DISORDERS LEADING TO INFERTILITY IN MALES AND FEMALES

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ABSTRACT

Objective: To determine the frequency of disorders causing infertility in patients reporting to CMH Bahawalnagar.

Study Design: Cross-sectional analytical study.

Place and Duration of Study: Department of Pathology and Gynaecology/Obstetrics, Combined Military Hospital (CMH), Bahawalnagar in collaboration with Armed Forces Institute of Pathology (AFIP) and Pak Emirates Military Hospital (PEMH), Rawalpindi, from Apr 2013 to Apr 2015.

Methodology: A total of 200 infertile couples who were married, living together and reported to CMH Bahawalnagar for the workup of infertility were included. Serum follicle stimulating hormone (FSH), luteinizing hormone (LH), prolactin (PRL), testosterone, thyroid stimulating hormone (TSH), free thyroxin (fT4) were performed in all patients. Serum estradiol, progesterone, liver function tests (LFTs), plasma glucose, high vaginal swab (HVS) and ultrasonography (USG) pelvis in all females. Semen analysis was performed in all males. Endocrinological profiles were analyzed by chemiluminescent enzyme immunoassay on Immulite 2000 at AFIP Rawalpindi.

Results: Out of total 200 infertile couples, 156 with infertility due to different identified causes comprised of 18 percent because of male factors, 37% female factors and 23% contributed by both partners and age of 30 ± 5 years in males, 28 ± 5 years in females and mean duration of marriage 6 ± 4 years. Varicocele was the cause of infertility in 12.5% males while poly cystic ovarian syndrome (PCOS) was the most common cause of infertility in 12.5% females.

Conclusion: Varicocele was found to be the commonest cause of infertility, followed by genital tract infection and immunological causes in males. Whereas polycystic ovarian syndrome was the commonest problem causing infertility in females.

Keywords: Infertility, Poly cystic ovarian syndrome, Semen analysis.

INTRODUCTION

Infertility is inability to conceive after one year of unprotected intercourse[1,2]. Twenty five percent of couples usually experience an episode of infertility in their lifetime. In 2010, 48.5 million infertile couples were estimated all over the world[3]. Worldwide prevalence of infertility is 10-15%, while in Pakistan infertility rate is 21.9%[4]. Relative abnormalities of infertility are found 50% in females, 40% in males and 10% in both partners[5]. Approximately 15% to 20% of couples are usually diagnosed with unexplained infertility after their complete diagnostic workups[6].

Male infertility factors include endocrine disorders[7], abnormal motility, anatomical /duct obstruction, abnormal spermatogenesis, psychosocial factors and drugs. Female infertility factors are ovarian/hormonal tubal cervical, uterine, psychosocial and immunological factors[8].

Although Pakistan is one of the most populous countries of the world, yet it has higher rate of infertility and couples are roaming around quacks. To relieve the stress, it is really required to investigate appropriately for the diagnosis of exact cause of infertility. As the prevalence of pathological conditions leading to infertility differ in various regions, and management depends on the cause. So knowing well the frequency of common causes of infertility in our setup could be helpful in early diagnosis of disease and further management of the patient. The objective

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of this study was to determine the frequency of disorders causing infertility in patients reporting to Combined Military Hospital Bahawalnagar.

METHODOLOGY

This cross-sectional analytical study was conducted at department of pathology and Gynae/Obs, CMH Bahawalnagar in collaboration with Armed Forces Institute of Pathology (AFIP) and Pak Emirates Military Hospital (PEMH), Rawalpindi, Pakistan from Apr 2013 to Apr 2015 after approval of the institutional ethical committee. A total of 200 infertile couples reported to CMH Bahawalnagar for the workups of infertility were included. All included patients were of fertile ages of either gender, who were married, living together and trying to conceive for more than one year and presented with primary or secondary infertility. Females using contraceptive methods, age <18 years or >55 years and males age <18 years were excluded.

Four hundred samples were consecutively collected from all the patients after their informed consent for the workup of infertility. All samples were collected in vacutainer tubes (BD, NJ USA). Blood samples were allowed to clot and then centrifuged for 10 min at 1,000g. The serum was separated and stored at –20°C until assayed. History of illness, physical examination, BMI and baseline routine investigations were carried out at the start of the study.

Serum collected in plain tubes for analysis of follicle stimulating hormone (FSH), luteinizing hormone (LH); (both on 2nd day of menses for females), prolactin (PRL), testosterone, thyroid stimulating hormone (TSH), free thyroxin (fT4) in all patients while gonadotropin releasing hormone (GnRH) stimulation test, anti-sperm antibody, anti mullerian hormone (AMH), magnetic resonance imaging (MRI) brain, genetic screening and karyotyping[9] were carried out in both males & females according to the requirements to confirm diagnosis.

Serum estradiol (on 2nd day of menses), progesterone (on 21st day of menses), liver function tests (LFTs), plasma glucose, high vaginal swab (HVS) and ultrasonography (USG) pelvis were performed in all females. While dehydroepian-drosterone sulphate (DHEAS), 17-OH-progesterone, papanicolaou (PAP) smear, hysterosalpingiogram and laparoscopy were carried out only in females according to the indications. Semen analysis (SA)[9,10] in all males while serum beta human chorionic gonadotropin (β-HCG), dihydrotestosterone (DHT), HCG stimulation test, semen culture sensitivity (C/S), USG of testes[11] and testicular fine needle aspiration cytology (FNAC)/biopsy were carried out only in males according to the indications to confirm diagnosis[12].

Plasma glucose and LFTs on metrolab, semen analysis by microscopy, HVS and USG pelvis were performed at CMH Bahawalnagar. Serum FSH, LH, PRL, testosterone, estradiol, progesterone, TSH, fT4, DHT, DHEAS, 17-OH-progesterone, β-HCG and AMH were analyzed by chemiluminescent enzyme immunoassay on random access immunochemistry analyzer (Immulite 2000) at AFIP, Rawalpindi. USG, hyste-rosalpangiogram and MRI brain were carried out at radiology department PEMH, Rawalpindi.

Statistical analysis of all the data was done using SPSS-20. Frequencies and percentages were calculated for qualitative variables. Median and inter quartile ranges (IQR) were calculated for quantitative variables. Mann-Whitney U-test was used for non parametric data. The *p*-value of <0.05 was considered significant.

RESULTS

Out of total 200 infertile couples, 156 couples with infertility because of different identified causes comprised of 36 due to male factors, 74 due to female factors and 46 due to both partners with mean age of 30 ± 5 years, ranged from 18 to 48 years in males and mean age of 28 ± 5 years, ranged from 18 to 44 years in females and mean duration of marriage 6 ± 4 years, ranged from 1 to 28 years. While in 44 couples no demonstrable cause was identified. Primary infertility was found in 63 percent cases while 37% presented with secondary infertility. In males sperm count,

motility, morphology and serum testosterone were found significantly ($p<0.05$) lower while pus cells, FSH and PRL significantly ($p<0.05$) higher in patients with known disorders of infertility. In females serum FSH and progesterone were found significantly ($p<0.05$) lower while serum PRL significantly ($p<0.05$) higher in patients with

infection in 20, obesity in 10, androgen excess in 8, hyperprolectinemias in 5, tubal occlusion in 4, fibroid uterus in 4, endometrial polyps in 3, endometriosis in 3, immunological causes in 3, liver disease in 3, PID in 2, ovarian failure in 2, hypothyroidism in 2, pituitary failure in 2, hypothalamic dysfunction in 1 and in 80 cases no demonstrable

Table-I: Baseline quantitative characteristics of male patients with disorders causing infertility and those with no demonstrable cause.

Parameter	No Demonstrable cause (n=118) Median (IQR)	Male Infertility disorder (n=82) Median (IQR)	*p*-value
Age (years)	30 (25-34)	29 (27-31)	0.916
Marital duration (years)	5 (2.5-8)	4 (3-7)	0.873
Sperm count (million/ejaculate)	60 (45-70)	40 (24-55)	<0.001
Sperm motility (%)	45 (40-50)	15 (3-40)	<0.001
Sperm morphology (%)	80 (60-100)	60 (36-80)	<0.001
PUS cells/high power field (HPF)	4 (3-6)	7 (4-12)	<0.001
Serum testosterone (nmol/L)	14.3 (13.1-16.7)	11.4 (6.5-17.0)	0.032
Serum Follicle-stimulating hormone (mIU/mL)	3.2 (1.7-3.7)	4.6 (2.6-6.9)	0.005
Serum Luteinizing hormone (mIU/mL)	4.4 (4.1-5.1)	6.6 (3.9-8.1)	0.093
Serum prolactin (mIU/L)	115 (97-168)	187 (139-307)	0.034

Note: IQR is inter quartile ranges.

Table-II: Baseline quantitative characteristics of female patients with disorders causing infertility and those with no demonstrable cause.

Parameter	No Demonstrable Cause (n=80) Median (IQR)	Female Infertility Disorder (n=120) Median (IQR)	*p*-value
Age (years)	27 (25-29)	28 (23-31)	0.361
Marital duration (years)	4 (2-7)	4 (3-8)	0.259
Serum Follicle-stimulating hormone (mIU/mL)	8.5 (7.0-11.4)	4.8 (2.9–8.1)	<0.001
Serum Luteinizing hormone (mIU/mL)	5.5 (2.5-9.5)	5.4 (3.0-10.0)	0.376
Serum prolactin (mIU/L)	159 (146-362)	258 (197-422)	0.010
Serum estradiol (pmol/L)	179 (104-206)	156 (96-325)	0.405
Serum progesterone (nmol/L)	26 (22-54)	10 (0.8-21)	0.001
Serum testosterone (nmol/L)	2.3 (1.9-2.3)	2.3 (1.4-3.8)	0.602

Note: IQR is inter quartile ranges.

known disorders of infertility (table-I & II).

In total of 200 males, varicocele was identified as the cause of infertility in 25 cases, genital tract infections in 22, immunological causes in 13, impotence in 10, duct obstruction in 4, testicular failure in 2, hypothalamic dysfunction in 2, hyperthyroidism in 2, idiopathic azoospermia in 2 and in 118 males no demonstrable cause was found (fig-1).

PCOS was the cause of infertility in 25 females, ovulatory dysfunction in 23, genital tract

cause was found in total of 200 females (fig-2).

DISCUSSION

Among the causes of infertility, genital tract infections, varicocele, immunological causes, impotence, duct obstruction and testicular failure are the main causes in males[13,14]. Ovulatory dysfunction, PCOS[15], infection, obesity, androgen excess, tubal occlusion[16,17], hyperprolectinemias, ovarian failure[18,19] and pituitary adenoma are the main causes of infertility in females[20-22].

Comparison of our data with the results of world health organization (WHO) investigations made in 33 centres in 25 countries, indicated that the female infertility level was higher than male infertility level[23]. In thirty percent cases of infer-
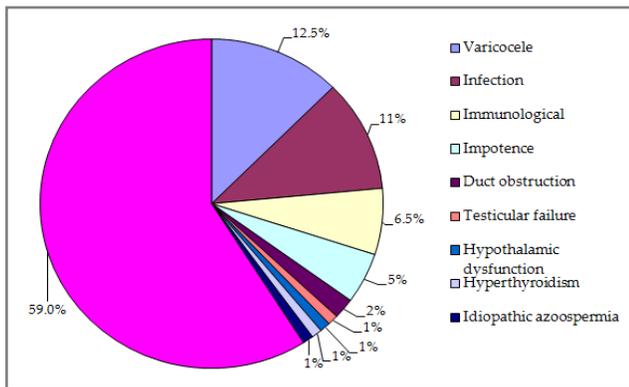

Figure-1: Different types of disorders causing infertility in 82 (41 %) male patients out of total 200 cases who reported to CMH Bahawalnagar, as in 118 (59%) patients no demonstrable cause found (n=200).

tility, pathology is in man alone, and in another 20% both man and woman are found abnormal while 50% contribution is from females[24]. This gender discrepancy is probably because of the

wth rate in Pakistan, and people with secondary infertility are not that much worried in comparison to primary infertility.

Nieschlag *et al* in a study at Europe in 2010 showed maldescended testes in 8.4% cases, varicocele in 14.8%, sperm autoantibodies in 3.9%, others known causes (infections) in 5%, idiopathic infertility in 30%, Klinefelter syndrome (47, XXY) in 2.6%, XX male in 0.1%, primary hypogonadism of unknown cause in 2.3%, secondary hypogonadism in 1.6%, Kallmann syndrome in 0.3%, idiopathic hypogonadotrophic hypogonadism in 0.4%, residual after pituitary surgery less than 0.1%, other causes of hypogonadism 0.8%, late-onset hypogonadism 2.2%, constitutional delay of puberty 1.4%, systemic disease 2.2%, testicular tumor 6.2%, lymphoma 1.5%, leukemia 0.7%, sarcoma 0.6%, disturbance of erection/ejaculation 2.4%, vasectomy 0.9%, cystic fibrosis 0.5%, others causes of obstruction in 0.8% cases[25].

Our study showed higher rates of genital tract infections in males, which may be due to poor hygienic conditions, immunological causes due to autoantibodies predisposition, impotence
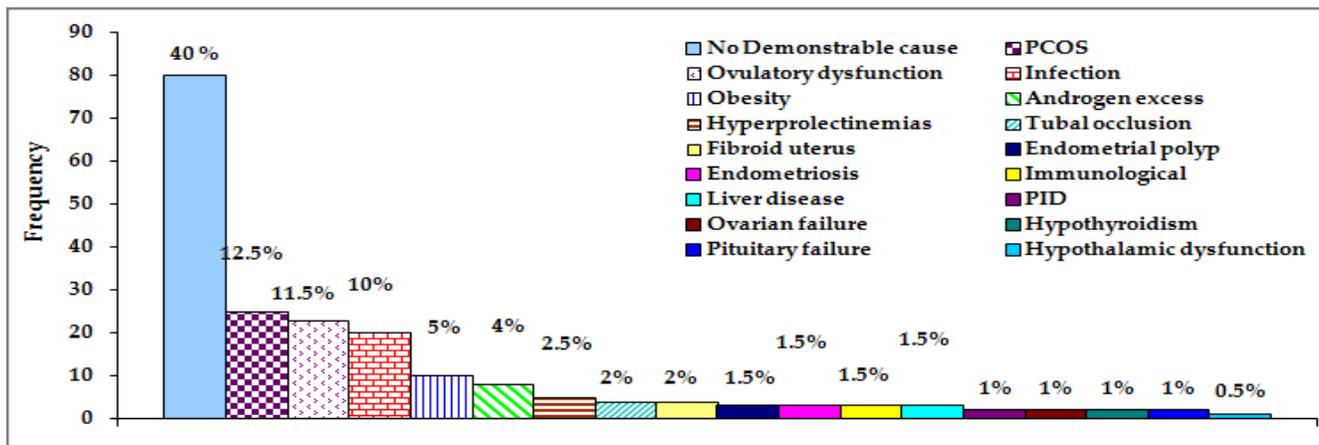

Figure-2: Disorders causing infertility in 120 (60%) female patients out of total 200 cases who reported to CMH Bahawalnagar, as in 80 (40%) patients no demonstrable cause found (n=200).

different risk factors and the intensity of their effects on both genders. Maxi-mum age group was 20 to 35 years as similar to different studies. In this study included patients showed higher rate of primary infertility than secondary infertility, that may be due to higher population gro-

may be due to psychosocial reasons in males, and as similar as varicocele, duct obstruction, hyperthyroidism and lower frequency for testicular failure, hypothalamic dysfunction and idiopathic azoospermia as compared to other studies in literature.

This study also showed higher rates of PCOS in females, which may be due to regional effects, sedentary life style, dietary imbalances and use of quackery formulations in females, genital tract infection due to poor hygienic conditions, obesity, androgen excess may be due to exogenous androgens intake in some diets and immunological causes due to autoantibodies as the commonest causes of female infertility, followed by as similar as ovulatory dysfunction, fibroid uterus, endometrial polyps, endometriosis, liver disease, pituitary failure, hypothalamic dysfunction and lower for hyperprolectinemias, tubal occlusion, PID, ovarian failure and hypothyroidism as compared to other studies in literature. Estimation of semen analysis in male while fertility hormonal profile in female provides the basis for early diagnosis of infertility in affected patients.

Limitation of the study was that complete tests were not carried out in all the patients but only required investigations were carried out step by step in order to reach the diagnosis of infertility. Further studies are required to find and compare the frequencies of all causes of infertility in different areas of Pakistan aiming to manage the diagnosed cases of infertility well in time accordingly.

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This original article was developed with some financial support of CMH Bahawalnagar and majority of patients paid themselves for their investigations. No external sources of funding and support have been involved. No honoraria or other reimbursements have been provided.

CONCLUSION

Varicocele is the commonest cause of infertility, followed by genital tract infection and immunological causes in males. Whereas PCOS is the commonest problem causing infertility, followed by ovulatory dysfunction, infection, obesity and androgen excess in female patients.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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