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Original Research Article

Evaluation of the complete profile of male partners in infertile couples with special emphasis on detection of genital tuberculosis

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ABSTRACT

Background: To evaluate the complete profile of male partners in infertile couples with special emphasis on detection of genital TB.
Methods: The study was conducted in the fertility clinic of department of obstetrics and gynaecology, Maulana Azad Medical College and Associated Lok Nayak and GB Pant Hospitals, New Delhi from August 2015 to December 2016 among 100 infertile couples. Detailed history, general physical and local examination of male partners was done. Routine blood and urine tests, combined with radiology examination of chest and mantoux skin test of male partners were done followed by investigations specific to male factor evaluation. Two semen samples collected after 3-5 days of sexual abstinence were analyzed to assess semen parameters such as volume, total sperm count, total motility and morphology. Ultrasound and colour Doppler of scrotum and hormone analysis was done in all cases of azoopermia, oligoasthenospermia or asthenospermia. Testicular FNAC was done for all cases of azoospermia and oligoasthenospermia to establish cause of male infertility.
Results: 72% couples had primary infertility. 34% males were daily tobacco chewers. 8 males had varicocele and 2 had undescended testes on examination. 60% males had semen analysis in the normal range and 19% had azoospermia. Tobacco chewing, testicular size abnormalities, varicocele, hydrocele were significantly associated with abnormal semen findings. A statistically significant relation was found between elevated S.FSH and semen analysis findings. A statistically significant association was found between penile meatal stenosis, chest X-ray, mantoux test with history of TB in male/female partner.
Conclusions: Primary infertility was more common than secondary infertility in our study group. Addiction was found to be an important factor in infertile men particularly tobacco chewing. Elevated Serum FSH levels were a common finding in males with azoospermia and oligoasthenospermia.

Keywords: Infertility, Sperm, TB, Genital

INTRODUCTION

Infertility is defined as the inability to conceive after one year of unprotected sexual intercourse during the fertile period. Infertility is estimated to affect between 8 and 12% of reproductive-aged couples worldwide.[1] Infertility is a global health issue which may affect both male and female partners. The agony of infertility is felt by the entire family, but the brunt is born by the female partner in the Indian society. When efforts to have children by infertile

couples are unsuccessful, it can lead to sexual dissatisfaction and psychological stress in the family.[2] An accurate profile of the prevalence, distribution, and trends of infertility is an important first step towards shaping evidence-based interventions and policies to reduce the burden of this neglected disability globally. It is therefore very pertinent to understand which male factors are contributing to infertility and this may help in alleviation of disease especially if the causes are reversible such as varicocele, cryptorchidism, infections including genital tuberculosis (TB), obstructive lesions, cystic fibrosis, trauma, oxidative stress and hypogonadism due to testicular causes. It also involves cases where the condition maybe just psychological or functional without any organic disease.[3]

Male partner evaluation is not extensive mostly and culminates with semen analysis, though it is the first step to investigate it.[3] Male partners are evaluated further if they are associated with azoospermia/oligospermia or have some complaint other than infertility. The prevalence of Genital tract TB in infertile women is reported to vary from 50-70% in developing countries to 1-2% in developed countries.[4] Infertility is the commonest symptom associated with genital TB and it seems to be an important under-diagnosed factor in infertility.[5,6] The diagnosis involves isolation of the organism by means of AFB (acid fast bacilli) smear and culture in the respective specimen. Hence the present study was conducted with the following objectives: to study complete profile of male partner of infertile couples attending Fertility clinic of Lok Nayak Hospital and to detect genital TB in male partner of infertile couples and to compare its occurrence in males with normal and abnormal semen parameters.

METHODS

The prospective observational study was conducted in the fertility clinic of department of obstetrics and gynaecology, Maulana Azad Medical College and Associated Lok Nayak and GB Pant Hospitals, New Delhi from August 2015 to December 2016 among 100 infertile couples attending the Fertility Clinic. Informed consent was taken from all patients before enrolling them for study. Male partners of 100 consecutive infertile couples irrespective of type of infertility (primary or secondary) attending the Fertility clinic outpatient department for the first time were included in the study. Patients who have received fertility treatment in past and currently taking anti-TB drugs were excluded from the study.

Procedure

Patients attending the fertility clinic were included in the study irrespective of age and type of infertility problem. The initial assessment was carried out according to the standard fertility clinic protocol. Detailed history in the form of structured medical questionnaire was taken including age, type of infertility, duration of infertility, sexual history, past medical/surgical history, history of pulmonary and genital TB, history of substance abuse. Socio economic status classification was done according to Modified Kuppuswamy scale.[7] BMI (body mass index) was evaluated according to global criteria.[8] General physical and local examination of the male partner was done. Presence or absence of gynaecomastia, hypospadias, varicocele, abnormalities of vas deferens and the epididymis and testicular location were evaluated. Testicular size was assessed with the use of a caliper or Prader wooden orchidometer and ultrasound (wherever indicated). Normal adult testes on an average are about 4.5 cm (length) by 2.5 cm (width). Routine blood and urine tests, combined with radiology examination of chest and mantoux skin test of male partners were done followed by investigations specific to male factor evaluation such as semen analysis, hormone analysis and FNAC.

For the Mantoux skin test a standard dose of five tuberculin units (0.1 ml) of purified protein derivative of tuberculin was injected intradermally into the left forearm using 28 or 26-gauge needle and tuberculin syringe. The test was read between 48 and 72 h after administration. An indurated area larger than 10 mm in diameter was considered a positive result. The Mantoux test does not measure immunity to TB but the degree of hypersensitivity to tuberculin and the size of in duration has no correlation and likelihood of current active TB disease. Semen analysis was done at least two times after 3-5 days of sexual abstinence. Sample obtained by masturbation was examined as per WHO guidelines. The parameters studied were appearance, liquefaction time, pH, volume, sperm counts (million/ml), motility (%) and morphology. Males with sperm parameters below the WHO normal values are considered to have male factor infertility. Absence of the spermatozoa in semen ejaculate was called azoospermia, a count less than 15 million/ml was called oligospermia, a total motility <40% was called asthenospermia and a combination of low total count and low total motility was called oligoasthenospermia.[9]

Colour Doppler scrotum

USG and colour Doppler of scrotum was done to measure testicular size, to rule out any testicular swelling including varicocoele, in all cases of azoopermia, oligoasthenospermia or asthenospermia. Testicular size was calculated by measuring height (H), width (W) and length (L) of testis and by calculating volume by formula: HxWxLx0.71. A total volume (both testes) of >30 ml and a single testicular volume of 12-15 ml is generally considered normal

Hormonal analysis

Nonfasting blood samples were drawn from the antecubital vein for the majority of the patients between 8 am and 2 pm for all cases of azoospermia, oligoasthenospermia or asthenospermia. Serum FSH, serum LH and serum Testosterone were estimated for indicated subjects by Electro chemiluminiscence band immunoassay using fully automated closed system.

Normal range for serum FSH was 1.5-12.4 mIU/ml, for serum LH was 1.7-8.6 mIU/ml and for serum Testosterone was 2.8-8 ng/ml.

FNAC

FNAC was done for all cases of azoospermia and oligoasthenospermia. The method of processing of FNAC material for complete cytological analysis was best described by Turek et al in 1997.[10] FNAC grading of spermatogenesis was done by Chandley's classification: Normal spermatogenesis: active spermatogenesis with mature cells, early/late maturation arrest: arrest at various stages of spermatogenesis, Hypospermatogenesis/germ cell hypoplasia: some tubules with sertoli cells only and Sertoli cell only syndrome: all tubules with sertoli cells only (SCOS).[11]

Open biopsy

Testicular biopsy was done in 10 cases of azoospermia out of 19 (6 males did not consent, 3 cases adequate tissue sample could not be obtained). Open biopsy was taken from anyone of the 8 segments of FNAC, whichever showed better grade of spermatogenesis. Grading of spermatogenesis was done according to Chandley's classification.[11]

Genital TB

A standard clinical criterion for the diagnosis of genital TB was used, which includes a high index of suspicion along with clinical, laboratory, and radiological evidence of genital TB.[12] All males were evaluated for urinary complaints, local examination for scrotal swelling, epididymal enlargement or irregularity, nodular vas was looked for. A complete hemogram, mantoux test and chest X-ray were done. All males were screened for TB using a semen staining for acid AFB and semen culture for TB. Male partners with a history of pulmonary TB or whose wives had a diagnosis of genital TB as the cause of infertility were taken to be the cases with suspicion of genital TB. Their clinical, laboratory and radiological parameters were recorded. A co-relation was attempted between all the parameters with history of TB.

Statistical analysis

Quantitative Data: Difference between the two means was compared by Students's t-test. Paired Observations: Wilcoxon paired test was done. Qualitative Data: Fisher test was done. Statistical significance was defined if the p value was <0.05.

RESULTS

A total 72% couples had primary infertility whereas 28% had secondary infertility. Primary infertility estimates were substantially higher than secondary infertility estimates in our study population. Mean duration of marriage was 6.96 years. Most (78%) of the men were in the age group of 20-35 years, whereas most women (71%) were in the age group of 20-30 years.

Table 1: Profile of the study subjects.

Parameters	N	%
Type of infertility		
Primary	72	72
Secondary	28	28
Age distribution (years)	**Men**	**Women**
<20	0	1
20-30	41	71
31-35	37	17
36-40	15	11
41-45	7	0
Socio economic class		
Upper class	0	0
Upper middle	34	34
Lower middle	33	33
Upper lower	33	33
Lower	0	0
BMI		
Underweight	4	4
Normal	76	76
Pre obese	16	16
Obese grade 1	4	4
History parameters		
Coital Problems	20	20
Dyspareunia	12	12
Premature ejaculation	7	7
Retrograde ejaculation	1	1
Systemic illness	1	1
TB	16	16
Smoker	13	13
Alcohol intake	12	12
Tobacco chewing	34	34

Only one female in our study was less than 20 years old. The mean age (±SD) of the men was 31.80±4.72 years (range, 22-42 years), and the mean age (±SD) of the women was 28.67±4.66 years (range, 19-40 years). Mean BMI was 23.17, range 18.91-32.28 kg/m^2 (Table 1).

Total 2 out of 100 males had penile meatal stenosis. 14 out of 100 cases had testicular abnormalities of which 8 males had either small or atrophic testes, 3 had enlarged testes and 2 males had undescended testes. 8 out of 100 males had varicocele and 4 out of 100 males had hydrocele on local examination. Mean values of the parameters were found to be; semen volume 2.82 ml, sperm concentration 51.53 million/ml, total motility 44% and total morphology 39.9%. The prevalence of azoospermia was found to be 19%. The prevalence of other abnormal semen parameters namely oligospermia, asthenospermia and oligoasthenospermia were 6%, 6% and 9% respectively. Type of infertility, coital problems, BMI and smoking history of men with abnormal semen analysis were not significantly different from those of men with normal semen analysis.

Abnormal findings on local genital examination such as varicocele (p=<0.01), hydrocele (p=0.01) or testes abnormalities (p=0.01) were found to be significantly associated with abnormal semen analysis in those males.

Table 2: Association between clinical and laboratory findings and semen analysis.

Parameters		Semen analysis		Total	Chi Square value	P value
		Normal (n=60)	Abnormal (n=40)			
Type of infertility	Primary	42	30	72	0.298	0.585
	Secondary	18	10	28		
Coital problems	Present	11	9	20	0.26	0.61
	Absent	49	31	80		
Smoking	Present	7	6	13	0.236	0.627
	Absent	53	34	87		
Tobacco	Present	16	18	34	3.595	0.058
	Absent	44	22	66		
BMI	Normal	49	31	80	2.135	0.344
	Overweight	10	6	16		
	Obese	1	3	4		
Testis examination	Normal	56	30	86	6.7	0.01
	Abnormal	4	10	14		
Varicocele	Present	0	8	8	13.043	<0.001
	Absent	60	32	92		
Hydrocele	Present	0	4	4	6.25	0.012
	Absent	60	36	96		
Urine physical examination	Normal	58	34	92	4.438	0.035
	Abnormal	2	6	8		

Table 3: Association between hormone analysis and semen analysis findings (n=34).

Parameters		Results			Total	Chi- Square	P value
		Asthenospermia	Azoospermia	Oligoasthenospermia			
Serum FSH	Normal	5	11	9	25	5.92	0.052
	Increased	1	8	0	9		
Serum LH	Normal	2	7	5	14	1.068	0.586
	Increased	4	12	4	20		
Serum total testosterone	Normal	6	16	9	31	2.598	0.273
	Decreased	0	3	0	3		
Total		6	19	9	34		

All the 8 male partners with varicocele for instance had abnormal semen parameters. Six males with abnormal urine analysis had abnormal semen findings as well (p=0.03) as shown in (Table 2). 9 out of 34 (26.5%) had increased S. FSH levels. 20 out of 34 (59%) had increased S. LH levels. 8 out of 19 (42%) males with azoospermia had increased S. FSH levels. 12 out of 19 (63%) males with azoospermia had increased S. LH levels. None of the males in our study had decreased S. FSH or S. LH levels as shown in (Table 3).

Age, coital problems and examination findings of varicocele and hydrocele were not found to be significantly different in males with primary or secondary infertility. Primary infertility was more common in younger females <30 years (46%), whereas primary and secondary infertility had equal prevalence in females older than 35 years. 34 out of 100 males were tobacco chewers of which 20 (59%) males had primary infertility. 13 out of 100 males were smokers of which 8 (61.5%) had primary infertility. Azoospermia was more common in primary infertile men (90%) as compared to secondary (10.5%) as shown in (Table 4). Of the 16 males who either had past history of pulmonary TB or whose wives had genital TB as cause of infertility, 10 were primary infertile, 2 had urinary complaints in form of dysuria, 1 male had penile meatal stenosis, 2 males had epididymal enlargement on local genital examination. 4 males had evidence of fibro nodular opacities on chest X-ray and 7 out of 16 (43.76%) had mantoux test positive. Most of the males had normal clinical findings, none had beaded/nodular vas or scrotal sinus formation. Bilateral spermatic cords were normal.

Table 4: Co-relation of demographic, clinical, laboratory and radiological findings with type of infertility.

Parameters		Type of infertility		Total	Chi Square value	P value
		Primary	Secondary			
Age (M) (years)	<30	24	7	31	0.856	0.652
	30-35	27	13	40		
	>35	21	8	29		
Age (F) (years)	<30	46	16	62	0.854	0.653
	30-35	18	7	25		
	>35	8	5	13		
Coital problems	Present	12	8	20	1.786	0.181
	Absent	60	20	80		
Smoking	Present	8	5	13	0.811	0.368
	Absent	64	23	87		
Tobacco	Present	20	14	34	4.437	0.035
	Absent	52	14	66		
Varicocele	Present	5	3	8	0.389	0.533
	Absent	67	25	92		
Hydrocele	Present	4	0	4	1.62	0.203
	Absent	68	28	96		
Semen analysis	Normal	42	18	60	4.649	0.325
	Asthenospermia	3	3	6		
	Azoospermia	17	2	19		
	Oligoasthenospermia	6	3	9		
	Oligospermia	4	2	6		

All 16 males with suspicion of genital TB had semen parameters such as volume, count, motility and morphology in the normal range. 3 out of 16 males were azoospermic and 1 case each of asthenospermia and oligoasthenospermia. Semen smear and culture examination to detect AFB in all 16 males was negative. On radiological examination 4 patients had fibro nodular opacities on chest X-ray which was found to be strongly associated with history of TB (p=0.01). Seven out of 14 men had an induration of more than 10 mm on tuberculin skin testing one which was also found to be significantly associated with history of TB. Two patients had abnormal findings on ultrasonography (one varicocele and one inclusion cyst). Fine-needle aspiration cytology (FNAC) testing in these cases revealed maturation arrest in 2 and normal spermatogenesis in two. There was no significant association between USG scrotal Doppler and FNAC findings with history of TB in male/female partner (Table 5).

DISCUSSION

Infertility has profound socio-economic and health consequences on affected couples and society. Research over the decades suggests that both the male and female partner is equally responsible for infertility. In view of the scarcity of data on male infertility, a prospective study was carried out to evaluate the complete profile of male partners in infertile couples with special emphasis on detection of genital TB. In our study we examined a total of 100 infertile couples and we found primary infertility (72%) to be more common than secondary. Bhattacharya et al reported 58.0% and 42.0% estimates of primary and secondary infertility respectively which was similar to our findings.[13] Cabrera et al found prevalence of primary infertility as 6.12% and that of secondary infertility was 11.33% however their major age group of analysis was 30-49 year old women, unlike our study where most women were in age group 20-30 years.[14] In another study conducted in Sub Saharan Africa by Larsen (2000) has also concluded higher estimates of secondary infertility in low- or middle-income countries.[15] This difference may be due to a very large sample size as they analyzed all women, fertile as well as infertile, aged 20-44 years. Most males (54%) included in the present study had normal BMI and only 4 males were obese. In our study also we observed no statistically significant association BMI and abnormal semen findings. In 2007, Danish et al and Norwegian et al cohorts illustrated an association between obesity and male infertility with ORs of 1.53 (95% CI 1.32-1.77) and 1.36 (95% CI 1.32-1.77), respectively.[16,17] Sermondade et al observed in a meta-analysis of 13,077 men that obese men had a significantly elevated risk of abnormal sperm count compared with normal weight men.[18] Chavarro et al however did not find statistically significant differences in sperm concentration, sperm morphology or sperm motility with BMI.[19] Pauli et al also found no significant co relation between BMI and semen analysis parameters.[20]

Our study found significant association between tobacco chewing and abnormal semen findings but we found no cases of teratospermia. Similarly, Sunanda et al studied the prevalence of abnormal sperms in tobacco chewers and found that, 66% of subjects were oligozoospermic, 85% asthenozoospermic and 28% teratozoospermic.

Table 5: Association between clinical, laboratory and radiological parameters with history of TB in male/female partner.

Parameters		H/O TB		Total	Chi Square value	P value
		Yes (n=16)	No (n=84)			
Coital problems	Yes	1	19	20	2.251	0.134
	No	15	65	80		
Smoking	Yes	3	10	13	0.557	0.456
	No	13	74	87		
Tobacco	Yes	4	30	34	0.688	0.407
	No	12	54	66		
Socio economic status	LM	5	28	33	0.104	0.949
	UL	5	28	33		
	UM	6	28	34		
BMI	Normal	12	68	80	0.391	0.823
	Overweight	3	13	16		
	Obese	1	3	4		
Penis examination	Normal	15	83	98	5.476	0.065
	Abnormal	1	1	2		
Varicocele	Present	0	8	8	1.656	0.198
	Absent	16	76	92		
Urine physical examination	Normal	14	78	92	0.524	0.469
	Abnormal	2	6	8		
Chest X-ray	Fibro nodular opacities	4	0	4	21.875	<0.001
	Normal	12	84	96		
Mantoux test	<10	9	83	92	33.076	<0.001
	>10	7	1	8		
Semen analysis	Normal	11	49	60	1.549	0.818
	Asthenospermia	1	5	6		
	Azoospermia	3	16	19		
	Oligoasthenospermia	1	8	9		
	Oligospermia	0	6	6		
USG Scrotum+Doppler	Normal	3	10	13	1.18	0.348
	Abnormal	2	20	22		
FNAC	Hypospermatogenesis	0	8	8	6.22	0.101
	Maturation arrest	2	2	4		
	Normal spermatogenesis	2	10	12		
	Sertoli cell only syndrome	0	4	4		

Sperm counts; odds ratio (OR)=2.2; 95% confidence interval (CI): 1.5-3.09, motility (OR=3.2; 95% CI: 2.05-4.9), and normal morphology (OR=8.4; 95% CI: 4.9-14.6) were significantly affected (p=0.001) in tobacco chewers than the non-chewing group.[21] Ramlau-Hansen et al also reported an association between smoking and decreased semen parameters such as semen volume, total sperm count, and sperm motility.[22] Dechanet et al have also pointed out that smoking was associated with decreased fertility by causing delay in conception and decreased IVF results, established by our findings of significant association between tobacco chewing and type of infertility (p=0.03).[23] In our study we found 8 cases of varicocele. In our study 20% patients with varicoceles had abnormal semen analysis results, although none of the patients with normal semen analysis had varicocele. Zargar et al report incidence of varicocele in 1 out of 66 cases (1.51%) and cryptorchidism in 4 out of 66 cases (6.06%), close to our finding of 2% cases of cryptorchidism.[24] In a Korean study by Lee et al varicoceles were diagnosed in 15.1% patients who presented with semen analysis in the normal range and 42.0% patients with semen analysis in the abnormal range.[25] Shafi et al found in their study that varicocele accounted for 32.2% (CI 95%, 29.3, 37.1) of patients with primary infertility and 28.5% (CI 95%; 26.5; 30.5) with secondary infertility i.e. no significant differences were seen between the type of infertility and varicocele.[26] This result is consistent with the findings of our study. Although, Kantartzi et al found that varicocele is more common in secondary infertile men.[27]

Out of 34 males whose hormone levels were estimated in our study, 36% had increased Serum FSH, 59% had increased Serum LH which was mirrored in the findings of Olesen et al who found 20.8% had increased LH levels in their analysis of 1213 infertile men.[28] In our study 42% men with azoospermia had elevated FSH. Zargar et al reported 66.7% men with azoospermia and 33.3% men with oligospermia had an elevated FSH level, suggesting failure of spermatogenesis, whereas 16.7% men with azoospermia had raised LH and FSH levels, suggesting testicular failure.[24] There is not much literature available on analysis of male genital TB in infertile couples, which was one of the reasons for initiation of this study. The analysis of genital TB was done in males who either themselves had a history of TB or the female partner had genital TB as the main cause of infertility (N=16). Mean age group in TB suspects was 31.4 years (22-41 years) similar to study of Sharma et al who found 75 % of their patients in age range of 20-45 years of age.[29] None of our patients had the evidence of clinical TB, except for one patient who had mediastinal lymphadenopathy, which was picked up on chest X-ray. All patients in our study were also asymptomatic on presentation. None of the cases had significant examination finding except 2 cases of penile meatal stenosis. Sinha et al have reported a case of ulceroproliferative lesion of the glans penis healing with meatal stenosis.[30]

In Christensen's review of 102 cases, 75% of patients had an abnormal chest radiograph, 88% tested had positive skin tests.[31] In the present study an abnormal chest radiograph was found in 4 patients and Mantoux test positive in 7 male partners. A significant association was found between chest X ray and mantoux testing was seen with past history of TB. In our study, 31% cases with suspicion of TB had abnormal semen analysis findings, however not statistically significant. Kumar et al found significant abnormalities in the semen analysis in the form of azoospermia, low volume ejaculate or leukocytospermia in patients with GUTB.[32] Regmi et al analysed male partners of 15 infertile women with a diagnosis of genitourinary TB as the cause of infertility and found only one case with abnormal semen analysis.[33] Sole-Balcells et al found in their study on male infertility that 75% of the patients without any lesion on genital examination had oligoasthenozoospermia.[34] We did not find any semen sample positive for AFB smear and culture. Sharma et al examined various clinical specimens to establish diagnostic value of genital TB.[29] They examined 17 semen samples and found positivity rate of AFB detection by semen smear or culture as 0%, like our study. They found PCR to be the method of choice for rapid diagnosis and management of genital TB. Ajantha et al examined 182 samples for extra pulmonary TB detection, found 22 positives out of which 3.3% were found to be positive by smear and 5% by culture.[35]

Future scope

In infertile couples, male partners with history of TB or whose female partner had genital TB as cause of infertility should be evaluated by more sensitive and rapid tests like semen PCR.

CONCLUSION

In conclusion primary infertility was more common than secondary infertility in our study group, with addiction found to be an important factor in infertile men particularly tobacco chewing. On examination of infertile males testicular size variations, varicocele, hydrocele were common and these were found to be significantly associated with abnormal semen findings as was abnormal urine microscopic examinations were found to be significantly associated with abnormal semen parameters. Elevated Serum FSH levels were a common finding in males with azoospermia and oligoasthenospermia, though we had cases with history of TB but semen smear and culture were negative in them.

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