Immunological and Hormonal Profile of Infertile Pakistani Males With Varicocele

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ABSTRACT

Aims: To compare the levels of serum FSH, Testosterone in infertile men with and without varicocele and to detect the Antisperm antibodies (ASA) in the serum of infertile men with and without varicocele.

Study Design & Settings: It is a Cross sectional prospective study the laboratory work was done at Physiology Department, University of Health Sciences, Lahore.

Methods: This Cross sectional study was conducted on ninety patients that fulfilled the inclusion criteria. The patients were chosen from the infertile couples reporting to the Combined Military Hospital Lahore and General Hospital Lahore for infertility. Detailed history was taken meticulous physical examination and semen analysis of was performed on all the subjects. Scrotal ultrasound was done to confirm varicocele. Serum FSH, testosterone and antisperm antibody determination were carried out by ELISA.

Results: Varicocele was found in 35 out of 99 infertile men by physical examination and confirmed by Scrotal Ultrasound. The infertile men with varicocele had higher levels of serum FSH than infertile men without varicocele. Levels of testosterone were lesser in subject with varicocele. All (99) infertile males with and without varicocele were subjected to ASA test. It was observed that out of 35 infertile men with varicocele 1 was positive, while 3 out of 64 men without varicocele were positive for ASA.

Conclusion: Our results suggest no relationship of varicocele with abnormal serum FSH & Testosterone levels and presence of ASA in infertile men with varicocele.

Keywords: Varicocele, Anti-sperm antibodies, Serum Testosterone, FSH, Infertile men.

INTRODUCTION

Internationally one out of every six couples reports in infertility clinics for treatment of infertility1, 2. Among these 40-50% are due to male factors, 25% cases are due to female, 20% are due to a combination of female and male factors while 10% have unexplained infertility3,4. The prevalence of varicocele is 25% in men with abnormal semen analysis5. In varicocele, there is enlargement and dilatation of veins of the pampiniform plexus in the spermatic cord6. In infertile men it is the commonest cause of infertility and occurs in approximately 30% to 81% of infertile men7. Several theories have been presented to explain the impairment of fertility by varicocele8. These theories include increased sperm DNA damage9, increase in apoptosis3, tissue hypoxia, oxidative stress degenerative changes in the seminiferous tubule, and decreased production of Fas protein resulting in immunological infertility10. In Varicoceles, seminal plasma antioxidant activity diminishes and sperm reactive oxygen species (ROS) production increases11. Excessive reactive oxygen species (ROS) can cause damage to DNA, proteins, and cellular lipids by inducing oxidative changes11. Surgical varicocelectomy decreases ROS production, increases levels of seminal plasma antioxidants and improves seminal parameters11. Presence of antibodies and deranged hormonal levels are blamed for decreased motility in infertility due to varicocele12. Hormonal imbalance and sperm autoimmunity affect each other and work in close association13. Antisperm antibodies are found in 11% of infertile men and its prevalence is 23.8% to 31% among infertile men with varicocele14. ASA decreases sperm motility hence inability to penetrate the cervical mucus resulting in reduced fertilizing potential15. Testosterone a steroid hormone, is essential for initiation and maintenance of spermatogenesis16. Moreover, it plays a key role in the development/maintenance secondary sexual characteristics of males17. Decrease levels of testosterone were found in infertile men having poor seminal parameters and varicocele17. Hence this study was designed to detect the hormonal levels and presence of ASA in infertile men with and without varicocele.

MATERIALS AND METHODS

This study was conducted on 99 subjects selected from Combined Military Hospital and Lahore General
Hospital. The subjects were 35 infertile males with varicocele aged between 20-40 years, and 64 age matched infertile males without varicocele. Serum samples were taken from all subjects and kept at -80c until assay was performed. Participants were instructed to come for semen sample collection after a restraint of three days from sexual intercourse. After collection in sterile containers semen was allowed to liquefy at 37 c for 30 minutes. Semen analysis was performed within one hour of sample collection. Physical examination of all subjects was performed before doing Scrotal Ultrasound

**Assay of serum:** All serum samples were analyzed for levels of FSH, testosterone and ASA by an enzyme linked immunosorbent assay (ELISA). Testicular ultrasonography was performed on all subjects.

**Inclusion Criteria:** Male subjects with abnormal semen parameters having primary infertility exceeding 2 years duration.

**Exclusion Criteria**
1. Male having infertility for less than a year.
2. Subjects having recent history of trauma or surgery of the genitourinary tract.
3. Subjects having intra-abdominal malignancy and chronic diseases.

**Statistical analysis:** Values represent the mean SD, statistical evaluation was done with Student’s t-test and Chi-square test. P < 0.05 was considered statistically significant. Statistical analyses were performed with SPSS version 21.0.

**RESULTS**

The mean age of infertile men as shown by age distribution was 30 years. All infertile men (99) underwent physical examination and scrotal USG, 35 subjects were found to have concomitant varicocele, while 64 males did not have varicocele. Serum FSH levels were found to be in normal range in all 99, however infertile men with varicocele had higher FSH levels but the difference was not significant (p value 0.06) between two groups (Table 1). In all the 99 males serum Testosterone levels were found to be in normal range (4 – 8 ng/ml). However estimates in relevance to varicocele were found to be lower but did not fall beyond the normal range (Table 2). The difference in serum testosterone level between two groups is not significant (p value 0.07). All (99) infertile males were subjected to ASA test. It was observed that ASA were found only in one infertile man with varicocele, while 3 out of 64 men without varicocele were positive for ASA (Table 3). The difference between the groups was not significant (p value 0.66).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Infertile Male (n=99)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FSH levels</td>
<td>Positive (n=35)</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>5.5 ± 6 miu/ml</td>
</tr>
</tbody>
</table>

**Table 1:** Comparison of serum FSH in infertile men with and without varicocele

<table>
<thead>
<tr>
<th>Variables</th>
<th>Infertile Male (n=99)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testosterone level</td>
<td>Positive (n=35)</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>7.5 ± 0.32</td>
</tr>
</tbody>
</table>

**Table 2:** Comparison of Serum Testosterone levels in infertile men with and without varicocele.

**DISCUSSION**

Multiple factors play role in pathogenesis of varicocele which is considered the most common cause of male infertility. Testicular damage or autoimmune process causes inhibition of spermatogenesis and leads to infertility in the males between 25 to 45 years of age. In the current study, 35(35%) males have varicocele. Similar results (30-40%) are shown in study conducted by Mohammad. In the current study sperm concentration was decreased in 16 subjects while 19 subjects have sperm motility defects in infertile men with varicocele. A Study conducted by Mohammad also showed similar results. Apoptosis in testis with varicocele may be the cause of decrease in sperm concentration. As far as the hormonal evaluation of these infertile subjects is concerned FSH levels were comparatively higher in subjects with varicocele but within normal range. These higher levels of FSH in infertile subjects with varicocele might be due to decrease in testicular volume, sperm concentration and sperm motility in these subjects. Testosterone levels are not statistically different in two groups, however some studies reported that varicoceles causes lydig cell dysfunction and subsequent decrease in testosterone biosynthesis. Certain studies showed that varicocele has a negative influence on the Leydig cell function thus indirectly decreasing testosterone production. It is reported that testosterone has a pivotal role in reproductive function as well as morphological development and in
males\(^{18}\) while other suggested that testosterone hormone has no connection with sperm concentration \(^{19}\). In the current study, ASA were found in only one infertile males with varicocele while they were present in three infertile men without varicocele. Multiple studies reported that varicocele-associated infertility has little or no relevance with ASA\(^{16, 17}\). A lot of contradiction exists in literature about varicocele induced ASA formation. The study conducted by Ishikawa showed no improvement in semen parameters after varicocelectomy in men with or without ASA\(^{19}\). Patients with a history of mumps, or either a fresh varicocele or a history of varicocele had statistically significant lower levels of MAR antisperm antibodies (ASAs) than patients with no such conditions\(^{16}\). As there is little evidence about association of varicocele with male infertility in local population therefore, further studies should be conducted on a larger sample of local infertile male to further explore this association.

### CONCLUSION

Estimates of Serum Testosterone were found to be lower while Serum FSH were higher in infertile men with varicocele but both fell within the normal range. A higher number of infertile men without varicocele were positive for ASA as compared to infertile men with varicocele.

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