

Causes of Primary Versus Secondary Infertility in Women Undergoing Diagnostic Laparoscopy

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Abstract:

Background: Infertility is defined as failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse. This study was planned to compare the frequency of different causes of infertility undergoing diagnostic laparoscopy and chromopertubation.

Objective: To compare the frequency of different causes of infertility in women with primary and secondary infertility undergoing diagnostic laparoscopy

Material and Methods: This study was a five-year retrospective observational study conducted in Lady Reading Hospital from January 2017 to December 2021. Data record of all patients who underwent diagnostic laparoscopy and chromopertubation for infertility was retrieved. Basic demographic features like age, type of infertility (primary or secondary) and duration of infertility were noted in all patients. During the procedure, any abnormal features of the uterus, ovaries, and fallopian tubes including patency, uterosacral ligaments, Pouch of Douglas, and any adhesions or endometriosis were also noted. Findings were recorded on proforma. IBM SPSS Version 22.0 was used for data analysis

Results: In this study, we got a record of 1945 patients, n=1427 (71.9%) patients had primary infertility while n=518 (26.1 %) had secondary infertility, mean age was 29.73 ± 4.37 . Regarding causes of infertility, abnormal findings in fallopian tubes were more common in patients with secondary infertility (31.46% versus 23.05% of cases of primary infertility), an ovarian abnormality was observed in 16.88% in primary versus 22.58 in secondary infertility, endometriosis was seen in 27.99% of cases of secondary infertility in comparison to 22.42% in primary infertility, fibroid uterus was noted in 11.5% of primary infertility and 8.5 % of cases of secondary infertility.

Conclusion: Tubal pathology and endometriosis are the most frequent abnormalities found in patients with secondary infertility, and uterine abnormalities are more common in patients with primary infertility.

Key words. Laparoscopy, Primary infertility, Secondary infertility, endometriosis

Cite this article: Hussain S S, Raees M. Causes of Primary Versus secondary Infertility in Women Undergoing Diagnostic Laparoscopy. BMC J Med Sci. 2024. 5(1): 22-26

Introduction:

For most married couples having infertility is agonizing, it affects their mental, physical and social life. Infertility is defined as failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse.¹ Worldwide it affects approximately 15% of couples, approximately 70 million population^{2,3}. The prevalence of primary and secondary infertility in Pakistan is nearly 5% and 18% respectively⁴. According to the American Society for Reproductive Medicine, in 40% of couples with infertility, the female partner has some pathology which contributes to infertility, in 40% it is the male partner and in the

remaining 20%, there are no identifiable reasons (unexplained infertility)³. Among females, the causes are classified into three major categories, i.e., ovulatory dysfunction (20-40 %), a problem with transport (20-40 %) and implantation failures.⁵ Management of an infertile couple comprises thorough history and examination, depending on age, duration of infertility and presence or absence of comorbidities further investigations are offered like semen analysis, serum progesterone, gonadotrophins (if prolonged irregular menstrual cycle), Anti-Mullerian hormone (test for ovarian reserve)⁶ Diagnostic hysterosalpingography and laparoscopy are the most common

Authorship Contribution: ^{1,2}Substantial contributions to the conception or design of the work; or the acquisition, data analysis, drafting the work or revising it critically for important intellectual content, Final approval of the version to be published & supervision

Funding Source: none
Conflict of Interest: none

Received: MArch, 25 2024
Accepted: June 22 2024
Published: July 2 2024

procedures used for the evaluation of tubal problems ,however, Laparoscopy and chromopertubation are considered the Gold standard for tubal, pelvic and Peritoneal problems⁷.

Tubal disease factor(62.8% of women with primary infertility and 54.8% of women with secondary infertility) is still the major cause of infertility in developing countries followed by endometriosis and polycystic disease^{8,10} pelvic inflammatory diseases, sexually transmitted infections,tuberculosis,unsafe abortions, deliveries in unsafe environments, and pelvic surgeries all contribute to tubal pathology. Early diagnosis and treatment of underlying factors improve outcomes and may prevent long-term complications¹¹.Infertility affects the quality of life of women very badly, especially in this part of the world, worst affected is their mental health because of fear of their husband remarrying, divorce and domestic abuse¹².

Precise and timely diagnosis and provision of adequate treatment facilities are needed. We need to have data to know the causes of infertility in our population and plan the provision of further treatment facilities, e.g.,till date, there is no specialized Centre for assisted conception in Khyber-Pakhtunkhwa. This study was planned to compare the frequency of different causes of infertility in women with primary and secondary infertility undergoing diagnostic laparoscopy and chromopertubation. The results of this study will help us create awareness among healthcare professionals and policymakers and will help in planning Fertility centres in this part of Pakistan.

Material and Method:

This study was a five-year retrospective observational study (January 2017- December 2021) conducted in Lady Reading Hospital after approval of the hospital ethical review (Ref:No 383/LRH/MTI). Data record of all patients who underwent diagnostic laparoscopy and chromopertubation for infertility was retrieved and included in the study, age 18 to 45 years. Cases, where the male partner has semen abnormalities, were excluded from the study. The Retrospective convenience sampling technique was used.

Basic demographic features like age, type of infertility (primary or secondary) and duration of infertility were noted in all patients. During diagnostic laparoscopy, the pelvis was inspected, including the uterus, ovaries, fallopian tubes, uterosacral ligaments, and Pouch of Douglas, any adhesions or endometriosis, or any abnormal features of these organs were recorded. The

patency of fallopian tubes was ascertained by injecting methylene blue into the uterine cavity and its spill through both of the fimbrial ends was checked.

Patients were diagnosed to have Polycystic ovaries, who had a history of infertility, irregular cycles, excessive hair growth or biochemical evidence of hyperandrogenism and naked eye appearance of smooth glossy thickened capsules, with the presence of multiple subcapsular cysts (2cm or more) on laparoscopy^{13,14}.

Endometriosis was classified according to the revised American Society for Reproductive Medicine (rASRM) classification and graded into stages 1-4 accordingly¹⁵. IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY) was used for data analysis. Categorical variables were reported as frequencies and percentages, while continuous variables were reported as mean and standard deviation. The Chi-square test and Pearson's correlation test were applied with the level of significance set at P- value < 0.05.

Results:

In this study, we got a record of 1945 patients, n=1427 (71.9%) patients had primary infertility, while n=518 (26.1 %) had secondary infertility, mean age was 29.73± 4.37 (primary infertility 28.64 ± 3.96, secondary infertility 32.75 ± 3.72, Range 25(minimum age was 18 while the maximum age was 43 years). The mean duration of infertility in years was 6.45± 2.92 (primary infertility 6.21 ±2.92. secondary infertility 7.14 ± 2.89) Range of 19(minimum 1 year and a maximum of 20 years) was noted.

Regarding pelvic organs, abnormal findings were observed most commonly in fallopian tubes (25.55%), followed by endometriosis in 24.06% of cases, ovarian pathology in 18.48%, pelvic adhesions in 17.78% and uterine abnormalities in 13.93% of patients. Further details of the frequency of these problems and type of abnormalities in patients of primary versus secondary infertility are mentioned in Table 1.

Mullerian duct abnormalities were observed in 1.37% of cases. Among congenital abnormalities,5patients had a unicorn ate uterus, 11 bicorn ate, and 4 had a uterus diadelphous (1.7% in secondary infertility versus 0.7% in primary infertility). while in three patients' the uterus was absent, in the other three it was rudimentary or very small.

Discussion:

13and even higher than the WHO global recommendation of 10-15%4.However, according to the WHO recent strategic

Table 1 (Frequency of causes of infertility in patients of primary versus secondary infertility along with silent features).

Pelvic structure	Feature	n= number of patients with % within type of infertility		Total	Pearson chi-square
		Primary infertility	Secondary infertility		
Uterus	• Missing data	1 (0.1 %)	0 (0 %)	1 (0.1 %)	0.04
	• Anteverted,normal looking	1080 (75.7 %)	392 (75.7 %)	1472 (75.7 %)	
	• Retroverted	139 (9.7 %)	63 (12.2 %)	202 (10.4%)	
	• Fibroid	164(11.5 %)	44 (8.5 %)	208 (10.7 %)	
	• congenital anomaly	10(0.7 %)	9 (1.7%)	19 (0.97%)	
	• not visualized (dense adhesions)	27(1.9 %)	10 (1.9 %)	37 (1.9 %)	
	• Infantile	3(0.2 %)	0 (0 %)	3(0.2 %)	
	• Absent	3 (0.2 %)	0 (0 %)	3(0.2 %)	
	• Total	1427	518	1945 (100%)	
	Fallopian tubes	• Missing data	2 (0.1 %)96 (76.8 %)	3 (0.6 %)	
• Normal-looking tubes, bilateral free spill		26 (1.8 %)	352 (68.0 %)	1448 (74.4 %)	
• bilateral hydrosalpinx with blocked tubes		58(4.1 %)	20 (3.9 %)	46 (2.4 %)	
• bilateral clubbed fimbrial ends, blocked tubes		30 (2.1 %)	28 (5.4 %)	86 (4.4%)	
• peri- tubal adhesions		40 (2.8 %)	18 (3.5 %)	48 (2.5 %)	
• Tubes adherent to ovaries or adjacent structures		120 (8.2 %)	16 (3.1 %)	56 (2.9%)	
• .one patent tube, one absent /blocked		20 (1.4 %)	67 (12.9 %)	187 (9.6%)	
• tubes not visualized because of dense adhesions		35 (2.5 %)	7 (1.4 %)	27 (1.4 %)	
• bilaterally blocked tubes without apparent abnormality		1427	7 (1.4 %)	42 (2.2 %)	
• total		1427	518	1945	
Ovaries	• Missing data	1(0.1 %)	0	1(0.1 %)	0.003
	• normal looking	1186 (83.1 %)	401 (74.1%)	1587 (87.6%)	
	• PCOS	84 (5.9%)	27 (5.2%)	111 (5.7%)	
	• endometriotic cyst	44 (3.1%)	28 (5.4%)	72 (3.7%)	
	• hemorrhagic cyst	16 (1.1%)	11 (2.1%)	27 (2.4%)	
	• simple cyst	45 (3.2%)	29 (5.6%)	74 (3.8%)	
	• tubo ovarian mass	21 (1.5%)	16 (3.1%)	37 (1.9%)	
	• not visualized because of dense adhesions	29 (2.0%)	6 (1.2%)	35(1.8%)	
	• streak ovaries	1 (0.1 %)	0	1 (0.1 %)	
	• total	1427	518	1945	
Adhesions	• Missing data	1(0.1 %)	0	1	<0.05
	• No adhesions	1212 (84.9%)	387 (74.7%)	1599 (82.2%)	
	• Fine, avascular transparent adhesions between two organs	126 (8.82%)	76 (14.4%)	202 (10.38%)	
	• Dense, thick, opaque vascular adhesions between two organs	54 (3.788%)	42 (8.10%)	96 (4.93%)	
	• Dense adhesions, involving multiple organs, no cleavage plane, fixed organs (Frozen pelvis)	34 (2.38%)	13 (2.50%)	47 (2.41%)	
	• Total	1427	518	1945	
Endometriosis	• No lesions	1104(77.36%)	373(72.00%)	1477(77.5%)	<0.05
	• Stage 1 (minimal, score 1-5)		73 (14.1%)	313 (16.1%)	
	• Stage 2 (mild Score 6-15)	240(16.8%)	10 (1.9%)	34 (1.7%)	
	• Stage 3 (moderate Score 16-40, includes > 3cm ovarian Endometrioma)	24 (1.7%)	28 (5.40%)	72 (3.69%)	
	• Stage 4	44 (3.08%)	0		
	• Additional Endometriosis (involvingthe gut)	2 (0.1%)	34 (6.6%)	2 (0.1%)	
	• Total	13 (0.9%)		47 (2.4%)	
	• Total	1427	518	1945	

The overall CS rate in our study population was 22.76% which was higher than the national average of Pakistan (19.6%) document more emphasis is on monitoring indications of CS for appropriateness14, 15. Moreover, in order to understand

the degree to which CS deliveries may be preventable, it is important to know why CS is performed¹³. In the present study the most common indication for CS delivery was history of previous CS/s which contributed for more than one third of CS (39.18%). Various studies conducted in Pakistan have also shown Repeat CS as the most common contributing indication to the overall CS rate. Jabeen J, et al (40.3%) and Bano S, et al (64.7%) have reported that the largest group of women contributing to repeat CS is that with history of previous Caesarean delivery^{4,16, and 17}. Another study by Karim F, et al has shown Repeat CS as the most common indication (47.17%)¹⁸. Several international studies have also found out "previous history of CS as the most common indication contributing to the increased CS rate". A cohort study conducted in Brazil showed Repeat CS as the most common contributor to the overall CS rate¹⁹. It is clear from the results that if we want to reduce overall CS rate, we have to reduce the rate of first CS in women, which accounted for 60.81% CSs in this study. Moreover, evidence-based steps should be taken to encourage women having previous one CS to deliver vaginally. National Institute of Clinical Excellence (NICE) and American College of Obstetricians and Gynecologists (ACOG) recommend that women with history of one CS should be given trial of labour and previous CS should not be the absolute indication for CS delivery in the index pregnancy^{20,21}. Researchers have shown different approaches that should be adopted in carefully selected cases such as External Cephalic Version (ECV) for breech presentation and promotion Trial of Labour after Caesarean delivery (TOLAC) and Vaginal Birth after Caesarean section (VBAC)²². According to the Royal College of Obstetricians and Gynecologists, VBAC should be considered a safe choice for the majority of women with a single previous lower segment caesarean delivery willing for vaginal delivery²³. Studies have shown a higher success rate of about 80% and much lower complication rate in women who underwent VBAC than those with repeat CS^{24,25}. We found that the 2nd most common contributor to the overall CS and the most common contributing indication to the primary CS, at our institute were fetal distress/non reassuring fetal heart tracing (18.01%). Several other studies have shown fetal distress as a common cause of emergency CS delivery with the global prevalence of about 20%¹¹. A study done by Gulfareen H et al, mentioned the same results as ours. Similarly, Studies conducted in India also found fetal distress to be the most common contributing indication^{26, 27}. Study conducted by Barber EL shows non reassuring fetal heart tracing (NRFHT) to be the most frequent cause (32%) adding to the burden of primary CS. The subjective variability in interpreting fetal heart tracing is a well-known fact^{28, 29, 30}. In our institution, we have protocol in place that we routinely do CTG on all women admitting in active Labour. Furthermore, there is lack of facilities for fetal scalp blood sampling which further adds to the subjectivity of CTG tracing. On the other hand, NICE guideline on intrapartum care clearly states: "reserve CTG for high-risk pregnancies/Labour". The guideline further stresses that to avoid unnecessary CS deliveries for presumed fetal distress, the facility of fetal blood sampling to measure p H /Lactate should readily be available so that CTG results can be interpreted properly³¹. Labour progress disorders (including failure of cervical dilation/decent of presenting part during active Labour) were the 3rd most common (14%) contributing cause to the overall burden of CS in the present study. Literature review has shown Labour progress disorder as one of the most common indications leading to emergency CS

delivery^{10,11}. Research conducted in a university hospital Karachi reveals Labour progress disorder as the 2nd most common cause contributing to the overall CS³¹. Literature review shows that the diagnosis of Labour progress disorder is relatively subjective and large variability exists among obstetricians. According to the WHO Labour care guide and ACOG, the more recent standards of normal Labour progress, from the Consortium on safe Labour should be practiced rather than traditional standards, if we want to prevent Primary caesarean delivery^{33, 34}. According to consortium on safe Labour both Nulliparous and multiparous women dilate at same rate from 4-6 cm, and more slowly than described by Friedman. However, multiparous women dilate more rapidly beyond 6cm. Similarly, according to new standards, the active phase of Labour starts at 6 cm of cervical dilatation^{33,34}. Thus in the first stage, slow but progressive Labour should not be an indication for CS. Hence, Caesarean delivery for active phase arrest of Labour, should be reserved for women at or beyond 6 cm dilatation with ruptured membranes, who fail to progress despite 4 hours of effective uterine contractions in the first stage of Labour/or at least 6 hours of oxytocin administration with ineffective uterine contractions and no cervical change³⁴. Furthermore, before diagnosing arrest of Labour in the second stage, if mother and fetus both doing well, at least 2 hours of pushing in multiparous and 3 hours in Nulliparous women should be allowed. Instrumental vaginal delivery in the second stage of Labour by well trained and experienced obstetrician should be considered a safe alternative approach to caesarean delivery³⁴. In our institute the instrumental delivery rate was 2.97%. ACOG has shown concerns regarding the significant decrease in instrumental vaginal deliveries during the past few years and recommends performing instrumental deliveries, so that the risk of CS in the second stage of Labour can safely be avoided. However, the trend of obstetricians is less towards instrumental delivery and more towards CS in the present environment of litigation. Hence, the number of healthcare providers who are adequately trained to conduct instrumental vaginal deliveries is decreasing. To curb this situation, skills and drills training related to instrumental vaginal delivery should be encouraged in tertiary care institutions^{34, 35}. The second most important indication for repeat CS was breech and other Malpresentations. In our institute we do offer ECV to women with non-scarred uterus, but reluctance is seen from the side of obstetricians to offer ECV to women with previous uterine scar. According to ACOG, ECV after one CS has no greater risk of uterine scar rupture than with unscarred uterus²². In the current study it has been noticed that the 3rd most common cause of repeat CS in women with history of Previous 1 CS is refused trial of Labour accounted for 15% of Repeat CS. Literature review shows wide variations in TOLAC uptake rates in different region of the world e.g. it is 20% in the US³⁶ and 70% in the Netherlands³⁷. Similarly, in Europe, TOLAC uptake rates differ considerably i.e. 14.8% to 52.2%³⁸. A Cochrane review established that counseling of women by obstetricians regarding TOLAC is the most important part of the informed decision-making process and has to be evidence based and according to the individual patient's need³⁹. Similarly, Induction of Labour (IOL) in women with history of CS, is a controversial intervention mainly because of the fear of uterine rupture which has been shown to be as high as 1.4%⁴⁰. Furthermore, there is uncertainty regarding efficacy/dosage of the different agents used for IOL in this special scenario. Till date, no agreed international/national

protocol for IOL in women with Previous CS birth is available and hospitals are using their own individually designed protocols⁴⁰. We are also using protocol designed locally for IOL in women with scarred uterus and this may be the reason for failed induction in our setup.

Conclusion:

Majority of the women who underwent CS had the history of prior CS deliveries. It is the need of the day to educate the obstetricians and counsel/encourage pregnant women in antenatal period regarding the safety of procedures like ECV, TOLAC and VBAC if we want to reduce repeat CS in our setup. Moreover, CTG should be used in high-risk pregnancies/labor and standardized terms/definitions should be used to avoid subjective variability in interpreting the CTG traces. Furthermore, adherence to 'WHO Labour care guide' regarding care/ monitoring of laboring women should be encouraged. Similarly, reviving the art of instrumental delivery by training obstetricians may curb the escalating rate of CS. Further research work is needed both at national and international levels to find out the most safe and effective method for Induction of Labour on scarred uterus.

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