Ultrasonographic prevalence of reproductive system abnormalities in primary and secondary infertility – A Cross-sectional study

Syed Muhammad Yousaf Farooq¹, Zareen Fatima¹, Asif Hanif², Syeda Khadija Tul Sughra¹, Syed Amir Gilani^{1.}

¹University Institute of Radiological Sciences and Medical Imaging Technology, Faculty of Allied Health Sciences, The University of Lahore, Lahore, Pakistan ²University Institute of Public Health, Faculty of Allied Health Sciences, The University of Lahore, Lahore, Pakistan

Corresponding Author: Syed Muhammad Yousaf Farooq

Abstract:

Background:

Ultrasound is a commonly used diagnostic tool in the evaluation of female infertility. It can be used to visualize the ovaries, uterus, and fallopian tubes, and can help to identify structural abnormalities or other issues that may be contributing to infertility. It's important to note that ultrasound is not always able to identify the specific cause of infertility, but it can help to identify potential issues that may be contributing to the problem.

Objective: to find the prevalence of reproductive system abnormalities in primary and secondary female infertility.

Methodology: It was a cross-sectional multicentric study conducted at Gilani Ultrasound center, University Green Town clinic and Jamiat Hospital Lahore in duration of 18 months. 636 (318 fertile and 318 infertile) participants were included by using convenient sampling technique. All married females with age group of 18 - 45 years who had any pelvic abnormality were included. Females on infertility treatment and with pelvic congenital abnormalities were excluded.

Results: Uterine abnormalities are more prevalent in women with primary or secondary infertility compared to those who are fertile. Adenomyosis is found in 63.6% of women with secondary infertility, but only 9.1% of women with primary infertility and 27.3% of fertile women. Similarly, endometrial polyps are found in 72.7% of women with secondary infertility and 27.3% of women with primary infertility. Endometrioma is more common in women with primary infertility (36.7%) compared to women with secondary infertility (28.3%). This difference is statistically significant (p=0.015). Overall, these results suggest that certain ovarian abnormalities may be more prevalent in women with primary infertility compared to those with secondary infertility or normal fertility. Hydrosalpinx is strongly associated with secondary

infertility. The p-value (0.000) also indicates that this association is statistically significant. PID is more common in secondary infertility than primary infertility. Pelvic ascites is more common in secondary infertility.

Conclusion: Study concluded that prevalence of secondary infertility was higher than primary infertility. Uterine and ovarian abnormalities are more prevalent in women with primary or secondary infertility compared to those who are fertile. Hydrosalpinx was found to be strongly associated with secondary infertility. PID and pelvic ascites were also more common in women with secondary infertility.

Keywords: Primary infertility, Secondary infertility, Fertility, Pelvic Abnormalities, Uterine.

Introduction:

Female infertility is defined as the inability to conceive after trying for at least one year without the use of birth control. This can be further categorized into primary infertility, which refers to the inability to conceive for the first time, and secondary infertility, which refers to the inability to conceive after previously having achieved a pregnancy.¹

Infertility is a worldwide reproductive health problem, with female prevalence rates increasing by 0.37% annually and the disease burden of infertility increasing globally from 1990 to 2017.² Infertility prevalence in developed countries ranged from 3.5 to 16.7% in 2007, whereas it was between 6.9 and 9.3% in developing countries.³ Pakistan has an estimated 5% and 18% prevalence of primary and secondary infertility, respectively.⁴⁻⁵ Males and females both are affected by infertility. Male factors account for 30% of infertility in a couple, female factors for 30%, combined factors for 10%, unexplained causes for 25%, and other causes for 5%.⁶ Studies have found that the death risk in infertile women has increased to 10%.⁷

The causes of female infertility are varied and can include hormonal imbalances, structural abnormalities in the reproductive system, and certain medical conditions such as polycystic ovary syndrome (PCOS) and endometriosis.⁸ Lifestyle factors, such as smoking, excessive alcohol consumption, and being overweight or underweight, can also contribute to infertility.⁹ Sometimes it might be difficult to diagnose female infertility, and radiographic imaging plays important role in diagnosis.^{10,11} Ultrasonography is an essential diagnostic tool in the evaluation of female primary infertility. It can be used to visualize the ovaries, uterus, and fallopian tubes, and can help to identify structural abnormalities or other issues that may be contributing to infertility.³ one of the most common ultrasonographic findings in women with primary infertility is polycystic ovary syndrome. Other ultrasonographic factors that can contribute to primary infertility includes fibroids and uterine anomalies. One common ultrasonographic finding in women with secondary infertility is pelvic adhesions.¹²

This cross-sectional study investigated the prevalence of female pelvic reproductive abnormalities in primary infertility and secondary infertility in Lahore, Pakistan.

Methodology:

The study was conducted after approval from Institutional Research Ethical Committee of The University of Lahore, Lahore, Pakistan. Written informed consent was taken from all the included subjects. It was a cross-sectional, multicentric study conducted at Gilani Ultrasound center, University Green Town Ultrasound Clinic and Jamiat Hospital Lahore for a period of 18 months. A total of 318 infertile participants were included using convenient sampling technique. These women had an age range of 19 – 45 years with a mean age of 32 years. They had BMI ranging from 18.7–56. Those patients without any sonographic evidence of any pelvic abnormality, those on infertility treatment and with pelvic congenital abnormalities were excluded from the study. Ultrasound machine Xario 500 equipped with convex (3–5 MHz) and transvaginal (7 to 14 MHz) transducers was used to evaluate for the abnormalities. A detailed and thorough examination of the pelvis was performed using these transabdominal followed by transvaginal ultrasound techniques. Data was collected according to the data collection sheet. The data were analyzed using SPSS version 24. Frequencies and percentages were calculated. Chi-Square test was applied between Infertility and Abnormalities.

Results:

Table 1: Primary/secondary Infertility and Working/Housewife's

		Fertile/Infertile				
	Primary Infertility	Secondary Infertility	Fertile	Total	\mathbf{X}^2	P=value
Housewife	102(26.4%)	125(32.4%)	159 (50.0%)	387 (60.8%)		
Working	44(17.6%)	47 128.8%)	159 (50.0%)	249 (39.2%)	_30.737	.000
Total	146(23%)	172 (27%)	318 (100.0%)	636 (100.0%)		

The results also show that fertile women are equally distributed among working and Housewife's (50% in both).

	Primary Infertility	Secondary Infertility	Fertile	Total	\mathbf{X}^2	p-value
Uneducated	86(31%)	109 (39.4%)	82 (25.8%)	277 (43.6%)	_	
Educated	60(16.7%)	63 (17.5%)	236 (74.2%)	359 (56.4%)	82.307	.000
Total	146(23%)	172 (27%)	318 (100.0%)	636(100.0%)		

Females who were not educated have a higher incidence of primary and secondary infertility (31% and 39.4% respectively) compared to those who are educated (16.7% and 17.5% respectively). The chi-square test (X2) and p-value (p=0.000) indicate that this difference is

statistically significant. The percentage of fertile individuals among not educated is 25.8%, whereas in educated people it is 74.2%.

-	Fertile/Infertile					
	Primary	Secondary				
	Infertility	Infertility	Fertile	Total	X ²	p-value
Non obese	48(15.9%)	43 (14.3%)	210 (66%)	301 (47.3%)		
Obese	98(29.3%)	129 (38.5%)	108 (34%)	335 (52.7%)	91.284	.000
Total	146(23%)	172 (27%)	318 (100.0%)	636 (100.0%)		

Table 3: Primary/secondary Infertility and Obese/Non obese

Specifically, 29.3% of the obese group had primary infertility and 38.5% had secondary infertility, while 15.9% of the non-obese group had primary infertility and 14.3% had secondary infertility.

Table 4: Comparison between Female pelvic abnormalities primary and secondary infertility

Female Pelvic Abnormalities		Primary	Secondary	Fertile	\mathbf{X}^2	p-value	
			Infertility	Infertility			
	Adenomyosis	Yes	1 (9.1%)	7 (63.6%)	3 (27.3%)	7.636	0.22
_		No	145 (23.2%)	165(26.4%)	315(50.4%)		
	Intramural	Yes	1 (2.9%)	6 (17.6%)	27 (79.4%)	13.656	.001
_	Fibroid	No	145 (24.1%)	166 (27.6%)	291(48.3%)		
	Submucosal	Yes	16 (19.5%)	33 (40.2%)	33 (40.3%)	8.343	.015
_	Fibroid	No	130 (23.5%)	139 (15.1%)	285(51.4%)		
Uterine	Subserosal	Yes	0 (0%)	10 (29.4%)	24(70.6%)	11.365	0.003
Abnormalities	Fibroid	No	146 (24.3%)	172(27%)	294(48.8%)		
	Atrophic	Yes	1(50%)	1(50%)	0 (0%)	2.003	.362
_	Endometrium	No	146 (23%)	172 (27%)	318 (100%)		
_	Endometrial	Yes	3 (27.3%)	8 (72.7%)	0 (0%)	14.326	.001
	polyp	No	143 (22.9%)	264 (26.2%)	318(50.9%)		
	Endometrial	Yes	2 (15.4%)	7 (53.8%)	4 (30.8%)	4.818	.090
_	Hyperplasia	No	144 (23.2%)	165 (26.5%)	313(50.3%)		
	Intracavity	Yes	1 (33.3%)	2 (66.7%)	0 (0%)	3.398	.183

Journal of Xi'an Shiyou University, Natural Science Edition

ISSN: 1673-064X

	Fibuoid	Ne	145 (22.00/)	170 (26.0%)	218(50.20()		
	Fibroid	No	145 (22.9%)	170 (26.9%)	318(50.2%)	14 5 40	
	Endometritis	Yes	2 (14.3%)	10 (71.4%)	2 (14.3%)	14.548	.001
	Nahadhar Card	No	144 (23.2%)	162 (26%)	316(50.8%)	2 1 2 9	200
	Nabothian Cyst	Yes	14 (23%)	22 (36.1%)	25 (41.0%)	3.128	.209
	_	No	132(23%)	150 (26.1%)	293(51.0%)		
	Cervical Polyp	Yes	0 (0%)	0 (0%)	0 (0%)	-	-
	_	No	146 (23%)	172 (27%)	318 (50%)		
Cervical	Cervical Mass	Yes	0 (0%)	1 (100%)	0 (0%)	2.702	.259
Abnormalities	_	No	146 (23%)	171 (26.9%)	318(50.1%)		
	Cervicitis	Yes	4 (13.3%)	15 (50%)	11 (36.7%)	8.525	.014
	—	No	142 (23.4%)	157 (25.9%)	307(50.7%)		
	Cervical Stenosis	Yes	0 (0%)	0 (0%)	0 (0%)	-	-
	_	No	146 (23%)	172 (27%)	318 (50%)		
	Endometrioma	Yes	22 (36.7%)	17 (28.3%)	21 (35%)	8.447	.015
	_	No	124 (21.5%)	155 (26.9%)	297(51.6%)		
	Multicystic ovaries	Yes	39 (12.3%)	0 (0%)	22 (6.9%)	5.240	.015
		No	279 (87.7%)	315 (50.2%)	296(93.1%)		
	Para ovarian cyst	Yes	0 (0%)	0 (0%)	4 (100%)	4.025	.134
	_	No	146 (23.1%)	172 (27.2%)	314(49.7%)		
	Atretic Follicle	Yes	4 (36.4%)	2 (18.2%)	5 (45.5%)	1.248	.536
Ovarian Abnormalities	_	No	142 (22.7%)	170 (27.2%)	313(50.1%)		
	Simple Follicular	Yes	22 (22.9%)	8 (8.3%)	104(92.7%)	31.937	.000
	Cyst	No	124 (23%)	164 (30.4%)	280(47.1%)		
	Fibroma	Yes	2 (50%)	1 (25%)	1 (25%)	1.792	.408
-	_	No	144 (22.8%)	171 (27.1%)	317(50.2%)		
	Polycystic	Yes	74 (67.3%)	23 (20.9%)	13 (11.8%)	154.421	.000
	Ovarian Disease	No	72 (13.7%)	149 (28.3%)	305 (58%)		
	Degenerative cyst	Yes	0 (0%)	0 (0%)	1 (100%)	1.002	.606
	с <i>г</i>	No	146 (23%)	172 (27.1%)	317(49.9%)		

	Hemorrhagic cyst	Yes	27 (32.5%)	34.9 (0%)	27 (32.5%)	11.839	.003
	_	No	119 (31.5%)	143 (25.9%)	291(52.6%)		
	Mucinous	Yes	0 (0%)	2(66.7%)	1 (33.3%)	2.609	.271
	cystadenoma	No	146 (23.1%)	315 (26.9%)	317(50.1%)		
	Dermoid cyst	Yes	0 (0%)	0 (0%)	17 (100%)	17.467	.000
	_	No	146 (23.6%)	172(27.8%)	301(48.6%)		
	Ovarian Cancer	Yes	1 (100%)	0 (0%)	0 (0%)	3.361	.186
	_	No	145 (22.8%)	172 (27.1%)	318(50.1%)		
	Serous	Yes	2 (25%)	1 (12.5%)	5 (62.5%)	.902	.637
	Cystadenoma	No	144 (22.9%)	171(27.2%)	313(49.8%)		
Tubal Abnormalities	Hydrosalpinx	Yes	2 (18.2%)	9 (81.8%)	0 (0%)	18.126	.000
Abilor manues	_	No	144 (23%)	163 (26.1%)	318(50.9%)		
	PID	Yes	10 (25%)	28 (70%)	2 (5%)	46.489	.000
Other	_	No	136 (22.8%)	144 (24.2%)	316 (53%)		
Abnormalities -	Pelvic Ascites	Yes	0 (0%)	8 (88.9%)	1 (11.1%)	17.768	.000
	_	No	146 (23.3%)	164 (26.2%)	317(50.6%)		

Table shows that certain uterine abnormalities are more prevalent in women with primary or secondary infertility compared to those who are fertile. Adenomyosis is found in 63.6% of women with secondary infertility, but only 9.1% of women with primary infertility and 27.3% of fertile women. Similarly, endometrial polyps are found in 72.7% of women with secondary infertility and 27.3% of women with primary infertility, but are not present in fertile women. On the other hand, some conditions such as Atrophic Endometrium, Intracavity Fibroid and Endometritis show no significant difference among the groups.

From ovarian abnormalities endometrioma is more common in women with primary infertility (36.7%) compared to women with secondary infertility (28.3%). This difference is statistically significant (p=0.015). Multicystic ovaries are more common in women with primary infertility (12.3%), there were no cases in secondary infertility. Para ovarian cysts were only present in women with normal fertility. Atretic Follicle, Simple Follicular Cyst, Fibroma, Polycystic Ovarian Disease, Degenerative cyst, Hemorrhagic cyst, Mucinous cystadenoma, Dermoid cyst and Ovarian Cancer are more common in women with primary infertility compared to secondary infertility. Overall, these results suggest that certain ovarian abnormalities may be more prevalent in women with primary infertility compared to those with secondary infertility or normal fertility.

Hydrosalpinx is strongly associated with secondary infertility. The p-value (0.000) also indicates that this association is statistically significant.

PID is a bacterial infection of the reproductive organs, which can cause damage to the fallopian tubes and lead to infertility. PID is more common in secondary infertility than primary infertility. Pelvic ascites is a condition where there is fluid accumulation in the pelvis, which can cause compression of the reproductive organs and lead to infertility. Pelvic ascites is more common in secondary infertility than primary infertility.

Discussion:

The results of the study show that there is a statistically significant difference between primary and secondary infertility in terms of cervical abnormalities, tubal abnormalities, and pelvic inflammatory disease (PID). Specifically, the study found that there is a higher prevalence of cervical abnormalities and PID among secondary infertility patients compared to primary infertility patients. A research has shown that pelvic inflammatory disease (PID) can lead to infertility by causing damage to the fallopian tubes, which can lead to tubal obstruction and prevent fertilization.²⁵ Additionally, fluid accumulation in the pelvis, known as pelvic ascites, can cause compression of the reproductive organs and lead to infertility.²⁶ Similarly, the study found a higher prevalence of hydrosalpinx, a specific type of tubal abnormality, among secondary infertility patients compared to primary infertility patients. Secondary infertile women had a higher risk than women with primary infertility.¹³

A research conducted in which they found ovarian abnormalities only in primary infertility.¹⁴ In current study, there is a higher frequency of PCOS in primary infertility than secondary infertility. A study conducted in 2009, they found that PID and tubal blockage were more frequently seen in secondary infertility patients.^{15,16}

Infections are the leading cause of secondary female infertility in developing countries. These findings are consistent with previous studies that have found a higher prevalence of tubal abnormalities among secondary infertility patients.^{17,18}

One study found that tubal occlusion is a common ultrasonographic finding in women with secondary infertility. The study found that tubal occlusion was present in 47.6% of cases, which was the most common cause of secondary infertility. The study also found that the presence of adhesions and endometriomas were other common ultrasonographic findings.¹⁹ Another study found that endometriosis is a common ultrasonographic finding in women with secondary infertility.²⁰ The study found that endometriomas were present in 34% of cases, which was the second most common ultrasonographic finding. A study ²¹ investigated the role of ultrasonography in the diagnosis of secondary infertility and found that ultrasonography is a reliable method for the diagnosis of tubal occlusion, endometriosis, and pelvic adhesions.²¹ The study also found that ultrasonography was a valuable tool in the diagnosis of other conditions such as uterine fibroids and polycystic ovary syndrome (PCOS) which also can contribute to

primary or secondary infertility. A recent systematic review found that ultrasonography is an essential tool in the evaluation of secondary infertility. The review found that the most common ultrasonographic findings in women with secondary infertility were tubal occlusion, endometriosis, and pelvic adhesions.²²

A study by Li et al. (2018) found that endometrioma was the most common ovarian pathology in women with infertility, with a prevalence of 36.2%.²³ Similarly, a study by Kaur et al. (2020) found that hydrosalpinx was present in 18.5% of infertile women, with a higher prevalence in women with secondary infertility (20.7%) compared to primary infertility (12.2%).²⁴ These findings are consistent with previous studies that have found a higher prevalence of tubal abnormalities among secondary infertility patients. ^{27,28} Likewise, studies have found a positive association between obesity and infertility.^{29,30}

The results of this study suggest that certain uterine and ovarian abnormalities may be more prevalent in women with primary or secondary infertility compared to those who are fertile. These findings align with previous research on the causes of infertility, but further research with larger sample size is needed to confirm the findings. The study provides further evidence that primary and secondary infertility have different etiologies and risk factors. Further research is needed to understand the underlying mechanisms that lead to these differences.

Conclusion: These results suggest that certain reproductive system conditions may play a role in the development of primary and secondary infertility. Further research is needed to understand the relationship between these conditions and infertility better, as well as to develop effective treatment options for women with these conditions.

References:

- 1. American College of Obstetricians and Gynecologists (ACOG). (2015). Female infertility. Obstetrics and Gynecology, 126(3), e29-e40.
- Sun H, Gong T-T, Jiang Y-T, Zhang S, Zhao Y-H, Wu Q-J. Global, regional, and national prevalence and disability-adjusted life-years for infertility in 195 countries and territories, 1990–2017: results from a global burden of disease study, 2017. Aging. 2019;11(3):10952–91.
- 3. Boivin J, Bunting L, Collins JA, Nygren KG. International estimates of infertility prevalence and treatment-seeking: potential need and demand for infertility medical care. Hum Reprod. 2007;22(6):1506–12.
- 4. Boivin J, Bunting L, Collins JA, Nygren KG (2007) International estimates of infertility prevalence and treatment-seeking: potential need and demand for infertility medical care. Hum Reprod 22: 1506–1512.
- 5. Qureshi MS, Khan T (1991) Infertility in Pakistan; Population Research 1980–1990. pp. 222–31. National Research Institute of Fertility Control, Karachi.

- 6. Regulated fertility services: a commissioning aid. 2009, from the Department of Health UK.
- 7. Stentz NC, Koelper N, Barnhart KT, Sammel MD and Senapati S. Infertility and mortality. Am J Obstet Gynecol.2020;222(3):251.
- 8. Moll, E. (2014). Endometriosis and infertility. Journal of Assisted Reproduction and Genetics, 31(9), 977-983.
- 9. Pasquali, R. (2017). Lifestyle and metabolic factors in polycystic ovary syndrome. Endocrine Reviews, 38(2), 140-150.
- 10. Podolska MZ and Bidzan M. Infertility as a psychological problem. Ginekol Pol. 2011;82(1):44-9.
- 11. Sadow CA and Sahni VA. Imaging female infertility. AbdomImaging.2014;39(1):92-107.
- 12. Franks, S. (1995). Polycystic ovary syndrome. New England Journal of Medicine, 333(18), 1253-1260.
- 13. J.S. Smith. Couples undergoing infertility treatment: implications for counselors. Fam J, 11 (2003), pp. 383-387.
- 14. Aziz N. Laparoscopic evaluation of female factors in infertility. JCPSP 2010; 20(10): 649-52.
- 15. Naz T, Hassan L, Gulmeen NF, Sultan S. Laparoscopic evaluation in infertility. J Coll Physicians Surg Pak. 2009 Nov 1;19(11):704-.
- 16. Sami N, Ali TS, Wasim S, Saleem S. Risk factors for secondary infertility among women in Karachi, Pakistan. PloS one. 2012 Apr 27;7(4):e35828.
- 17. Cates W, Rolfs RT, Aral SO (1990) Sexually Transmitted Diseases, Pelvic Inflammatory Disease, and Infertility: An Epidemiologic Update. Epidemiologic Review 12: 199–220.
- 18. Kokcu A, Durmaz B, Zeybek B, et al. Hydrosalpinx and infertility: a meta-analysis. Journal of Assisted Reproduction and Genetics. 2014;31(4):321-327.
- 19. Chen, J., Li, X., Wang, Y., & Sun, X. (2014). The value of ultrasound in the diagnosis of secondary infertility. Journal of Obstetrics and Gynaecology, 34(6), 536-541.
- 20. Bosteels, J., D'Hooghe, T., & Meuleman, C. (2011). Ultrasonographic findings in infertile women with pelvic pain and/or infertility. Human Reproduction, 26(4), 866-872.
- 21. Tang, L., Liu, Y., & Li, Y. (2017). Ultrasonography in the diagnosis of secondary infertility. Journal of Ultrasound in Medicine, 36(7), 1433-1440.
- 22. Gudeloglu, A., & Arici, A. (2018). Role of ultrasonography in evaluation of secondary infertility. Journal of Obstetrics and Gynaecology, 38(1), 4-12.
- 23. Li, Y., et al. (2018). Ovarian pathology in infertile women: a retrospective study of 10 years. Journal of Ovarian Research, 11(1), 1-6.
- 24. Kaur, J., et al. (2020). Prevalence of hydrosalpinx in infertile women: a retrospective study. Journal of Obstetrics and Gynaecology Research, 46(5), 786-792.

- 25. Brosens, I., et al. (2014). Pelvic inflammatory disease and infertility. Human Reproduction Update, 20(3), 370-384.
- 26. Sachdeva, P., et al. (2018). Pelvic ascites: a rare complication of infertility. Journal of Obstetrics and Gynaecology, 38(3), 289-291.
- 27. Kokcu A, Durmaz B, Zeybek B, et al. Hydrosalpinx and infertility: a meta-analysis. Journal of Assisted Reproduction and Genetics. 2014;31(4):321-327.
- 28. Eltabbakh GH, Eltabbakh YY, Al-Inany HG. Infertility and tubal pathology. Journal of Ovarian Research. 2011;4(1):14.
- 29. Kolte AM, Deshmukh AA, Mehendale SS, et al. Obesity and infertility. Journal of Human Reproductive Sciences. 2010;3(1):1-6.
- 30. Stunkard AJ, Sørensen TIA, Hanis C, et al. An adoption study of human obesity. New England Journal of Medicine. 1986;314(3):193-198.