

RISK FACTORS FOR INFERTILITY IN WOMEN IN A PERUVIAN HOSPITAL

FACTORES DE RIESGO PARA INFERTILIDAD EN MUJERES EN UN HOSPITAL PERUANO

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ABSTRACT

Introduction: Infertility is defined as the failure to achieve pregnancy after 12 months of unprotected sex, according to the World Health Organization (WHO). Between 60 to 80 million couples annually suffer from this problem. In Peru there are no updated reports that allow to know these figures and there are few studies that allow to know the causes of this condition. **Objective:** To determine the risk factors associated with infertility in female patients treated in outpatient offices in the gynecology service of the Vitarte hospital, period January 2015 to April 2019. **Methods:** An observational, analytical, retrospective case-control study was conducted, considering a sample of 82 cases and 82 controls. Clinical, demographic and habits of harmful consumption factors were considered and, to measure the association, the crude and adjusted odds ratios were used, for which the statistical package SPSS was used. **Results:** Based on the adjusted OR, dyspareunia was identified (OR: 4.16, 95% CI 1.56-11.14), dysmenorrhea, (OR: 4.22, 95% CI 1.79-9.93), pelvic inflammatory disease (OR: 5.59, 95% CI 2.11-14.84), and alcohol consumption (OR: 2.87, 95% CI 1.10-7.49), as statistically significant risk factors for the development of infertility. **Conclusion:** The factors associated with infertility in the gynecology service of the Vitarte hospital during the period from January 2015 to April 2019 are dyspareunia, dysmenorrhea, the history of pelvic inflammatory disease and alcohol consumption.

Key words: Infertility; Pelvic Inflammatory Disease; Ectopic pregnancy (source: MeSH NLM).

RESUMEN

Introducción: La infertilidad se define como el no logro del embarazo posterior a 12 meses de relaciones sexuales sin protección, según la Organización Mundial de la Salud (OMS). Entre 60 a 80 millones de parejas anualmente sufren este problema. En el Perú, no existen reportes actualizados que permitan conocer estas cifras y hay pocos estudios que permitan conocer las causas de esta afección. **Objetivo:** Determinar los factores asociados a infertilidad en pacientes mujeres atendidas en consultorios externos en el servicio de ginecología del hospital Vitarte, periodo enero 2015 a abril del 2019. **Métodos:** Se realizó un estudio observacional, analítico, retrospectivo de casos y controles, considerando una muestra de 82 casos y 82 controles. Se consideraron factores de riesgo clínicos, demográficos y de hábitos de consumo nocivo y, para medir la asociación, se utilizó los odds ratio crudos y ajustados, para lo cual se usó el paquete estadístico SPSS. **Resultados:** En base a los OR ajustados, se identificó a la dispareunia (OR:4,16, IC95% 1,56- 11,14), dismenorrea, (OR:4,22, IC95% 1,79-9,93), enfermedad pélvica inflamatoria (OR:5,59, IC95% 2,11- 14,84), y el consumo de alcohol (OR:2,87, IC95% 1,10-7,49), como factores de riesgo estadísticamente significativos para el desarrollo de infertilidad. **Conclusión:** Los factores asociados a la infertilidad en el servicio de ginecología del hospital Vitarte durante el periodo de enero 2015 a abril 2019 son la dispareunia, dismenorrea, el antecedente de enfermedad pélvica inflamatoria y, el consumo de alcohol.

Palabras clave: Infertilidad; Enfermedad Inflamatoria Pélvica; Embarazo ectópico (fuente: DeCS BIREME).

INTRODUCTION

We can define infertility as couple inability, whether one of them or both, to conceive naturally in a certain period. According to American Society for Reproductive Medicine (ASRM)⁽¹⁾, female infertility occurs within a period of 12 months or more in

women under 35 years old, or within a period of 6 months in women over 35 years old. Its etiology may be primary when the inability of achieving a spontaneous gestation occurs since the beginning of relationships without contraceptives. Or, it may be secondary, when the inability of achieving a

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spontaneous gestation occurs after a conception⁽²⁾.

The WHO exhorts to consider infertility as a worldwide health problem⁽³⁾. Fifteen percent of couples of reproductive age are infertile, worldwide. This represents from 60 to 80 million of infertile couples⁽³⁾. In Latin America, we notice high rates of secondary infertility. We can explain this due to sexual and reproductive health⁽⁴⁾. In Peru, we suspect that the situation is very similar, but there are not any updated reports that allow knowing the number of couples affected with this problem. A 2013 study reported that 4% of women between 15 and 49 years old are infertile, but it did not consider men^(5,6).

Factors that lead to infertility are not clearly known. Studies performed in Asia, Latin America and Middle East reveal that the main factors that predispose to infertility are: pelvic factor 35% (includes prior tubal disease and endometriosis), male factor with abnormalities in sperm production 40%, cervical factor 7.5%, and with no known cause 5%⁽⁷⁻¹⁰⁾. Besides, in the last years, women have had a change in their outlook on life, thus, they postpone their motherhood due to career goals and evolution in work⁽¹¹⁾. Regarding this, we carried out the present study, aiming to determine factors associated: demographic, clinical and habits of harmful consumption, associated to female infertility.

METHODS

Study design

An observational, analytical, case-control and retrospective study was prepared. Data were obtained through the review of medical records and the application of a data collection card that recorded information on demographic aspects, clinical history, and habits of harmful consumption.

Population and sample

The population was made up of all the women who attended the gynecology service of the Vitarte Hospital for female infertility during the period from January 2015 to April 2019. A simple random sample was selected for the case-control groups.

Cases: Women between 18 and 50 years old who come with a diagnosis of infertility to the gynecology service of the Vitarte Hospital during the period January 2015 to April 2019.

Controls: Women between 18 and 50 years attended in the gynecology service of the Vitarte Hospital during the period January 2015 to April 2019 who do not have the diagnosis of infertility and mediated puerperal women.

Exclusion criteria

Patients with a history of hysterectomy or bilateral tubal block, and patients whose partner has been diagnosed as infertile. Additionally, incomplete medical records and illegible handwriting were excluded.

Variables

Through a review of national and international literature; The following variables were considered: sociodemographic factors (age, educational level); gynecological factors (dysmenorrhea, dyspareunia); pathological factors (history of pelvic inflammatory disease, history of ectopic pregnancy, history of endometriosis); environmental factors (consumption of caffeine, alcohol, tobacco, and drugs).

Process

The instrument used was a data collection sheet. The data collected was recorded in an Excel spreadsheet; Then, the generated base was processed by a statistical program for analysis.

Statistic analysis

The collected data was recorded in an Excel sheet and analyzed with the SPSS 23 statistical software, considering a significance level of 95%. Frequency tables and descriptive statistics were used. For the association of risk factors, we used the non-parametric statistical test Chi square X², Odds Ratio raw or bivariate (OR) the adjusted OR (ORa) through a binary logistic regression model.

Research ethics

In this work, personal data was treated with confidentiality; the protocol of this research was approved by the Research Institute of Biomedical Sciences (INICIB), the Faculty of Human Medicine and the Ethics Committee of the Vitarte hospital.

RESULTS

We reviewed 184 medical records of women who attended to gynecology service from Vitarte Hospital. 82 of them with diagnosis of infertility and 82 without this diagnosis or puerperal ones. Regarding general features: patients from 35 to 50 years old represent 60.9% of total of the cases group's total. Average age of cases was 35.17 ($s=4.96$) and of controls, 30.4 ($s=6.31$). Patients with secondary school completed or higher education represent 75.6% of all cases. Likewise, of all cases, 34.1% presented dyspareunia, 74.4% showed dysmenorrhea, 46.3% submitted pelvic inflammatory disease, 18.3% had ectopic pregnancy and 25.6% showed endometriosis. In addition, 65.9% consume caffeine, 12.2% use tobacco, 39% drink alcohol and 29.3% use pharmaceuticals. See Table 1.

Table 1. General features of female assisted patients at Gynecology Service at Vitarte Hospital because of female infertility.

Factors	Infertility (cases)		No infertility (controles)		Total	
	n	%	n	%	n	%
Age						
>35 – 50 years	50	60.9%	22	26.82%	72	43.90%
≤ 35 years	32	47.6%	60	73.17%	92	56.09%
Media (DE)	35.17 (4.96)		30.4 (6.31)			
Level of education						
Incomplete secondary	20	24.4%	32	39.0%	51	31.70%
Complete secondary or higher education	62	75.6%	50	61.0%	113	68.30%
Dyspareunia						
Yes	28	34.1%	12	14.6%	40	24.4%
No	54	65.9%	70	85.4%	124	75.6%
Dysmenorrhea						
Yes	61	74.4%	33	40.2%	94	57.3%
No	21	25.6%	49	59.8%	70	42.7%
PID						
Yes	38	46.3%	11	13.4%	49	29.9%
No	44	53.7%	71	86.6%	115	70.1%
Ectopic						
Yes	15	18.3%	1	1.2%	16	9.8%
No	67	81.7%	81	98.8%	148	90.2%
Endometriosis						
Yes	21	25.6%	23	28.0%	44	26.8%
No	61	74.4%	59	72.0%	120	73.2%
Caffeine						
Yes	54	65.9%	43	52.4%	97	59.1%
No	28	34.1%	39	47.6%	67	40.9%
Tobacco						
Yes	10	12.2%	2	2.4%	12	7.3%
No	72	87.8%	80	97.6%	152	92.7%
Alcohol						
Yes	32	39.0%	14	17.1%	46	28.0%
No	50	61.0%	68	82.9%	118	72.0%
Pharmaceuticals						
Yes	24	29.3%	15	18.3%	39	23.8%
No	58	70.7%	67	81.7%	125	76.2%
Total	82	100.0%	82	100.0%	164	100.0%

SWe noted that the factors associated were maternal age over 35 years old; dyspareunia, dysmenorrhea; history of pelvic inflammatory disease; alcohol consumption. Although, it is true that we found statistically significant association with ectopic pregnancy, described by a p value <0.01, we do not consider it a risk factor associated to infertility due to low amount of sample from patients. We can observe this in so wide confidence interval (95%) that ranges from 2.33 to 140.8. The same happens with tobacco use: it has a p value = 0.02, and a risk quantified by

an OR 5.56 and a confidence interval (95%) that ranges from 1.18 to 26.2. In a similar way, we display adjusted OR, result of the binary logistic regression model. In this one, we identified as factors statistically significant for infertility development the following ones: dyspareunia (OR: 5.64, CI95% 2.01- 17.32), dysmenorrhea (OR: 8.55, CI95% 3.44-23.77), pelvic inflammatory disease (OR: 10.07, CI95% 3.75- 30.75) and alcohol consumption (OR: 4.39, CI95% 1.64-12.67) (Table 2) (Figure 1).

Table 2. Factors associated to infertility in patients treated in Gynecology Service at Vitarte Hospital.

Factors associated		P value ^{/1}	OR	OR CI 95%	Adjusted OR	Adjusted OR CI 95%
Age	>35 – 50 years old	0.001	4.21	2.11-8.38	3.56	1.44-9.32
	≤ 35 years old					
Level of education	Incomplete secondary	0.064	0.53	0.27-1.04	0.35	0.13-0.88
	Complete secondary or higher education					
History of Dyspareunia	Yes	0.004	4.16	1.40-6.49	5.64	2.01-17.32
	No					
History of Dysmenorrhea	Yes	0.001	4.21	2.22-8.37	8.55	3.44-23.77
	No					
History of Pelvic inflammatory disease	Yes	<0.01	5.57	2.58-12.03	10.07	3.75-30.75
	No					
History of Ectopic pregnancy ^{/2}	Yes	<0.01	18.13	2.33 -140.8	-	-
	No					
History of Endometriosis	Yes	0.6	0.83	0.41-1.65	0.79	0.29-2.15
	No					
Caffeine consumption	Yes	0.11	1.66	0.88-3.12	2.05	0.87-5.03
	No					
Tobacco use ^{/2}	Yes	0.016	5.56	1.18- 26.2	-	-
	No					
Use of pharmaceuticals	Yes	0.1	1.84	0.88-3.85	1.27	0.47-3.51
	No					
Alcohol consumption	Yes	0.002	3.1	1.50-6.42	4.39	1.64-12.67
	No					

/ 1 Level of significance obtained through the chi-square test of association.

/ 2 Due to the low sample for its calculation, the logistic regression model was omitted and, for illustrative purposes only, the crude OR is shown.

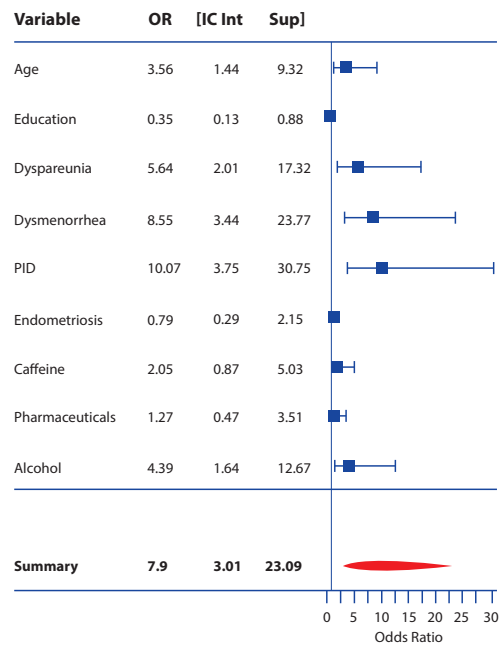


Figure 1. Adjusted Odds Ratio for infertility in patients treated in Gynecology Service at Vitarte Hospital.

DISCUSSION

This study has great relevance in both clinical-practical field and theoretical field, since because of this we have better vision regarding determinants associated to infertility. We discovered significant association in women over 35 years old. Similar result to research by Ramos et al⁽¹²⁾ with OR = 1.9, CI 95%: 1.3-4.1, $p < 0.001$ and research by Cabrera⁽¹³⁾ who also found association between these two variables. Martínez⁽¹⁴⁾ determined that 67% of people with infertility were between 30 and 39 years old. Likewise, Malo and Marín⁽¹⁵⁾ identified that age was a risk factor associated to infertility given by a p value < 0.05 . Finally, Toledo⁽¹⁶⁾ in his study established that patients who most attended to examination were 39-year-old women. Regarding level of education, we did not statistically significant association in our sample. However, He X et al⁽¹⁷⁾ in their study identified that high level of education was a protector factor in women with infertility (OR = 0.522, IC 95%: 0.391-0.696). Moreover, Toledo⁽¹⁶⁾ states that most women who attended to examination due to infertility had a complete academic level. On the other side, we discovered statistically significant association with dyspareunia. These results confirm the findings by HE X⁽¹⁷⁾, who also identified association with these two variables (OR = 2.447, CI 95%: 1.201-4.986). Mayhuasca⁽¹⁸⁾ did not find any association between dyspareunia and infertility in his retrospective descriptive study. In addition, we discovered statistically significant association between dysmenorrhea and infertility.

We confirm this thanks to the study by Mallikarjuna et al⁽¹⁹⁾ with a (OR: 6.08, $p = 0.009$). HE X⁽¹⁷⁾ on his own, also discovered association with this factor (OR = 1.62). Furthermore, history of pelvic inflammatory disease turned out to be statistically significant in our study, confirming the findings by HE X⁽¹⁷⁾ who also identified an association between these two variables with (OR = 7.07, IC95% 3.4-14.46). Ramos et al⁽¹²⁾ found out that it was not statistically significant with a p value over 0.05. Martínez⁽¹³⁾ reported a 23% incidence as well as Benavides⁽²⁰⁾ who stated a 19% incidence. This contrasts our results, which suggest in our group of cases a 49% incidence. Regarding ectopic pregnancy, although we discovered statistically significant association, this may have been due to few sample of patients with this history. This is reflected in the so wide confidence interval. Safarinnejad et al⁽²¹⁾ discovered association with ectopic pregnancy (OR = 2.45; CI 95%: 1.90-3.44; $p = 0.04$). Thounneau⁽²²⁾ found out association given by a OR: 9.9. Roa Huapaya⁽²³⁾ also identified association with this factor with a risk quantified by OR: 2.59. History of endometriosis resulted non-significant with infertility, in contrast with the findings by Franco et al⁽²⁴⁾. According to their study, one of the diseases associated to female infertility with higher incidence was endometriosis with a 43.4%. Roa Huapaya⁽²³⁾ discovered association given by a (OR: 4.1). Mayhuasca⁽¹⁸⁾ found out association with a p minor than 0.05. Caffeine consumption is not statistically significant, confirming with studies by Soyly et al⁽¹²⁾, who discovered that regular coffee portions were not

a risk (OR: 1.00; IC: 0.97 – 1.03). Ramos et al⁽¹²⁾, on their own, confirm our results stating that caffeine is not associated to infertility. Lyngsø et al⁽²⁶⁾, in their study, did not find out any association between caffeine consumption and infertility. However, caffeine consumption increases miscarriage according to daily intake. In our study, alcohol consumption is statistically significant. Greenlee et al⁽²⁷⁾ studied associated factors of female infertility in 322 cases and 322 controls, mentioning association between alcohol consumption and infertility with (OR= 1.8 IC 95% 1.2- 16.3%). Contrasting with research by Ramos et al⁽¹¹⁾, who discovered that there is not any statistically significant association between alcohol consumption and infertility, given by p values over 0.05. Although, we found statistically significant association with tobacco use, this was due to a few sample of patients regarding tobacco use. Thus, we appreciate a confidence interval so wide, which we should improve performing more studies that calculate an accurate sample size. Moreover, Greenlee et al's⁽²⁷⁾ study did not find out statistically significant association between tobacco use and infertility (OR= 1.6 IC 95% 0.9-2.9). Use of pharmaceuticals is not statistically significant unlike study by He X et al⁽¹⁷⁾, who discovered association with history of drug treatment (OR= 23.57, IC 95%: 12.32-45.10). Benito⁽²⁹⁾ reports that pharmaceuticals possibly related to sterility are numerous, such as, anti-inflammatories, chemotherapeutic, hormones, antibiotics, and others like, caffeine, chlortetracycline, dapson, phenothiazines, nifedipine, cimetidine, cyclosporine or spironolactone. We could recommend try to avoid its use in patients with difficulty conceiving, unless it is strictly necessary. Nevertheless, we should consider that sometimes it could be the case of a patient with underlying disease. We recommend that health service professionals register the age of the couple, since it also represents an associated factor

according to the literature. At the methodological level, we suggest validating these results in other sample populations and considering associated factors such as ectopic pregnancy and tobacco use, in order to guarantee an accurate representation and results that are more precise.

We state that limitations of this research are the fact that patients who attend due to infertility are referred to a more complex center that has a specialized service of infertility for further studies. There were also medical records with missing information, which did not embrace the total of factors to evaluate.

CONCLUSION

In the study, we identified dyspareunia, dysmenorrhea, history of pelvic inflammatory disease, and alcohol consumption as significant risk factors for infertility.

We did not find out statistically significant association between age, level of education, ectopic pregnancy, endometriosis, tobacco use and use of pharmaceuticals with infertility.

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