rose initially and then decreased for every 5 years added to women's age. Women aged 35–39 years had the highest infertility rate. When the participants were grouped by age of marriage, the infertility rate increased

as the age of marriage increases. Among all participants the contraceptive prevalence rate was high at all ages, and the rate of women who still hope to conceive decreases as they get older. Characteristics of the difference between the fertile and infertile group are presented in Table II.

The prevalence of primary infertility and secondary infertility was about 5.8% and 19.6%, respectively. Among the infertile women, the difference between primary and secondary infertility was statistically significant by household registry, age, age of marriage, age of first sexual intercourse ( $p < 0.05$ ) (Table III). It was found that among those women who had primary infertility, more were from rural than urban, while for secondary infertility women the situation was reversed. Among infertile women 55.3% went to hospital seeking medical help regardless of the outcome after treatment. From data obtained, the main causes of infertility were fallopian tube factor (27.3%), ovulation disorders (31.7%), endometriosis (18.1%), male factor (13.7%), and unexplained factors (9.2%). Characteristics of primary and secondary infertile groups are shown in Table III.

### RISK FACTORS FOR INFERTILITY

In this study Table IV showed the odds ratio (OR) and 95% confidence interval (CI) for the factors associated with infertility in logistic multivariate regression analyses. Infertility was associated with age as shown in logistic regression analysis. Compared with women aged 20–24 years, the adjusted OR for women aged 30–34 years was 5.036 (95% CI, 1.163–21.83) and the adjusted OR for women aged 35–39 years was 6.862 (95% CI, 1.557–30.248). History of gynecological surgery was associated with infertility. Also, ovarian dysfunction was associated with infertility. There were differences among factors associated with infertility, primary infertility and secondary infertility. The factors associated with primary infertility were age of marriage ( $p = 0.006$ ), age of first sexual intercourse ( $p = 0.003$ ), long-term air-conditioning environment ( $p < 0.001$ ), decreased ovarian reserve ( $p = 0.005$ ) and age ( $p = 0.002$ ). A factors associated with secondary infertility were history of gynecological surgery ( $p < 0.001$ ) and decreased ovarian reserve ( $p = 0.002$ ). (data not shown).

**Table I.** Prevalence of infertility by region of Ukraine (2019–2021)

Region	All (n=6,885)	Fertile (n = 5,139)		Infertile (n = 1,746)		p-value
		n	%	n	%	
West	1,465	1,216	81.7	249	18.3	0.012
East	1,487	1,186	77.4	301	22.6	
North	1,305	1,031	80.7	274	19.3	
South	1,331	912	68.7	419	31.5	
Central	1,297	794	63.7	503	36.3	
Total	6,885	5,139	74.6	1,746	25.4	

**Table II.** Characteristics of fertile and infertile group in Ukraine (2019-2021)

Characteristics	All (n=6,885)	Fertile (n = 5,139)		Infertile (n = 1,746)		p-value
		n	%	n	%	
Age (years)						
20–24	315	297	5.8	18	1.0	< 0.001
25–29	1,620	1,422	27.7	198	11.3	
30–34	2,358	1,629	31.7	729	41.8	
35–39	1,341	855	16.6	486	27.8	
40–44	855	639	12.4	216	12.4	
45–49	396	297	5.8	99	5.7	
Place of residence						
Urban	3,609	2,715	52.8	894	51.2	0.569
Rural	3,276	2,424	47.2	852	48.8	
Occupation						
Unemployed	936	666	13.0	270	15.5	0.541
Head of enterprises	972	711	13.8	261	14.9	
Professional worker	2,574	1,980	38.5	594	34.0	
Clerk	261	216	4.2	45	2.6	
Service worker	945	711	13.8	234	13.4	
Agricultural worker	180	117	2.3	63	3.6	
Operator	45	36	0.7	9	0.5	
Other	972	702	13.7	270	15.5	
Educational level						
Primary	972	675	13.1	297	17.0	0.391
High school	1,044	819	15.9	225	12.9	
Junior college degree	1,512	1,150	22.4	362	20.7	
Bachelor's degree and above	3,357	2,495	48.6	862	49.4	
Smoking						
No	90	72	1.4	18	1.0	0.582
No, secondhand smoke	1,602	1,251	24.3	351	20.1	
Yes	5,193	3,870	75.3	1,323	75.8	
Drinking						
No	801	666	13.0	135	7.7	0.072
Yes	6,084	4,473	87.0	1,611	92.3	
BMI <sup>a</sup> (kg/m <sup>2</sup> )						
Thin	495	351	6.8	144	8.2	0.486
Normal	4,347	3,303	84.3	1,044	59.8	
Overweight	1,557	1,125	21.9	432	24.7	
Obese	486	360	7.0	126	7.2	
Age of marriage (years)						
≤ 24	3,429	2,717	52.9	712	40.8	0.041
25–29	3,177	2,251	43.8	926	53.0	
≥ 30	279	171	3.3	108	6.2	
Age of first sexual intercourse						
< 20	864	702	13.7	162	9.3	0.197
20–25	4,545	3,384	65.8	1,161	66.5	
> 25	1,476	1,053	20.5	423	24.2	
History of gynecological surgery						
No	6,183	4,788	93.2	1,395	79.9	< 0.001
Yes	702	351	6.8	351	20.1	
History of endometriosis						
No	6,696	5,031	97.9	1,665	95.4	0.048
Yes	189	108	2.1	81	4.6	
Long-term air-conditioning environment						
No	2,601	1,827	36.6	774	44.3	0.009
Yes	4,284	3,312	64.4	972	55.7	
DOR <sup>b</sup>						
No	6,525	4,995	97.2	1,530	87.6	< 0.001
Yes	360	144	2.8	216	12.4	
Total	6,885	5,139	74.6	1,746	25.4	

<sup>a</sup>BMI, Body Mass Index<sup>b</sup>DOR, Decreased ovarian reserve

**Table III.** Characteristics of primary and secondary infertile groups in Ukraine (2019–2021)

Characteristics	All (n=1,746)	Primary infertility (n = 472)		Secondary infertility (n = 1,274)		p-value
		n	%	n	%	
Age (years)						
20–24	18	18	3.6	0	0.0	< 0.001
25–29	198	143	30.3	55	4.3	
30–34	729	189	40.0	540	42.4	
35–39	486	91	19.3	395	31.0	
40–44	216	22	4.7	194	15.2	
45–49	99	9	1.9	90	7.1	
Place of residence						
Urban	868	173	36.7	695	54.6	0.014
Rural	878	299	63.3	579	45.4	
Age of marriage (years)						
≤ 24	702	135	28.6	567	44.5	0.014
25–29	936	274	58.1	662	52.0	
≥ 30	108	63	13.3	45	3.5	
Age of first sexual intercourse (years)						
< 20	182	36	7.6	146	11.5	< 0.001
20–25	1172	207	43.9	965	75.7	
> 25	392	229	48.5	163	12.8	

**Table IV.** Logistic multivariate regression analyses of risk factors associated with infertility in Ukraine (2019–2021)

Characteristics	p-value	Unadjusted OR <sup>a</sup> (95% CI)	p-value	Adjusted OR (95% CI)
Age (years)				
	< 0.001		< 0.001	
20–24		Ref		Ref
25–29	0.269	2.297(0.515–10.249)	0.587	1.523 (0.335–6.943)
30–34	0.012	6.618(1.549–28.274)	0.031	5.036 (1.163–21.83)
35–39	0.003	9.379 (2.165–40.619)	0.011	6.862 (1.557–30.247)
40–44	0.025	5.577 (1.244–25.011)	0.109	3.49 (0.758–16.071)
45–49	0.035	5.50 (1.131–26.752)	0.174	3.096 (0.607–15.797)
History of gynecological surgery				
No		Ref		Ref
Yes	< 0.001	3.611 (2.234–5.831)	< 0.001	3.063 (1.819–5.158)
DOR <sup>b</sup>				
No		Ref		Ref
Yes	< 0.001	5.131 (2.662–9.878)	< 0.001	3.835 (1.908–7.712)
Constant			0.003	0.109

<sup>a</sup>OR, Odd Ratio<sup>b</sup>DOR, Decreased ovarian reserve

## DISCUSSION

This is the first multicentre study was aimed to estimate the prevalence and both primary and secondary infertility rate among Ukrainian married women and identify the

factors associated with vulnerability of infertility. In this study the current prevalence of infertility among couples of reproductive age in Ukraine was 25.4%. The prevalence of primary infertility among women was 5.8%, and the

prevalence of secondary infertility was 19.6%. The levels of infertility in the regions of Ukraine had significant differences. It was detected the high level couples infertility rate in South and Central regions, and low level in West, East and North regions of Ukraine. It was found that among those women who had primary infertility, more were from rural than urban, while for secondary infertility women the situation was reversed. Infertility was associated with age, history of gynecological surgery, ovarian dysfunction, age of marriage, long-term air-conditioning environment, and history of endometriosis. There were differences among factors associated with infertility, primary infertility and secondary infertility. The factors associated with primary infertility were age of marriage, age of first sexual intercourse, long-term air-conditioning environment, decreased ovarian reserve and age. A factors associated with secondary infertility were history of gynecological surgery and decreased ovarian reserve.

Reports about the prevalence of infertility are rare currently in Ukraine. According to national statistical reports, the prevalence of current infertility has increased in 3.0 times for the last five years (2012-2017) in Ukraine. Our estimates of infertility are broadly in line with those found by previous studies although prevalence estimates differ as a result of diverse definitions and study populations.

The prevalence of infertility varies greatly in different countries and regions, and change all the times. The infertility estimates use different definitions considering different periods, which make direct comparisons difficult between various studies. The definition, as well as the etiological causes associated with infertility, differs from region to region. Infertility affects both men and women, and approximately 10% to 15% of couples in industrialized countries are infertile. The percentage of infertile men ranged from 2-5% to 12% [7]. Infertility rates were highest in Africa and Central/Eastern Europe. Additionally, according to a variety of sources, rates of male infertility in North America, Australia, and Central and Eastern Europe varied from 4 5-6%, 9%, and 8-12%, respectively [7]. The infertility prevalence rate was in the United States 15.5% [15], in Canada 11.5-15.7% [16], in Britain 12.5% [8], in China 24,6% [17]. In Scotland, nearly one in five women attempting conception experienced infertility [18]. The percentage of infertility, based on data collected in demographic surveys, varies between different countries as well as gender, with the higher being in men, examples being >10% and 17% for Finland and 18% and >21% for Switzerland [13]. Prevalence of infertility among women in Norway, Poland, Romania, Czech Republic has been recorded as between 5-8%, which increases to >10% in Sweden and Canada. The large differences among countries could be attributable to large differences involuntary infertility [13]. Other studies have reported higher and lower estimates but, because of differences in study groups and outcome measures, comparison is not possible. In our study prevalence of infertility was 25,4%.

Previous studies have shown that age, history of gynecological surgery, decreased ovarian reserve, age of marriage,

long-term air-conditioning environment, and history of endometriosis, age of first sexual intercourse are factors associated with infertility [17]. Fertility problems were associated with endometriosis and pelvic surgery [17, 18]. The risk of primary infertility proportionally increases by age since reproduction capability is biologically decrease when a woman ages [19]. Some former studies also demonstrated that young women were frequently exposed to sexual dysfunction and ovulatory disorders, which had already been known as leading causes of infertility [17, 20]. The risk factors of infertility detected in our study are comparable with those obtained in other previous similar studies.

We found that ever experience of infertility and of help seeking were associated with few current health factors for women. In Ukraine little more than half of women who had experienced infertility had sought medical or professional help for the problem. Those who did so were better educated and in higher status occupations. Our estimate that 55.3% of women sought medical help for infertility is close to that reported by an international review which estimated that 56% of women in more developed countries sought help [5], and by a Finnish study [21], and by a Britain study [8] which found that 57% of all subfertile women did so. Other studies [22, 23] have reported higher and lower estimates but, because of differences in study groups and outcome measures, comparison is not possible.

According to literature, interventions to encourage help seeking include raising public awareness about reproductive risks and strategies to minimize them [24], general practitioners taking opportunities to discuss fertility with patients, greater access to fertility treatments [25]. Ukraine is a country that lays particular emphasis on the issue of infertility, especially after experiencing a dramatic fertility decline over the last two decades. The Ukrainian State program for infertility treatment by budget funds was approved in Ukraine since 2004. However, most infertile women do not have access to this program. This means that many women have to pay out-of-pockets. Reproductive healthcare for young women should be strengthened with promotion of health education to provide them with sufficient knowledge related to reproductive health problems including potential risk factors to develop primary infertility.

## STUDY STRENGTHS AND LIMITATIONS

Our study investigation has several strengths. First, this is the first multicentre study was aimed to estimate the prevalence and both primary and secondary infertility rate among Ukrainian married women and identify the factors associated with vulnerability of infertility. Second, size of the sample and the fact that it is population-based. Our findings will be useful to resource allocation and health services planning for the growing number of patients with infertility. However, the limitations of this study also need to be noted. First, the estimation of prevalence of infertility was based on questionnaire-based interview method. The

current study relied on women's response to these questionnaires; these assumptions may be inaccurate, as women may not reveal accurately on this sensitive topic such as past voluntary abortions. Self-reported data may be subject to recall bias. Second, men were not included in the study, although they may also cause infertility. Despite some limitations, this study is helpful to understand infertility dynamics and some influencing factors increasing the risk of infertility in Ukraine. We expect that our findings will be invaluable to health professionals toward their efforts to reduce the burden of infertility in their respective regions of Ukraine.

## CONCLUSIONS

The results of this study revealed high level the prevalence rate of infertility among couples of reproductive age in Ukraine is high. This applies to both primary and secondary infertility of married women. The most women who had experienced infertility have not sought medical or professional help for the problem. The main reason for this is the high cost for infertility treatment. There should be taken practical measures at policy level for education to improve literacy level related to sexual and reproductive health including prevention of infertility among young women. There should be developed a specific health policy to focus on the support for infertile couples to promote better access to infertility diagnosis and treatment service in Ukraine. Further research is required to determine which set of interventions minimize factors increasing the risk of infertility.

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*The Authors declare no conflict of interest*

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