ORIGINAL ARTICLE

Causes of Male and Female Sub Fertility in the Couples who Underwent 'In Vitro Fertilization' at Life Clinic; a Statistical Study from Lahore, Pakistan

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ABSTRACT:

Objective: To explore the causes of male and female sub fertility in the couples undergoing 'In Vitro Fertilization' at LIFE clinic

Materials and Methods:In this retrospective, cross-sectional, observational study from Lahore, Pakistan all couples coming for evaluation and treatment for sub-fertility from 1st January to 30th April 2015 at Lahore institute of fertility and endocrinology LIFE with n=344 patients were included Fertility and Endocrinology (LIFE). Sampling method was non probability consecutive. The data collection instrument was an especially designed Performa. Causes of Sub fertility male and female were studied and data was extracted from the files of LIFE.

Results:Out of 344 patients 138(40.1%) had female factors, 122(35.5%) had male factor, 38(11.0%) had combined factors whereas 46(13.4%) had unexplained infertility. Out of 138, 55(39.85%) females had tubal factor, 2(1.45%) had endometriosis, 21(15.22%) had PCO and 60(43.47%) had unexplained causes of sub-fertility. Out of 122 males, 90 (74.4%) had oligospermia/asthenospermia and 32(25.6%) had azoospermia.

Conclusion: Tubal factor was a major cause of sub-fertility in females whereas in 2/3 of the females, cause of sub-fertility was not explained. Among the males, oligospermia was the most common cause and was found in 74.4%. Health education about menstrual hygiene should be imparted early in life to prevent Sub-fertility due to infection. Premarital counseling and testing should be made easily available. Andrology should be made part of the Gynecology courses and curricula. Community based Sub-fertility research should be encouraged to assess the disease burden and frequency of preventable causes. **Keywords:** Sub fertility, Females, Males, Causes, Lahore, Pakistan

INTRODUCTION:

Mothering and motherhood have been regarded as issues of prime importance regardless of religion, geography, culture, art, mythology and literature. To become a parent and have children is a desire that leads goals and life plans of a common man and inability to achieve that desire may jeopardize the whole life of a person or a family. Inability to have a kid even after 12 months of unprotected intercourse without use of contraceptives is known as subfertility. Subfertility evaluation is usually started by the gynecologist or the couple is referred to a fertility center where the couple is evaluated for subfertility. If age of the female is more than 35 years

or there is history of menstrual irregularities or there is a known male factor for subfertility then evaluation may be commenced earlier. Subfertility has two types, primary and secondary subfertility. Primary subfertility is the inability to have a child despite unprotected vaginal intercourse for twelve months among women of reproductive age (15 to 49 years).

Secondary subfertilitymeans the inability to have a child after at least one pregnancy. Globally, primary subfertility is commoner than secondary subfertility. 5

The process of conception in human beings is quite complicated and a firm understanding of anatomy and physiology of male and female reproductive system is

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essential for evaluating clinician to identify the investigations needed for a correct diagnosis of cause of infertility. 6,7,8 Modern laboratory and sonology/ radiology can help an intelligent clinician to think about the treatment strategies after reaching a meaningful diagnosis. 9,10 The whole record of the couple is to be scrutinized to look for co-morbid conditions and associated diseases. Sometimes it is very difficult to make the couple understand the mechanics of the male and female genital tract. Conception is the result of interplay between many physical and biochemical processes gauged by the biological clock. 11,12 The journey of the egg starts after well-timed ovulation and successful picking up by the fallopian tubes. ^{13,14} If semen has been deposited in the vaginal tract the spermatozoa are needed to travel all the way through the cervix and uterus to reach the fallopian tube having the egg. 15,16 After fertilization the embryo travels to the uterus to be implanted there and the process of pregnancy starts. So subfertility evaluation may be a long, tedious and expensive process. A well prepared couple should have the awareness and patience to bear the process. When a couple is labelled to be subfertile stress, anger, jealousy and frustration may be the usual result that may overwhelm the couple due to social response or resentment of close relatives. ¹⁷ Subfertility may be an important cause of marital conflict and may lead to an unwanted divorce and polygamy. ^{18,19,20}. In eastern culture motherhood qualifies womanhood and so women are blamed and victimized on being responsible for childlessness of the couple. ²¹ World Health Organization affirmed in 2001 that if subfertility rate exceeds 15% it may be declared to be a public health problem. Subfertility is a social stigma and a couple is afraid to accept it and here comes into play the role of the family physician. A general practitioner or a family physician has a unique opportunity to help a childless couple. Initial workup and support can help the scared subfertile couple to think about visiting a fertility physician. An early visit to a fertility center may be of great value in terms of right and timely investigation.²³ The sub fertile couple is needed to be evaluated before detailed investigations. A detailed history and physical examination may point towards an area to be investigated if analyzed thoughtfully with an inquisitive mind. A well concerted effort may help the clinician to tailor the treatment strategy to have a fruitful outcome.²⁴ Couples across the globe are affected by the sub-ability to have children which is a source of personal discontent and social resentment. ² A well prepared couple has the awareness and patience to bear the process. 25 The couple may need psychosocial counseling which may include family counseling.²⁶ Anatomy and physiology of the reproductive system may be compromised as a cause of subfertility. Sometimes genes may be implicated.²⁷ Prevalence of subfertility in different regions is different mainly due to environmental factors as well as reproductive behaviors, smoking and pollution etc.²⁸ Present study was designed to explore the causes of male and female sub fertility in the couples undergoing

'In Vitro Fertilization' at Lahore institute of fertility and endocrinology LIFE clinic.

MATERIALS AND METHODS:

In this retrospective, cross-sectional, observational study from Lahore Pakistan all couples coming for evaluation and treatment for subfertility from 1st January to 30th April at Lahore institute of fertility and endocrinology (n=334) were included. Sampling method was non probability consecutive. The data collection instrument was a specially designed performa validated by biostatistician and epidemiologist of LIFE research center. Causes of male and female subfertility were studied. Data was extracted from the files of LIFE. Data was entered into SPSS version 15.0 and descriptive analysis was done for frequencies and percentages for categorical variables. Mean, S.D and variance were calculated for numerical variables.

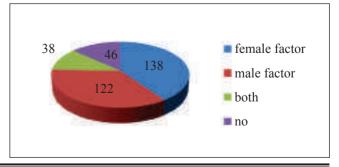
RESULTS:

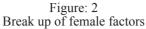
In this study unexplained subfertility was seen in 13.4% (46) of the couples, both males and females were implicated in 11.0% (38) of the couples, only females were said to be responsible in 40.1% (138) of the cases where as in 35.5% (122) couple males were implicated (n=344). In the females 43.47% (60) had unexplained subfertility, in 39.85% (55) tubal factors were said to be responsible, 15.22% (21) had PCO and 1.45% (2) had endometriosis (n=138). Amongst the males oligospermia was found in 74.4% (90) and azoospermia in 25.6% (32) (n=122) (Table 1, Figure 1,2 & 3)

Table: 1

Sr.	Variable	Frequency	Percentage
1	Female factor	138	40.1
	Tubal factor	55	39.85
	Endometriosis	2	1.45
	PCOS	21	15.22
	Un-explained	60	43.47
2	Male factor	122	35.5
	Oligospermia	90	74.4
	Azoospermia	32	25.6
3	Both responsible	38	11.0
4	No cause found	46	13.4
	(female/male/unexplained)		
Tota		344	100 %

Figure: 1 Breakup of causes of subfertility





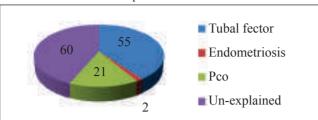
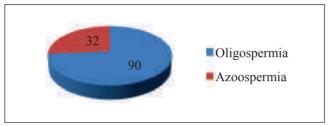


Figure: 3
Break up of male factors



DISCUSSION:

In our study only females were found to be responsible for subfertility in 40.1% of the couples, only males in 35.5% (122), both males and females in 11.0% (38) and unexplained subfertility was seen in 13.4% (46) of the couples. In males oligospermia was found in 74.4% (90) and azoospermia in 25.6% (32). In females unexplained subfertility was found in 43.47% (60), tubal factors in 39.85% (55), PCOS in 15.22% (21) and endometriosis in 25.6% (32).

Subfertility may be primary or secondary depending on the history of pregnancy in the past.²⁹Primary subfertility is more common in developed countries as compared to developing countries where secondary subfertility is also prevalent. ^{30,31}

Zargar has shown that primary subfertility is quite common in India as compared to secondary subfertility but most of the subfertile couples delay to consult the fertility physician. Male factor was found to be responsible in 22.4 % whereas ovulatory dysfunction (17.2%), tubal factor (7.2%), failure of ovaries (8.8%) and hyperprolactinemia (8.4%) were the causes found in sub fertile females.³²

In a study done in Mongolia, used WHO protocol 'Standardized Investigation of the Infertile Couple' to explore causes of sub fertility, female factor was responsible for subfertility in 45.8% of couples, male factor was responsible in 25.6% of couples and unexplained subfertility was seen in 9.8% of couples whereas in 18.8% of couples both the partners contributed to subfertility. History of STI (sexually transmitted infection) and PID (pelvic inflammatory disease) were found to be 33.5% and 25.1%, respectively. History of STI (sexually transmitted infection) in males was present in 42% whereas previous testicular damage was seen in 27.7% of the males.³³

Another study done in Mongolia in 2004 also used

WHO protocol. Primary subfertility was seen in 62.4% and secondary subfertility in 37.6%. Female factor was responsible for subfertility in 52.7% of couples, male factor in 6.4% of couples and unexplained subfertility was seen in 2.2% of couples whereas in 38.7% of couples both the partners contributed to subfertility. In the female factor, tubal block was found in 36.5%, pelvic adhesions in 23.6% and endocrine disorders in 32.8. Females showed to have four times more inflammatory complications as compared to males. ³⁴

Elussein analyzed 710 Sudanese couples at Khartoum Fertility Center in Sudan to explore causes of infertility. Primary subfertility was seen in 62.4% and secondary subfertility in 37.6%. Female factor was responsible for subfertility in 49.3% of couples, male factor in 36.2% of couples and unexplained subfertility was seen in 13.0% of couples whereas in 1.5% of couples both the partners contributed to subfertility. Female subfertility was found to be mostly due to ovulation failure i.e. 60.3%. Male subfertility was found to be due to Oligozoospermia (16.8%) and asthenozoospermia (17.5%). Whitman-Elia examined the diagnosis of the couples after evaluation and found that male factors caused subfertility in 40% of the subfertile couples, female factors in 40-55% and unexplained factors in around 10%. In a very small percentage i.e. 5% mixed factors were found to be responsible. Female factors responsible for subfertility were tubal disease, endometriosis and pelvic adhesions, ovulatory dysfunction and cervical factors. Hypothyroidism, luteal phase defect and immunologic factors were also implicated in a small percentage i.e. 5%. In 10% of the couples cause of subfertility remained unexplained even after all investigations. 23

The diagnosis of idiopathic infertility in males reflects a poor understanding of the factors involved in regulation of spermatogenesis. Single gene mutations and chromosomal aberrations are some of the genetic causes of impairment of spermatozoa, which constitute ten to fifteen percent of severe subfertility in the males. ³⁵

CONCLUSION:

Tubal factor is the major cause of subfertility in the females whereas in 2/3rd of the females, cause of subfertility was not explained. Among the males oligospermia was the most common cause and was found in 74.4%. Health education about menstrual hygiene should be imparted early in life to prevent Subfertility due to infection. Premarital counseling and testing should be made essential. Andrology should be made part of the Gynecology obstetrical courses and curricula. Community based Sub fertility research should be encouraged to assess the disease burden and frequency of the preventable causes.

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REFERENCES:

- Begum BN, Hasan S. Psychological problems among women with infertility problem: a comparative study. J Pak Med Assoc.2014;64(11): 1287-91
- Mascarenhas MN, Flaxman SR, Boerma T, Vanderpoel S, Stevens GA. National, regional, and global trends in infertility prevalence since 1990: a systematic analysis of 277 health surveys. PLoS Med. 2012;9(12):e1001356
- Maheshwari A, Hamilton M, Bhattacharya S. Effect of female age on the diagnostic categories of infertility. Hum Reprod 2008;23(3):424-538
- Bhattacharya S, Maheshwari A, Mollison J .Factors Associated with Failed Treatment: an Analysis of 121,744 Women Embarking on TheirFirst IVF Cycles. PLoS ONE 2013;8(12): e82249
- 5. Adamson PC, Krupp K, Freeman AH, Klausner JD, Reingold AL, Madhivanan P. Prevalence & correlates of primary infertility among young women in Mysore, India. Indian J Med Res. 2011;134:440-6
- Son WY, Das M, Shalom-Paz E, Holzer H. Mechanisms of follicle selection and development. Minerva Ginecol. 2011;63(2):89-102
- Stouffer RL, Bishop CV, Bogan RL, Xu F, Hennebold JD. Endocrine and local control of the primate corpus luteum. Reprod Biol. 2013;13(4):259-71
- Zeleznik AJ. The physiology of follicle selection. Reprod Biol Endocrinol. 2004; 16;2:31
 Abou-Setta AM, Mansour RT, Al-Inany HG, Aboulghar
- Abou-Setta AM, Mansour RT, Al-Inany HG, Aboulghar MM, Aboulghar MA, Serour GI. Among women undergoing embryo transfer, is the probability of pregnancy and live birth improved with ultrasound guidance over clinical touch alone? A systemic review and meta-analysis of prospective randomized trials. Fertil Steril. 2007; 88(2):333-41
- Ammar T, Sidhu PS, Wilkins CJ. Male infertility: the role of imaging in diagnosis and management. Br J Radiol. 2012;85 Spec No 1:S59-68
- 11. Gratton RJ, Nisker JA, Daniel S, Toth S, Gunter J, Kaplan BR, et. al. An aggressive philosophy in controlled ovarian stimulation cycles increases pregnancy rates. Hum Reprod. 1993;8(4):528-31
- Campbell S Ash Monga; Gynaecology by Ten Teachers (18th ed.). Hodder Education. 2006 ISBN 0-340-81662-7
- Psychoyos A Endocrine control of egg implantation. In: Handbook of Physiology 1973 Volume II, Part 2 pp 187-215 Eds RO Greep, EG Astwood and SR Geiger. American Physiological Society, Washington DC
- Hickey M, Balen A. Menstrual disorders in adolescence: investigation and management. Hum Reprod Update. 2003;9(5):493-504
- Williams M, Hill CJ, Scudamore I, Dunphy B, Cooke ID, Barratt CL. Sperm numbers and distribution within the human fallopian tube around ovulation. Hum Reprod. 1993; 8(12):2019-26
- Suarez SS, Pacey AA. Sperm transport in the female reproductive tract. Hum Reprod Update.2006;12(1):23-37
- 17. Ali S, Sophie R, Imam AM, Khan FI, Ali SF, Shaikh A, et al. Knowledge, perceptions and myths regarding infertility among selected adult population in Pakistan: a cross-sectional study. BMC Public Health. 2011;(4);1
- 18. Chester R. Is there a relationship between childlessness

- and marriage breakdown? J Biosoc Sci. 1972;4(4):443-54
- Ibeh U O, Obidoa M A. Marital Disharmony: Causes and resolution strategies in Enugu State of Nigeria. Research on Humanities and Social Sciences; 2013; 3(22), 40-8
- Khan HL, Khan YL, Suhail S, Awais A, Khawaja AR. Characteristics of Female Patients Visiting for Assisted Reproductive Technology in a Private Clinic in Lahore Pakistan. J SZMC. 2014; 5(4): 715-20
 Hasanpoor-Azghdy SB Vedadhir A. The emotional-
- 21. Hasanpoor-Azghdy SB Vedadhir A. The emotional-psychological consequences of infertility among infertile women seeking treatment: Results of a qualitative study. Iran J Reprod Med 2014; 12(2): 131-8
- 22. Bergstrom S. Childlessness. In: Lawson J B, Harrison K A, Bergstrom S, editors. Maternity care in developing countries. RCOG PRESS; 2001. pp. 360-8
- 23. Whitman-Elia GF, Baxley EG. A primary care approach to the infertile couple. J Am Board Fam Pract. 2001;14(1):33-45
- Swerdloff RS, Wang C, Kandeel FR. Evaluation of the infertile couple. Endocrinol Metab Clin North Am. 1988; 17(2):301-37
- Cousineau Tara M, Domar AD. Psychological impact of infertility. Best Pract Res Clin Obstet Gynaecol, 2007; 21: 293-308
- Greil A L, Slauson-Blevins, K, Mc Quillan J. The experience of infertility: A review of recent literature. Sociol Health Illn. 2010;32(1):140-62
- 27. Masoumi SZ, Parsa P, Darvish N, MokhtariS, Yavangi M, Roshanaei G. An epidemiologic survey on the causes of infertility in patients referred to infertility center in Fatemieh Hospital in Hamadan. Iran J Reprod Med. 2015;13(8):513-6
- 28. Macaluso M, Wright-Schnapp T, Chandra A, Johnson R, Satterwhite C, Pulver A, et al. A public health focus on infertility prevention, detection, and management. Fertil Steri 2010; 93: 16
- 29. Elussein EA, Magid YM, Omer MM, Adam I. Clinical patterns and major causes of infertility among Sudanese couples. Trop Doct. 2008;38(4):243-4
- 30. Templeton A, Fraser C, Thompson B. Infertility-epidemiology and referral practice. Hum Reprod. 1991;6(10):13 91-4
- Menuba IE, Ugwu EO, Obi SN, Lawani LO, Onwuka CI. Clinical management and therapeutic outcome of infertile couples in southeast Nigeria. Ther Clin Risk Manag. 2014;10:763-8
- 32. Zargar AH, Wani AI, Masoodi SR, Laway BA, Salahuddin M. Epidemiologic and etiologic aspects of primary infertility in the Kashmir region of India. Fertil Steril. 1997;68(4):637-43
- 33. Bayasgalan G, Naranbat D, Tsedmaa B, Tsogmaa B, Sukhee D, Amarjargal O, et al Clinical patterns and major causes of infertility in Mongolia. J Obstet Gynaecol Res. 2004;30(5):386-93
- Philippov OS, Radionchenko AA, Bolotova VP, WHO Estimation of the prevalence and causes of infertility in western Siberia. Bull 1998; 76: 183-7
- 35. Ferlin A, Arredi B, Speltra E. Molecular and clinical characterization of Y chromosome microdeletions in infertile men: a 10-year experience in Italy. J Clin Endocrinol Metab. 2007;92:762-70

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