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SPERM DISORDERS AND TRENDS OF MALE FACTOR INFERTILITY: META-ANALYSIS AND REVIEW

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Abstract:
Infertility and sperm disorders have been a serious concern for a long period and are still a perplexing issue at present. Approximately 8 to 12% of couples are affected by this issue around the globe. The malefactor is 40- 50% in all the infertility cases and almost 2% of all men show the suboptimal sperm parameters. The reason might include poor sperm motility, low sperm concentration, or abnormal morphology with deformed sperm shape. In the underdeveloped or developing countries, the ratio of infertility is marked higher by WHO and it is found associated with infectious diseases. This review paper will aid in understanding the trends of male infertility factor in developing countries like Pakistan, and to sort out the future in this niche along with various factors responsible for male infertility.

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INTRODUCTION:

Infertility is a reproduction disorder linked with economic, psychological, and medical implications causing stress, specifically in a social system like in Pakistan, where the emphasis is super strong on childbearing. According to the World Health Organization (WHO), and International Committee for Monitoring Assisted Reproductive Technology, infertility is a disease of the reproduction system characterized by the inability to conceive/ achieve a clinical pregnancy after one year of regular unprotected sexual intercourse. It can also be elaborated as regular unprotected sexual intercourse with the partner of age <35 years for 12 or more months; and 6 months of regular intercourse without contraceptive usage with the female partner ≥35 years. [1, 2]

Global Male Infertility Incidence

No reliable figures are present to reveal the percentage of male infertility. But, an estimated suggestion is presented by WHO depicting that an average of 72.4 million couples faces infertility issues around the globe per year. [3, 4] About 60 to 80 million couples are experiencing the infertility issue. It is observed to be highest in countries where the fertility rate is higher; "barrenness amid plenty" is a famous term coined by the specialists. In recent years, infertility and sperm disorders have impacted a huge number of couples. Almost 10% of couples in the USA fall under the infertile category based upon the inability to achieve a clinical pregnancy after one year of unprotected sexual intercourse. [5, 6]

Data revealed by the National Center for Health Statistics has shown that the absolute figures of impaired fecundity have risen from 4.56 million in 1982 to 7.26 million in 2002, which is about 2.7 million in females. This figure slightly fluctuated and fell to 6.71 million from 2006 to 2010. Moreover, in men with age below 30 years, the fertility rate has also decreased in them by 15% all around the globe. [7, 8]

Trends of Male Infertility in Pakistan

In Pakistan, the infertility rate is rising and becoming a common problem. It is affecting almost 21.9% of Pakistan's population with 3.5% primary and 18.5% secondary infertility. In many of the 30% cases, both partners are found to be infertile. While the male factor accounts for 20 to 25% of infertility in couples. [9]

Various factors like chromosomal and genetic disorders, smoking, drug abuse, mental stress, obesity, malnutrition, cryptorchidism, Sexually Transmitted Diseases (STDs), contraceptive procedures, accessory gland infections, accessory gland infection, germ cell malignancies, varicocele, a disorder of ejaculation, testicular cell calcification, endocrine disruption, and autoimmunity. [10]

Various mental and physical issues are linked with infertility which often leads to separation in couples. A recent analysis of data regarding the prevalence of etiological factors and spermatogenic abnormalities of infertility in men in Pakistan has shown conflicting results. But, somehow these results aided in figuring out the responsible causes of infertility and aided to move one step further towards its treatment. [11, 12]

Male Infertility: An Imperative Factor

Male infertility means failure to make his fertile female partner pregnant. In the tests and analysis of sperm, samples gathered 1 and 4 weeks apart, "male infertility" is observed as an alteration in sperm morphology, motility, or concentration. In humans, almost 40 to 50% of infertility is owing to these reasons and it affects almost 7% of all men. Deficiencies in the semen quality are the common reason behind male infertility, and this quality level is used as a surrogate measure level of male fecundity. [13]

WHO has presented values for normal sperm parameters and males with a sperm count less than those values have infertility factors. The most common and significant of these are abnormal sperm morphology (teratozoospermia), low sperm concentration (oligospermia), and poor sperm motility (asthenospermia). Some other factors also exist, that are less associated with infertility, those are semen volume and semen markers of prostatic, seminal vesicle function, and epididymal functions. Almost 90% of all the infertility cases are linked with the sperm count. Moreover, the issue of sperm morphology, motility, and the count is associated with an anomaly in control mechanisms like testicular, ore-testicular, and pos testicular functions.
Therefore, a semen analysis is considered as one of the most imperative and fundamental investigation methods which have 89.6% sensitivity and can detect 90% of the genuine male infertility cases. This test is quite simple which deals with sperm maturity and its interaction with the seminal fluid. This test elaborates aspects like sperm count and sperm quality.

Abnormalities of Sperm Count and Morphology

There are different sperm abnormalities which play a critical role in defining male infertility:

- **Abnormalities Linked with Sperm Count**

- Azoospermia: Absence of sperm in seminal plasma
- Low sperm count (oligozoospermia: <15 million sperms/mL)

- **Anomalies Linked with Sperm Motility**
  Rapid progressive motility is the key to the efficient passage of spermatozoa through cervical mucus. It means spermatozoa has a forward and rapid progression of at least 25 µm/s. Persistent poor motility of sperm shows the male infertility factors because normal semen must have at least 50% of grade A and B sperms. [15]
- **Abnormal Sperm Shape and Structure**
  WHO classification can be used to smear the morphology of sperms or the classification presented by Kruger's strict criteria. Morphology is not the single factor but falls along with other factors to collectively define male infertility.

Factors of Male Infertility

Multiple studies were conducted in different cities of Pakistan to gather some data about the male infertility ratio in the region as well as to know about the prevalent factors responsible for this infertility issue.

Based on this data the cumulative meta-analysis was carried out and the following factors were gathered along with the statistical variables and percentages of the current ratio in the country:

- **Varicocele**

Four different studies were carried out in 1205 patients. The studies revealed that out of these patients 82 had a varicocele. It was then concluded that varicocele might be the reason for infertility in 9.84% of infertile men. [16]

- **Abdominal or Inguinal Surgery/ Trauma**

Two different studies showed that trauma or abdominal/inguinal surgery also adds up to one of the causes of infertility in 12.06%, a total of 1055 men. A study in Islamabad was also conducted that showed that trauma was responsible for 10.8% of infertility, out of which 4.4% went through inguinal surgery. The study also showed that out of this percentage 5.1% had inguinal trauma and 3.49% went through abdominal surgery. [17]

- **Congenital testicular Disorder**

The cumulative analysis of the study of infertile male patients depicted that congenital testicular disorder was prevalent in 17.41%, and out of this percentage 12.68% had ectopic testis, 3.4% had undescended testis, 0.53% had retractile testis, and 1.06% had single testis. [17]

- **Infections**

3 different studies depicted that in 1105 patients the infection ratio was 23.08% prevalent. These infections include tuberculosis as 2.11%, urinary tract infection 26%, and mumps 9%. When it comes to the semen infection, then issues like Neisseria gonorrhea 2.3%, 0.59% Proteus spp., Providencia spp., and 1.3% E. coli in infertile men were found.

- **Genetic Mutations**

In different studies, under the genetic mutation subject, the Y chromosome microdeletion issue was prominently found. In Islamabad, a study was conducted on patients which revealed azoospermia factors deleted on the Y chromosome. Almost in 2% of subjects, AZF regions were deleted, and AZFb, AZFc were also found deleted in 1.925 of men. All these deletions were present in men with non-destructive azoospermia.

In another second study, no microdeletion Y chromosome factor was observed in 55 male patients. However, when the study was conducted in most populace provinces of Pakistan inc, using Punjab, Sindh, and KPK, it was found that 3% of men were with severe oligozoospermia and 5.5% had AZFc region deleted on the Y chromosome.

- **Iatrogenic effects**

Deep multiple evaluations of different studies have depicted that medicine was found in 26.8% of cases as one of the underlying causes of infertility in men. Moreover, 12.41% of cases were using herbal medicine and 10.7% were using allopathic medicine. 4.4% were using both medicines.

- **Immunological effects**

Another 2 different studies shown a shocking result. It was observed that 8.25% of infertile men had anti-sperm antibodies in their blood and 8.02% of infertile men had anti-sperm antibodies in their seminal plasma. Besides, almost 49% of infertile men were found with puss cells in their semen.

CONCLUSION:

Reproduction is important for the continuity of genome and genetic factors among species including humans. The desire to transfer this genome is so strong in humans that those who are unable to do so have poor social, psychological, and physical life. They become a victim of depression and this abruptly affects their married life as well. A few studies have shown the factors responsible for male infertility in men in Pakistan with variable results. But, these results also showed the reluctance of men's inappropriate treatment and even identification of the issues in the first place.

The main reasons found for infertility in men included infections, genetic mutations, congenital testicular disorder, varicocele, abdominal surgery/ trauma, iatrogenic effects, and immunological effects. Other reasons like diabetes, hernia, etc contributed collectively to less than 2% of infertility in men.

Oligoasthnospermia was observed in 7.99% of infertile men in Pakistan while 2.06% in Punjab [11,12,17,18]. Asthenoteratospermia was observed in 17.53%, oligoasthenoteratospermia in 11.69%, necrospermia in 1.32% and polyspermia in 1.91% [11,14,15].Varicocele: Four studies included 1204 infertile men, of which 81 had varicocele. Data showed that varicocele may be a cause of infertility in 9.74% (95% CI=4.33, 15.14) of infertile men [12,15,17,19].

Inguinal or abdominal surgery/Trauma: Two studies showed that inguinal or abdominal surgery/trauma was found responsible ofVaricocele: Four studies included 1204 infertile men, of which 81 had varicocele. Data showed that varicocele may be a cause of infertility in 9.74% (95% CI=4.33, 15.14) of infertile men [12,15,17,19].

Inguinal or abdominal surgery/Trauma: Two studies showed that inguinal or abdominal surgery/trauma was found responsible of According to data from three studies, di□erent infections were prevalent in 23.85% (95% CI=17.93, 29.78) of 1105 infertile men [15,17,19]. □ese infections included urinary tract infections (25.88%), mumps (8.96%) and tuberculosis (2.11%) [11,15,17,19]. Semen culture had infections, including 2.4% Neisseria
gonorrhea, 1.2% E. coli, 0.59% Proteus spp., and Providencia spp., each in infertile men [19]

Infertility is a common problem a□ecting about 21.9% of the Pakistani population with 3.5 primary and 18.5% secondary infertility. Both partners are found to be infertile in 30% of the cases, while male factor is responsible of infertility in 20 to 25% of the couples

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