



Review Article



Diagnostic Approaches and Causes of Male Infertility: A Comprehensive Clinical Review

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ABSTRACT

Male infertility accounts for approximately 30–50% of infertility cases worldwide and poses a significant reproductive health challenge. This review synthesizes current knowledge on the etiology of male infertility, emphasizing the pivotal role of diagnostic imaging, particularly ultrasonography, in identifying structural and functional abnormalities. Common causes include varicocele, testicular failure, genetic abnormalities such as chromosomal defects and Y-chromosome microdeletions, obstructive pathologies, and idiopathic factors. Ultrasound techniques, especially scrotal and transrectal ultrasonography, have become essential tools in detecting conditions often missed during routine examinations, thereby facilitating accurate diagnosis and targeted management. Despite advancements, standardization of imaging protocols and access remain limited in resource-constrained settings. An integrated diagnostic approach, combining semen analysis, hormonal profiling, genetic testing, and imaging, enhances diagnostic precision, reduces unexplained cases, and guides personalized treatment. Early identification of causative factors is crucial for optimizing reproductive outcomes.

INTRODUCTION

Infertility is one of the most triggering issues in the world that is affecting couples all over the world, about their overall health. At an average of 15%, most couples do not conceive after one year or later efforts. Male infertility, as defined by the World Health Organization (WHO), is a man's inability to conceive a child by means of a fertile woman, following unprotected and inconsistent sexual activity for at least one year. Around 20% cases of male infertility contribute to another 30 – 40% independently, combined with female factors. Country-Specific / Regional Data: About 25–30% of couples who seek fertility treatment are affected by Male factor infertility, with varicocele being

especially prevalent at rates up to 40% [1]. Infection-related obstructive pathologies and causes are more common, especially in sub-Saharan Africa, which is impacting up to 15–20% infertile men regarding the prevalence [2]. Higher rates of genetic abnormalities, in Middle Eastern populations, with Y-chromosome microdeletions are shown to be higher in research, with an average of 10–12% of severe oligozoospermia cases [3]. Male infertility may result in physical problems with reproductive organs, genetic disorders, hormonal imbalances, or sperm production or movement issues [4]. The general initial evaluation in this case mostly consists of



blood hormone tests, semen analysis, and physical examination of the affected individual. Whereas helpful information is provided by means of these tests, in many cases, the information regarding deeper problems is missed in such cases and may not be noticeable without specific medical imaging techniques or diagnosis [5].

Despite significant advances in understanding male infertility, major research gaps remain, particularly in low-resource settings. Standardized imaging protocols for scrotal and transrectal ultrasonography are lacking, leading to variability in diagnostic accuracy and underdiagnosis of structural or obstructive abnormalities. Idiopathic infertility continues to account for a large proportion of cases, highlighting limitations in current genetic, imaging, and functional sperm assessments. Additionally, access to advanced diagnostic tools such as MRI, AI-assisted imaging, and comprehensive genetic testing is limited, restricting personalized treatment strategies. Addressing these gaps is essential to improve early detection, reduce unexplained infertility, and optimize reproductive outcomes globally.

Male Infertility Etiology

Among the most prevalent causes of male infertility, varicocele is considered to be a more treatable and common cause, which is characterised by enlargement of veins in the scrotum [6]. Some varicoceles can be felt during physical examination, but many subclinical varicoceles are too small to detect without ultrasound and can still harm sperm production [7]. Men with high-grade varicoceles were significantly weaker with their semen quality, presenting 45% severe azoospermia or oligozoospermia, as shown in Nigerian research [8]. It was observed in studies that surgical correction supported several men recovering sperm parameters by gaining natural pregnancy as a result of their marital intercourse [9, 10], yet normal sperm parameters are still maintained by some men with varicocele [11]. When the testicles do not function properly, testicular failure happens, and it is because of genetic mutations, hormone problems, or developmental issues in the male reproductive system. Testicular texture, blood flow, and size can be assessed by the ultrasound, which can provide signs pertaining to conditions like Leydig cell damage or Sertoli cell-only syndrome [12]. One can identify hormone imbalances like elevated prolactin through blood tests or low testosterone, and they can mostly be correlated with abnormalities of the ultrasound [13]. Obstructive pathologies in the epididymis, the ejaculatory ducts, or the vas deferens do not allow sperm release and cannot be detected by semen analysis alone. These problems can be identified by Transrectal ultrasound (TRUS), which is specifically beneficial to

diagnose obstructive azoospermia [14]. Important diagnostic information can be provided by testicular size. Decreased sperm production is indicated by reduced testicular volume generally. According to research, low sperm count shows correlation with smaller testicles, mostly by depicting hormonal abnormalities such as elevated LH or FSH [15]. Research conducted on 1,000 infertile men revealed the outcome of abnormalities through ultrasound, in the seminal vesicles and prostate, among almost 30–35% cases [16]. So, scrotal ultrasonography is considered a safer and more effective tool. The testicular abnormalities like microlithiasis, varicocele, epididymal cysts, and undescended testicles can be tested through it. One cannot directly feel during a regular examination. According to a study, during physical examination, 58% of such abnormalities were not found during the test, but those were examined clearly by means of ultrasound [17]. In a significant number of cases, men may still be infertile, even with normal semen tests. It depends upon undiagnosed conditions such as previous mumps infection, testicular injury, or congenital abnormalities during the examination. These hidden problems can be identified in genetic and ultrasound testing [18]. Sperm DNA may be damaged, even in subclinical cases, because of oxidative pressure, which raises testicular temperature, exacerbated by varicocele [19].

Diagnostic Strategies in Male Infertility

Investigations – Structured Order: A systematic hierarchy is followed in a comprehensive diagnostic approach. In the first-line investigations, factors that need to be included like detailed sexual and medical history, semen analysis, followed by physical examination. While, incorporates hormonal profiling is incorporated in the second-line testing (LH, FSH, testosterone, and prolactin), post-ejaculatory urinalysis, followed by scrotal ultrasonography with Doppler also required. For surgical and advanced investigations, testicular biopsy for azoospermia, genetic testing (karyotyping, Y-chromosome microdeletion analysis), and vasography for suspected obstruction are needed [20]. Diverse causes and diagnostic approaches are required in male infertility measurement. In about 30–50% infertility cases, male factors are responsible, mostly, with etiologies following endocrine disorders, genetic syndromes, anatomical abnormalities, and infections [21]. Cryptorchidism is a major risk factor that affects 1–4% of newborn males. It is because of abnormal maturation and germ cell loss at the earlier stage. It leads to higher testicular cancer risk and future infertility [22]. One of the most frequent chromosomal abnormalities linked with male infertility is Klinefelter syndrome (47, XXY, which

causes testicular failure, reduced azoospermia, and testosterone production [23]. Prolactinoma lowers testosterone levels and disrupts sperm production; it interferes with the hypothalamic-pituitary-gonadal axis [21]. With the reduction of hypogonadism symptoms through testosterone treatment, it also reduces fertility and suppresses gonadotropins. A viral infection, known as mumps orchitis, may cause persistent azoospermia due to irreversible testicular damage [24].

Expanded Discussion About MRI

A crucial role is played by imaging techniques in diagnosis. Pertaining to this, for the detection of obstructive factors and anatomical features, TRUS and ultrasound are first-line modalities, where MRI becomes the first priority when ultrasound findings become unclear or inconclusive. In this case, superior soft tissue characterization is provided by MRI and becomes particularly significant to assess undescended testes and evaluate complex obstructions, by mapping anatomy and finding out subtle tumors before reconstructive surgery [25]. Concerning such benefits, the limited availability of MRI and its higher cost in low-resource settings do not fully allow its routine use. Limitations of Biopsy Techniques: To differentiate obstructive from non-obstructive azoospermia Testicular and to guide about assisted reproductive interventions, biopsy becomes necessary test. In this way, two major practices are common: needle biopsy and open surgical biopsy. Larger tissue samples are provided by open biopsy, with means of lower risk of sampling error and better and precise histological assessment. For this, hiring costs with operating room facilities are required. Needle biopsy (Tru-cut or fine needle aspiration) under local anaesthesia can be performed as an office procedure, giving lower cost and greater convenience. Although there are risks in needle biopsy with infection, potential sampling error due to smaller tissue volumes hematoma formation [26]. All about the process is dependent on local expertise, clinical indication, along complete planning of simultaneous sperm retrieval for ICSI [27].

Vaso Graphical Role in Surgical Management

Technical Details: Water-soluble radiopaque contrast media is employed by Vasography employs, such as iohexol or iopamidol, which may be directly injected into the vas deferens. Normally, plain radiography or fluoroscopy is used as an imaging technique for visualizing the seminal vesicles, vas deferens, and ejaculatory ducts. In such a technique, puncture with a fine needle, surgical exposure of the vas deferens, or intraoperative protocol is utilized (characteristically 27-30 gauge), under fluoroscopic guidance, generally, slow injection of 1-3 ml contrast is injected, and immediate assessment of obstruction and

patency sites is conducted [28]. To manage male infertility, vasography becomes a significant therapeutic and diagnostic tool, especially in obstreperous azoospermia cases. In such cases, localized obstruction sites and vas deferens patency are assessed primarily, which is considered to be extremely important to plan for proceeding surgical procedures like vasoepididymostomy or vasovasostomy. These microsurgical techniques are mostly used in vasography, which is often performed alongside, where immediate correction of enabling enhancing fertility restoration and identifying obstructions and likelihood is performed [28]. The benefits of combining surgical treatment with vasography have been highlighted by recent advancements in andrology clinics, particularly in settings with constrained medical facilities. With such techniques, patients' enhanced outcomes are achieved compared with those formerly deprived of adequate access to specialized care [29]. Even, rather its great significance, vasography has declined because of less invasive imaging modalities as a self-contained diagnostic system like MRI and transrectal ultrasound, where preoperative evaluation is mostly offered [30]. When direct visualization of vasal anatomy is required or non-invasive imaging is inconclusive, during surgery there vasography remains indicated. Vasography, rather than an outpatient procedure to minimize complications, is generally recommended intraoperatively, with the recommendation of immediate surgical intervention when needed. Vasography becomes very important for obstructive male infertility treatment when incorporated into comprehensive treatment plans, coupled with microsurgical advancements [31].

Associating Diagnostics with Treatment

Therapeutic strategies are directly guided by diagnostic findings. With abnormal semen parameters, ultrasound-detected varicocele of grade 2 or 3, by which varicolectomy is indicated, and natural conception is improved in 40-60% of cases [28]. Biopsy results confirm an obstruction that shows normal spermatogenesis in azoospermic men. Also, it guides about sperm retrieval techniques for ICSI, where fertilization rates of 50-70% are achieved in the process [32]. The influence of the choice between vasoepididymostomy (for epididymal obstruction) and vasovasostomy (for vas obstruction) is calculated by vasography findings of complete obstruction, with patency rates of 85% and 65% respectively [33]. The treatment selection is optimized by this integrated approach, and reproductive outcomes are improved to a great extent [34]. To identify underlying causes of male infertility, the importance of clinical imaging is emphasized by this review, specifically in

ultrasound imaging. The routine integration into fertility assessments helps improve patients' outcomes by addressing diagnostic gaps in male reproductive health.

Pathologic Conditions for Male Infertility

Among the main pathologic conditions responsible for male infertility, the main contributing factors are idiopathic infertility (35.6%) and testicular disorders (38%), that encountered most frequently, closely followed by cases of varicocele (Grade 2/3), which affects 35.5% of infertile men approximately [34]. According to some research, around 10% of cases account for Cryptorchidism [35], whereas there are major genetic causes related to Y-chromosome microdeletions and chromosomal abnormalities (such as Klinefelter syndrome), with a percentage of 3.2% and 10-15% cases, accordingly [36, 37]. This study shows consolidated percentage and frequency of the data, referring to the most prevalent pathological conditions that are linked with male infertility, as reflected by means of the studies conducted between the years 2000-2025 (Table 1).

Table 1: Main Pathologic Conditions Responsible for Male Infertility

Pathologic Condition	Frequency (%)
Idiopathic (Unexplained) Infertility	356 (35.60%)
Testicular Disorders	380 (38%)
Cryptorchidism (Undescended Testes)	100 (10%)
Varicocele (Grade 2/3)	355 (35.50%)
Chromosomal Abnormalities	100 (10%)
Y Chromosome Microdeletions	32 (3.20%)
Leydig Cell Insufficiency	25-50 (2-5%)
Hydrocele (via ultrasound)	~60 (~6%)
Epididymal Cysts (via ultrasound)	~90 (~9%)
Testicular Atrophy (via ultrasound)	~120 (~12%)

It was found that Leydig cells contribute to hypogonadism insufficiency, giving poor spermatogenesis, with an average of 2-5% of cases similarly [38]. Of these characteristics, acquired factors like trauma, endocrine tumors, and infections result differently among many individuals [39]. Transrectal and scrotal ultrasonography have been considered non-invasive and essential diagnostic techniques, which significantly enhance the abnormalities like: testicular atrophy, hydrocele, and epididymal cysts, and these techniques are not only apparent through clinical examination but also being practiced in ultrasonic diagnosis [40]. Both obstructive and non-obstructive causes are identified by ultrasound, which provides vascular flow analysis by means of techniques like Doppler ultrasound, which is especially significant in azoospermia assessments [41]. Sonography remains underutilized, and instead of clinical utility, wider adoption of standardized imaging protocols is

recommended by experts in infertility evaluations [39]. Scrotal Causes of Male Infertility: mechanism/pathology and clinical impact on fertility are very important (Table 2).

Table 2: Scrotal Causes of Male Infertility

Scrotal Cause	Mechanism/Pathology	Clinical Impact on Fertility
Varicocele	Dilated pampiniform plexus veins, increased scrotal temperature, oxidative stress	Most common; impairs spermatogenesis, reduces sperm count/motility.
Hydrocele	Fluid accumulation around the testis, possible local temperature elevation	May impair spermatogenesis
Epididymal-orchitis	Inflammation/infection of the epididymis/testis	Obstructs sperm transport, damages tissue
Epididymal cysts	Cystic lesions in the epididymis	May obstruct sperm passage
Trauma	Physical injury to the scrotum/testes	Disrupts testicular function
Cryptorchidism	Undescended testis, abnormal scrotal development	Reduces testicular volume, impairs spermatogenesis
Testicular microlithiasis	Microcalcifications in testicular tissue	Associated with abnormal sperm parameters
Scrotal AVM	Abnormal arteriovenous connections, local hyperthermia, or pressure effects	Can cause oligospermia /infertility
Chronic scrotal hyperthermia	Prolonged elevation of scrotal temperature	Causes oxidative stress, spermatogenic arrest
Scrotal wall pathology	Abnormalities in scrotal wall layers	Mechanical/inflammatory effects, hyperthermia

Table II shows different scrotal problems that can yield male infertility. It shows that amongst various causes of male infertility, varicocele is the most prevalent, which causes oxidative stress in testicles, raises temperature, and affects sperm production [40]. There are also many other issues, including epididymo-orchitis, hydrocele, injuries, cryptorchidism, and cysts, which can block sperm movement by damaging the sperm-making environment, and this leads to weak fertility among couples [33]. In this way, important but less common causes are scrotal arteriovenous malformations, testicular microlithiasis, and chronic scrotal hyperthermia. These factors combine, and the quality and number of sperm are reduced in fertile couples. Also, fertility can be affected by scrotal wall problems when local conditions, through inflammation and pressure, are changed. Concerning these issues, proper treatment by early detection is very important; often, using scrotal ultrasound helps cure male infertility by improving their health [1, 28]. Sonographic findings and clinical significance were analyzed (Table 3).

Table 3: Sonographic Patterns in Male Infertility

Sonographic Finding	Cause of Infertility	Clinical Significance
Varicocele (Dilated Pampiniform Plexus)	Varicocele	The most common ultrasound finding associated with poor sperm production
Reduced Testicular Volume	Non-obstructive azoospermia, testicular failure	Indicates sperm production failure; helps rule out obstructive causes
Heterogeneous Testicular Echotexture	Atrophy, chronic orchitis, trauma	Suggests old damage or inflammation affecting fertility
Epididymal Enlargement	Epididymitis, obstructive azoospermia	Indicates inflammation or blockage of the sperm passage
Testicular/ Epididymal Cysts	Obstruction, post-infection changes	May block sperm transport if large; sometimes incidental
Dilated Rete Testis/ Epididymal Tubules	Obstructive azoospermia	Strongly suggests blockage at the epididymal or duct level
Dilated Vas Deferens	Obstructive azoospermia	Shows distal blockage, like an ejaculatory duct cyst or absence
Hydrocele	Hydrocele	May impair fertility by raising local temperature
Reduced Testicular Vascularity (Doppler)	Testicular failure	Points to severe damage or primary testicular failure
Inflammatory Changes (Orchitis/Epididymitis)	Orchitis, epididymitis	Suggests acute inflammation that can damage sperm production

The study presents sonographic patterns in male infertility. It depicts that by identifying both obstructive and non-obstructive causes, sonographic evaluation plays a significant role in the assessment of male infertility [41]. Regarding this, the table portrays many vital characteristics like reduced testicular volume, indicating atrophy, varicocele, testicular echotexture suggestive of chronic damage, and heterogeneous [33]. Research findings indicate obstruction through epididymal enlargement, dilated rete testis, and dilated vas deferens, causing male infertility. Furthermore, testicular blood flow assessment is carried out by using Doppler ultrasound, which helps differentiate between primary testicular failure and obstructive conditions affecting male fertility [32]. Moreover, diagnostic precision is enhanced using hydrocele additional detection, cysts, signs of acute inflammation, and guides management [23, 42]. Diagnostic accuracy is enhanced meaningfully by integrating these sonographic patterns into clinical evaluation, and better targeted treatment is enabled. The findings discuss the prevalence of the main causes of male infertility. It reports Idiopathic infertility to be the most frequently occurring category, which is reflected in certain subgroups up to 75% cases, particularly its range observed among men with oligozoospermia, and hence, current

diagnostic approaches show major gaps in likewise cases [43]. Varicocele is the most potentially correctable and common identifiable cause in this sense [44]. Other factors are also very important, along with primary testicular failure and genetic defects, which contribute to male infertility the most [40]. Although among the less common causes are endocrine and obstructive causes, due to the potential for effective interventions, they remain clinically significant [33]. There is also the role of infections and sexual dysfunction, particularly in specific populations [45]. The environmental influences and lifestyle are a severe concern for male infertility. Although due to overlapping risk factors, the exact prevalence remains unclear. The multifactorial origin of male infertility is emphasized by these findings, and personalized treatment planning and thorough evaluation are highlighted by means of all such factors about male infertility [36]. The Findings are shown (Table 4).

Table 4: Prevalence of Major Causes of Male Infertility

Cause of Male Infertility	Prevalence Among Infertile Men (%)	Notes/Comments
Idiopathic (Unknown cause)	30-75	Most common; up to 75% in oligozoospermia cases remain unexplained
Varicocele	15-40	Most frequent identifiable cause; higher in secondary infertility
Genetic causes (chromosomal, Y deletion)	10-15	Includes Klinefelter syndrome, Y-chromosome microdeletions
Testicular failure (primary)	10-20	Includes Sertoli cell-only syndrome, maturation arrest
Obstructive azoospermia	7-13	Includes congenital bilateral absence of vas deferens, post-infectious causes
Endocrine disorders	1-2	Hypogonadotropic hypogonadism, pituitary/hypothalamic dysfunction
Sexual dysfunction	8-17	Erectile/ejaculatory disorders; higher in some populations
Infections (orchitis, epididymitis)	5-15	Can cause temporary or permanent infertility
Congenital anomalies	2-5	Cryptorchidism, hypospadias, other urogenital malformations
Lifestyle/ environmental factors	Variable	Smoking, obesity, toxins, heat, and medications often overlap with other causes.

Table V above shows clinical utility & diagnostic value in key male infertility tests. A comprehensive diagnostic strategy, consisting of sperm function tests such as DNA fragmentation assessment, semen analysis, and advanced imaging techniques, enhances the diagnostic ability of fundamental causes of male infertility. With this proportion of unexplained (idiopathic) cases is reduced to a great extent [41]. Moreover, valuable information about DNA fragmentation testing on sperm quality is depicted in the

table, which can be missed by conventional semen analysis, while a central role is played in detecting vascular and structural abnormalities through ultrasonography. It shows the importance of genetic testing, particularly among those patients who severely face azoospermia or sperm abnormalities, by supporting the uncovering of Y-chromosome microdeletions or chromosomal defects, particularly those not evident in such cases [22]. A patient-specific infertility management strategy is developed by incorporating these diagnostic tools, which enhances clinical outcomes [40] (Table 5).

Table 5: Clinical Utility and Diagnostic Value, in Key Male Infertility Tests

Diagnostic Test/Approach	Diagnostic Value & Clinical Utility	Sensitivity/Specificity
Semen analysis	Cornerstone for initial assessment; identifies oligozoospermia, asthenozoospermia, teratozoospermia, and azoospermia	Moderate sensitivity/specificity
Sperm DNA fragmentation (sDF)	Higher accuracy than conventional semen analysis for detecting sperm dysfunction; predicts FSH therapy response	Sensitivity 79%, specificity 86%
Oxidation-Reduction Potential (ORP)	Novel marker for oxidative stress; correlates with poor sperm parameters; aids in diagnosis and management	Sensitivity 69-81%, specificity 66-83%
Genetic testing (karyotype, Y del.)	Essential for severe oligo/azoospermia; guides prognosis, treatment, and genetic counseling	High for known mutations
Comprehensive andrological assessment	Reduces idiopathic cases, enables targeted therapy, and increases natural pregnancy rates	Reduces the idiopathic rate to 8%
Seminal plasma biomarkers	Emerging non-invasive markers: potential to improve diagnosis beyond standard semen analysis	Under investigation
Imaging (scrotal US, Doppler)	Detects varicocele, obstruction, and testicular atrophy; refines diagnosis and guides management	High for structural causes

The study depicts selected studies on sonographic techniques used in the evaluation of male infertility. The above selected studies are fully pertinent to identify functional and primary structural causes of male infertility using sonographic techniques, including TRUS, grey-scale ultrasound, and elastography. Key infertility factors are highlighted through these studies, consisting of testicular atrophy, varicocele, microlithiasis, obstructive azoospermia, and epididymal cysts, by highlighting major prevalence-related pathologies reported in different studies. The inclusion of these studies is justified because clear evidence is provided about the value of diagnostic imaging in detecting both obstructive and non-obstructive causes, helping reduce idiopathic cases. Research conducted on parenchymal inhomogeneity, testicular echotexture, and elastography showed a correlation between spermatogenic findings with sonographic function; while, need for population-specific reference values is emphasized by regional studies, specifically, in low-resource settings as Pakistan (Table 6).

Table 6: Selected Studies on Sonographic Techniques used in Evaluation of Male Infertility

Sr. No.	Study Title	Study Type	Sample Size/ Design	Ultrasound Technique	Infertility Focus	Key Findings	Gaps/Future Direction
1	Colour Doppler Ultrasonography as a Routine Exam	Clinical Study	Not Reported	Colour Doppler US	Varicocele, Obstruction	Improved detection of vascular issues	Needs protocol standardization
2	Sonographic Spectrum of Scrotal Abnormalities	Imaging Review	Narrative	Grey-Scale US	Hydrocele, Varicocele, Epididymal Cysts	Detected lesions missed in the physical exam	Require training and structured reporting
3	Imaging in Male-Factor Obstructive Infertility	Focused Clinical Review	Clinical Cases	TRUS, Scrotal US	Obstructive Azoospermia	Algorithms for imaging of obstruction are defined	Prospective validation lacking
4	Testicular Ultrasound Inhomogeneity	Observational Study	Not Provided	Grey-Scale US	Testicular Function, Spermatogenesis	Inhomogeneity correlates with reduced sperm quality	Requires large-scale validation
5	Ultrasound Evaluation of Varicoceles	Systematic Review	40+ Studies	Doppler US	Varicocele Grading	Standard grading criteria established	Implement in low-resource clinics
6	Sonography as an Underutilized Diagnostic Tool	Prospective Clinic Study	60 men	TRUS, Scrotal US	Obstructive vs Non-Obstructive Azoospermia	Specific resistive index and volume cut-offs defined	Promote in routine evaluations
7	Role of the US in Male Infertility Detection	Review	Clinical Synthesis	Scrotal US, TRUS	Broad Male Infertility Causes	Diagnostic thresholds clarified for the US	Clinician curricula development is recommended
8	Role of Testicular Elastography	Comparative Study	42 patients	Elastography	Spermatogenic Health	Stiffness reflects functional sperm production	Regional baseline values required

9	Advanced Sonographic Techniques	Review	Narrative	TRUS, Elastography	Idiopathic Infertility	Discussed advanced methods (elastography, microvascular imaging)	Validation in South Asia is needed
10	Varicocele & Semen Quality Study	Prospective Study	~150 men	Doppler US	Varicocele	Blood flow associated with semen parameters	Follow-up studies needed
11	Genetic Causes + US Features	Retrospective Cohort	~200 men	TRUS, Scrotal US	Genetic Infertility	Imaging models developed to predict genetic defects	Integration into genetic workups is required
12	Prospective Sonographic Evaluation	Prospective Study	120 men	Scrotal US, TRUS	Mixed Infertility Causes	Comprehensive imaging increased diagnostic accuracy	Adaptation in local clinical protocols
13	West African Scrotal Abnormalities	Observational	80 subfertile/ 40 fertile	Scrotal US	Regional Male Infertility Patterns	Higher varicocele rates in subfertile men	Regional imaging databases needed
14	Central Role of the US in Function/ Obstruction	Retrospective Cohort	320 men	TRUS, Scrotal US	Ductal Obstruction, Testicular Function	Imaging features correlated with hormonal profiles	Link imaging with lab and endocrine results
15	Super Resolution Ultrasound Microscopy	Experimental Study	Lab Based	Super-Resolution US	Microvascular Evaluation	Visualized tiny testicular blood vessels (early stage)	Clinical trials pending

Overall, clinical understanding of infertility causes is developed through these studies, which supports and strengthens the incorporation of imaging technology with hormonal assessment and genetic evaluation to diagnose precisely and personalize treatment.

DISCUSSION

Almost half of the infertility cases are prone to the margin line. The natural conception rates are significantly maintained by early ultrasound detection of varicocele. Observed through different studies, Abnormal semen parameters and varicocelectomy in men with Grade 2/3 varicocele result in 40–60% pregnancy rates that naturally occur within post-surgery along 12–18 months post-surgery [35]. Similarly, appropriate surgical intervention is enabled by ultrasound-guided diagnosis of obstructive azoospermia with vasovasostomy, achieving pregnancy rates of 40–50% and patency rates of 85% [2]. Assisted reproduction, including imaging, improves ICSI outcomes, identifying specific causes through comprehensive evaluation, following fertilization rates reach almost 65–75% when biopsy confirms normal spermatogenesis [3]. In the most common diagnosis, Idiopathic infertility is observed in up to 75% of certain populations, specifically among men who are detected with oligozoospermia, and diagnostic gaps are identified [44]. In the leading specific cause, the testicular disorders are common, where 38% of infertile men are affected seriously, with varicocele and in a treatable condition, being the most frequent occurring in 35–40% cases. Sperm production is impaired by Varicocele with the increase in oxidative stress and scrotal temperature. Other important causes include cryptorchidism (10%), Leydig cell dysfunction (4%), and testicular atrophy (12%) [44]. Chromosomal defects and Y-chromosome microdeletions reported as genetic abnormalities contribute to 10–15% cases, where the need for genetic testing is stressed in severe azoospermia or oligospermia cases. Obstructive causes, though less common (7–13%), are clinically relevant due to the potential

for assisted reproductive or surgical treatment [40]. Infections, congenital anomalies, and hormonal imbalances also give prevalence in many cases. In beneficial diagnostic approaches, Doppler imaging and Scrotal ultrasound are essential non-invasive tools to detect varicocele, hydrocele, testicular atrophy, and epididymal cysts, which may not be found while doing the examination. These modalities help identify obstructive azoospermia and assess testicular damage or vascular flow abnormalities [42]. However, challenges remain, including operator dependency, interpretation variability, and lack of standardized imaging criteria.

As per research, in developing countries as Pakistan, there are many limitations, including trained personnel and restricted access to technology that hinder diagnosis further [13]. By identifying chromosomal abnormalities in unexplained infertility, genetic analysis complements imaging techniques to probe into the prevalence among infertile men. Combining semen analysis, advanced sperm tests, imaging, and genetic evaluation reduces idiopathic cases and guides personalized treatment. Overall, male infertility is multifactorial. A thorough diagnostic approach enhances detection of causes, minimizes unexplained cases, and supports individualized management strategies [45]. Future recommendations should prioritize the development and implementation of standardized imaging protocols for scrotal and transrectal ultrasonography to ensure consistent diagnostic accuracy across diverse clinical settings. Increased accessibility to advanced diagnostic tools, such as genetic sequencing and AI-assisted imaging, is essential, particularly in resource-limited regions. Furthermore, integrating

multimodal diagnostics combining imaging, genetic testing, and sperm function analysis—into routine clinical practice can reduce idiopathic cases and support personalized treatment strategies. Finally, fostering interdisciplinary collaboration and specialized training for healthcare providers will enhance the comprehensive evaluation and management of male infertility.

CONCLUSION

The emerging technologies are prospectively promised to revolutionize management and diagnose male infertility cases across the globe. Detection accuracy can be improved by using artificial intelligence-assisted imaging analysis, and operator dependency can be reduced in ultrasound interpretation. Advanced genetic sequencing technologies, including whole-exome sequencing and next-generation sequencing panels are being utilized. It will explore currently disruptive causes of novel genetic issues to male infertility as idiopathic. Standardized diagnostic protocols are urgently needed for the improvement of consistency, particularly for imaging techniques, and accessibility of care across the globe, particularly in contexts with limited resources for health improvement.

Authors' Contribution

Conceptualization: MIUH

Methodology: MIUH, MM

Formal analysis: MIUH

Writing and Drafting: MIUH, SMYF, MM

Review and Editing: MIUH, MM, SMYF

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

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REFERENCES

- [1] Bakhtawar K and Arshad N. Role of Ultrasonography in Detection of Male Infertility: Ultrasonography in Detection of Male Infertility. *Pakistan BioMedical Journal*. 2023 May; 6(5). doi: 10.54393/pbmj.v6i05.870.
- [2] Muteshi C and Chesire A. Approach to Evaluation and Management of Male Infertility in Sub-Saharan Africa. *International Journal of Gynecology and Obstetrics*. 2025 Jun; 169(3): 913-20. doi: 10.1002/ijgo.16196.
- [3] Duvuru R, Halabi M, Omolaoye TS, Du Plessis SS. The Genetic Causes of Male Infertility: A Middle East and North Africa Perspective. *F1000Research*. 2022 Jun; 11: 125. doi: 10.12688/f1000research.106950.2.
- [4] Jarow JP, Sharlip ID, Belker AM, Lipshultz LI, Sigman M, Thomas AJ et al. Best Practice Policies for Male Infertility. *The Journal of Urology*. 2002 May; 167(5): 2138-44. doi: 10.1016/S0022-5347(05)65109-9.
- [5] Koziół-Kozakowska A, Januś D, Stępniewska A, Szczudlik E, Stochel-Gaudyn A, Wójcik M. Beyond the Metabolic Syndrome: Non-Obvious Complications of Obesity in Children. *Children*. 2023 Dec; 10(12): 1905. doi: 10.3390/children10121905.
- [6] Sakamoto H, Saito K, Shichizyo T, Ishikawa K, Igarashi A, Yoshida H. Color Doppler Ultrasonography as A Routine Clinical Examination in Male Infertility. *International Journal of Urology*. 2006 Aug; 13(8): 1073-8. doi: 10.1111/j.1442-2042.2006.01499.x.
- [7] Qublan HS, Al-Okoor K, Al-Ghoweri AS, Abu-Qamar A. Sonographic Spectrum of Scrotal Abnormalities in Infertile Men. *Journal of Clinical Ultrasound*. 2007 Oct; 35(8): 437-41. doi: 10.1002/jcu.20326.
- [8] Ogunjimi MA, Abudu OA, Jeje EA, Ojewola RW, Arogundade RA. A Prospective Study of the Association Between Varicoceles and Semen Quality in Men with Infertility. *African Journal of Urology*. 2024 Sep; 30(1): 50. doi: 10.1186/s12301-024-00452-z.
- [9] Majzoub A, Viana MC, Achermann AP, Ferreira IT, Laursen RJ, Humaidan P et al. Non-Obstructive Azoospermia and Intracytoplasmic Sperm Injection: Unveiling the Chances of Success and Possible Consequences for Offspring. *Journal of Clinical Medicine*. 2024 Aug; 13(16): 4939. doi: 10.3390/jcm13164939.
- [10] Munoz-Lopez C, Wong A, Lewis K, Bole R, Vij SC, Lundy SD. The Evolving Landscape of Male Varicocele Pathophysiology in the Era of Multi-Omics: A Narrative Review of the Current Literature. *Biology*. 2024 Jan; 13(2): 80. doi: 10.3390/biology13020080.
- [11] Minhas S, Bettocchi C, Boeri L, Capogrosso P, Carvalho J, Cilesiz NC et al. European Association of Urology Guidelines on Male Sexual and Reproductive Health: 2021 Update on Male Infertility. *European Urology*. 2021 Nov; 80(5): 603-20. doi: 10.1016/j.euro.2021.08.014.
- [12] Sudhakar DV, Shah R, Gajbhiye RK. Genetics of Male Infertility—Present and Future: A Narrative Review. *Journal of Human Reproductive Sciences*. 2021 Jul; 14(3): 217-27. doi: 10.4103/jhrs.jhrs_115_21.
- [13] Del Giudice F, Kasman AM, De Berardinis E, Busetto GM, Belladelli F, Eisenberg ML. Association Between Male Infertility and Male-Specific Malignancies: Systematic Review and Meta-Analysis of Population-Based Retrospective Cohort Studies. *Fertility and*

- Sterility. 2020 Nov; 114(5): 984-96. doi: 10.1016/j.fertnstert.2020.04.042.
- [14] Donkol RH. Imaging in Male-Factor Obstructive Infertility. *World Journal of Radiology*. 2010 May; 2(5): 172. doi: 10.4329/wjr.v2.i5.172.
- [15] Boeri L, Capogrosso P, Ventimiglia E, Cazzaniga W, Pozzi E, Belladelli F et al. Testicular Volume in Infertile Versus Fertile White-European Men: A Case-Control Investigation in the Real-Life Setting. *Asian Journal of Andrology*. 2021 Sep; 23(5): 501-9. doi: 10.4103/aja.aja_93_20.
- [16] Lam IS, Trost LW, Casalino DD, Brannigan RE. Ultrasound in Male Infertility. In *Ultrasound Imaging in Reproductive Medicine: Advances in Infertility Work-up, Treatment and ART*. Cham: Springer International Publishing. 2019 Jul: 213-235. doi: 10.1007/978-3-030-16699-1_13.
- [17] Sihag P, Tandon A, Pal R, Bhatt S, Sinha A, Sumbul M. Sonography in Male Infertility: A Useful Yet Underutilized Diagnostic Tool. *Journal of Ultrasound*. 2022 Sep; 25(3): 675-85. doi: 10.1007/s40477-021-00646-z.
- [18] Agarwal A, Mulgund A, Hamada A, Chyatte MR. A Unique View on Male Infertility Around the Globe. *Reproductive Biology and Endocrinology*. 2015 Apr; 13(1): 37. doi: 10.1186/s12958-015-0032-1.
- [19] Shiraishi K, Takihara H, Matsuyama H. Elevated Scrotal Temperature, But Not Varicocele Grade, Reflects Testicular Oxidative Stress-Mediated Apoptosis. *World Journal of Urology*. 2010 Jun; 28(3): 359-64. doi: 10.1007/s00345-009-0462-5.
- [20] Esteves SC, Miyaoka R, Agarwal A. An Update on the Clinical Assessment of the Infertile Male. *Clinics*. 2011 Jan; 66(4): 691-700. doi: 10.1590/S1807-59322011000400026.
- [21] Pathak UI, Gabrielsen JS, Lipshultz LI. Cutting-Edge Evaluation of Male Infertility. *Urologic Clinics*. 2020 May; 47(2): 129-38. doi: 10.1016/j.ucl.2019.12.001.
- [22] Kolettis PN. Evaluation of the Subfertile Man. *American Family Physician*. 2003 May; 67(10): 2165-72.
- [23] Khatun A, Rahman MS, Pang MG. Clinical Assessment of Male Fertility. *Obstetrics and Gynaecology Science*. 2018 Mar; 61(2): 179. doi: 10.5468/ogs.2018.61.2.179.
- [24] İbiş MA and Yaman Ö. Evaluation of Male Infertility. *Duzce Medical Journal*. 2022 May; 24(Special Issue): 1-6. doi: 10.18678/dtfd.1181407,
- [25] Lotti F, Studniarek M, Balasa C, Belfield J, De Visschere P, Freeman S et al. The Role of the Radiologist in the Evaluation of Male Infertility: Recommendations of the European Society of Urogenital Radiology-Scrotal and Penile Imaging Working Group (ESUR-SPIWG) for scrotal imaging. *European Radiology*. 2025 Feb; 35(2): 752-66. doi: 10.1007/s00330-024-10964-5.
- [26] Punjani N, Kang C, Lamb DJ, Schlegel PN. Current Updates and Future Perspectives in the Evaluation of Azoospermia: A Systematic Review. *Arab Journal of Urology*. 2021 Jul 3; 19(3): 206-14. doi: 10.1080/2090598X.2021.1954415.
- [27] Woodward PJ, Schwab CM, Sesterhenn IA. From the Archives of the AFIP: Extratesticular Scrotal Masses: Radiologic-Pathologic Correlation. *Radiographics*. 2003 Jan; 23(1): 215-40. doi: 10.1148/rg.231025133.
- [28] Garolla A, Grande G, Palego P, Canossa A, Caretta N, Di Nisio A et al. Central Role of Ultrasound in the Evaluation of Testicular Function and Genital Tract Obstruction in Infertile Males. *Andrology*. 2021 Sep; 9(5): 1490-8. doi: 10.1111/andr.13060.
- [29] Lotti F, Bertolotto M, Maggi M. Historical Trends for the Standards in Scrotal Ultrasonography: What Was, What Is, and What Will Be Normal. *Andrology*. 2021 Sep; 9(5): 1331-55. doi: 10.1111/andr.13062.
- [30] Akcar N, Turgut M, Adapınar B, Ozkan IR. Intratesticular Arterial Resistance and Testicular Volume in Infertile Men with Subclinical Varicocele. *Journal of Clinical Ultrasound*. 2004 Oct; 32(8): 389-93. doi: 10.1002/jcu.20059.
- [31] Maiolino G, Fernández-Pascual E, Ochoa Arvizo MA, Vishwakarma R, Martínez-Salamanca JI. Male Infertility and the Risk of Developing Testicular Cancer: A Critical Contemporary Literature Review. *Medicina*. 2023 Jul; 59(7): 1305. doi: 10.3390/medicina59071305.
- [32] Bier S, Wolff A, Zitzmann M, Kliesch S. Normozoospermic Men in Infertile Couples: Potential Benefit of Early Medical Diagnostic Procedures. *Andrology*. 2025 Mar. doi: 10.1111/andr.70035.
- [33] Jain B, Gaddi M, Nallathambi N, Palande A, Holebasu B, Prasad R et al. Advanced Sonographic Techniques in the Comprehensive Evaluation and Diagnosis of Male Infertility. *Cureus*. 2024 Jun; 16(6). doi: 10.7759/cureus.62848.
- [34] Mittal PK, Little B, Harri PA, Miller FH, Alexander LF, Kalb B et al. Role of Imaging in the Evaluation of Male Infertility. *Radiographics*. 2017 May; 37(3): 837-54. doi: 10.1148/rg.2017160125.
- [35] Sharma A, Minhas S, Dhillon WS, Jayasena CN. Male Infertility Due to Testicular Disorders. *The Journal of Clinical Endocrinology and Metabolism*. 2021 Feb; 106(2): e442-59. doi: 10.1210/clinem/dgaa781.
- [36] Babakhanzadeh E, Nazari M, Ghasemifar S,

- Khodadadian A. Some of the Factors Involved in Male Infertility: A Prospective Review. *International Journal of General Medicine*. 2020 Feb; 13: 29-41. doi: 10.2147/IJGM.S241099.
- [37] Eisenberg ML, Esteves SC, Lamb DJ, Hotaling JM, Giwercman A, Hwang K *et al*. Male infertility. *Nature Reviews Disease Primers*. 2023 Sep; 9(1): 49. doi: 10.1038/s41572-023-00459-w.
- [38] Behboudi-Gandevani S, Bidhendi-Yarandi R, Panahi MH, Vaismoradi M. A Systematic Review and Meta-Analysis of Male Infertility and the Subsequent Risk of Cancer. *Frontiers in Oncology*. 2021 Oct; 11: 696702. doi: 10.3389/fonc.2021.696702.
- [39] Agarwal A, Baskaran S, Parekh N, Cho CL, Henkel R, Vij S *et al*. Male infertility. *The Lancet*. 2021 Jan; 397(10271): 319-33. doi: 10.1016/S0140-6736(20)32667-2.
- [40] Fuchkar Z. Sonography in Male Infertility. In *Ultrasound and Infertility*. 2020 Aug: 189-206. doi: 10.1201/9781003068204-9.
- [41] Sihag P, Tandon A, Pal R, Jain BK, Bhatt S, Kaur S, Sinha A. Sonography in Male Infertility: A Look Beyond the Obvious. *Journal of Ultrasound*. 2018 Sep; 21(3): 265-76. doi: 10.1007/s40477-018-0294-5.
- [42] Diaz P, Dullea A, Chu KY, Zizzo J, Loloi J, Reddy R *et al*. Future of Male Infertility Evaluation and Treatment: Brief Review of Emerging Technology. *Urology*. 2022 Nov; 169: 9-16. doi: 10.1016/j.urology.2022.06.036.
- [43] Concepción-Zavaleta M, Ibarra JL, Ramos-Yataco A, Coronado-Arroyo J, Concepción-Urteaga L, Roseboom PJ *et al*. Assessment of Hormonal Status in Male Infertility. An Update. *Diabetes and Metabolic Syndrome: Clinical Research and Reviews*. 2022 Mar; 16(3): 102447. doi: 10.1016/j.dsx.2022.102447.
- [44] Shi S, Chen W, Tian J, Liang Z, Wu J, Li J *et al*. Risk Factors Associated with Varicocele: A Narrative Review. *Translational Andrology and Urology*. 2025 Jun; 14(6): 1807. doi: 10.21037/tau-2025-120.
- [45] Ammar T, Sidhu PS, Wilkins CJ. Male Infertility: The Role of Imaging in Diagnosis and Management. *The British Journal of Radiology*. 2012 Nov; 85(special_issue_1): S59-68. doi: 10.1259/bjr/31818161.