

Review

## Status of Azoospermia in Saudi Arabia: A Retrospective Narrative Mini-Review

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**Academic Editor:** Elisavet Kouvidi

**Special Issue:** [Chromosomal Abnormalities and Infertility](#)

*OBM Genetics*

2024, volume 8, issue 3

doi:10.21926/obm.genet.2403265

**Received:** April 19, 2024

**Accepted:** September 05, 2024

**Published:** September 30, 2024

### Abstract

The total lack of spermatozoa in the ejaculate is known as Azoospermia. It is the most severe and significant contributor to male infertility. Therefore, the purpose of this study is to assess



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the status of Azoospermia and its etiologic factors that contribute to male infertility in Saudi Arabia. This study included all published studies written in English that were published in Saudi Arabia. Online searches via PubMed and Google Scholar were conducted from their inception to 15 January 2023. A total of 624 studies were found and reviewed, of which only 57 were eligible for the review. Studies were eligible if they provided the prevalence of infertility in Saudi Arabia. A total of 57 articles reported cases diagnosed with male infertility were identified with a sample size of (n = 9441), and only nine studies reported patients diagnosed with Azoospermia. Retrospectively, from our review, the reported cases of Azoospermia in Saudi Arabia are (n = 1030) between 1989-2022. The Klinefelter syndrome was reported in 46 cases and only 9 cases with Y-chromosome microdeletion. A total of 6 studies reported cases of non-obstructive Azoospermia (NOA) (n = 843). Among NOA cases, three studies reported sperm retrieval rates (SRR) were 43.9%, 44.3%, and 47.2%, respectively; the most common histology pattern was Sertoli cell-only (SCO) (n = 120). A total of 3 studies reported cases of obstructive Azoospermia (OA) (n = 187); the most common cause of OA was a history of a genital infection (n = 90). After the microsurgical intervention, two studies reported overall patency rates of 37.3% and 59%, respectively, and three studies reported overall paternity rates of 6%, 10.4 and 36%, respectively. Azoospermia reporting is low in Saudi Arabia. Estimates of male infertility are crucial in helping governments and healthcare decision-makers implement the right social and economic policies. A nationwide azoospermia registry in Saudi Arabia is recommended.

### **Keywords**

Fertility; azoospermia; non-obstructive azoospermia; obstructive azoospermia; Saudi Arabia

## **1. Introduction**

Azoospermia is characterized by the total lack of sperm in the ejaculate following at least two assessments of centrifuged semen. Despite the lack of an implied underlying cause, Azoospermia invariably results in infertility [1, 2]. After a year of unprotected sex, over 15% of couples are unable to conceive and are consequently classified as infertile [3]. About 20–30% of these cases have an isolated male factor, whereas another 20–30% have a link between the male and female variables. As a result, the male component is present in about 50% of cases of infertility in marriage [3]. Azoospermia affects roughly 1% of males overall, while between 10 and 15 percent of infertile men have the condition [3]. Idiopathic Azoospermia, or the absence of mature sperm cells (spermatozoa) in seminal fluid, affects about 15% of men seeking treatment at infertility clinics [4]. There is a vital hereditary component to infertility in males with azoospermia and severe oligozoospermia (sperm counts of fewer than 5 to 10 million per ejaculate) [4].

Even males with potentially curable causes of infertility are typically treated with assisted reproductive methods (ARTs) rather than specific therapy. However, once Azoospermia is diagnosed, no sperm can be found in the ejaculate; hence, ARTs cannot be used due to the lack of sperm in the ejaculate unless surgical sperm retrieval is applied [5]. To direct appropriate management strategies and to assess the advantages, risks, costs, and prognosis of the treatment

success, the diagnosis of Azoospermia and systematic evaluation of patients are essential [5]. The couple should receive enough counseling from the urologist, and patients with male-factor infertility should receive substantial assistance. Men with Azoospermia were previously thought to be sterile. The profession and the medical literature know that various reasons for Azoospermia can be treated [5].

Although in some clinical protocols, etiologies of Azoospermia fall under pre-testicular, testicular, and post-testicular categories, Azoospermia is often divided into obstructive and non-obstructive categories [6]. This classification directs patient management and treatment outcomes, making it clinically significant [7]. Remarkably, nonobstructive Azoospermia (NOA) refers to a considerable testicular defect caused by several conditions that ultimately hurt sperm production. The severe spermatogenic deficiency seen in NOA patients is usually due to primary testicular failure primarily affecting spermatogenic cells (spermatogenic failure (STF)) or dysfunction of the hypothalamus-pituitary-gonadal axis (hypogonadotropic hypogonadism (HH)). Hereafter, the acronyms STF and HH will be used to differentiate these types of NOA, as appropriate [2, 8].

The frequency of male infertility among infertile couples varies geographically, reaching as high as 59% in France, 36% in South Africa, Indonesia, and Finland, and between 26% and 3% in the UK and Kashmir. Furthermore, the mean sperm concentration varies regionally in France and the USA, according to several studies [9].

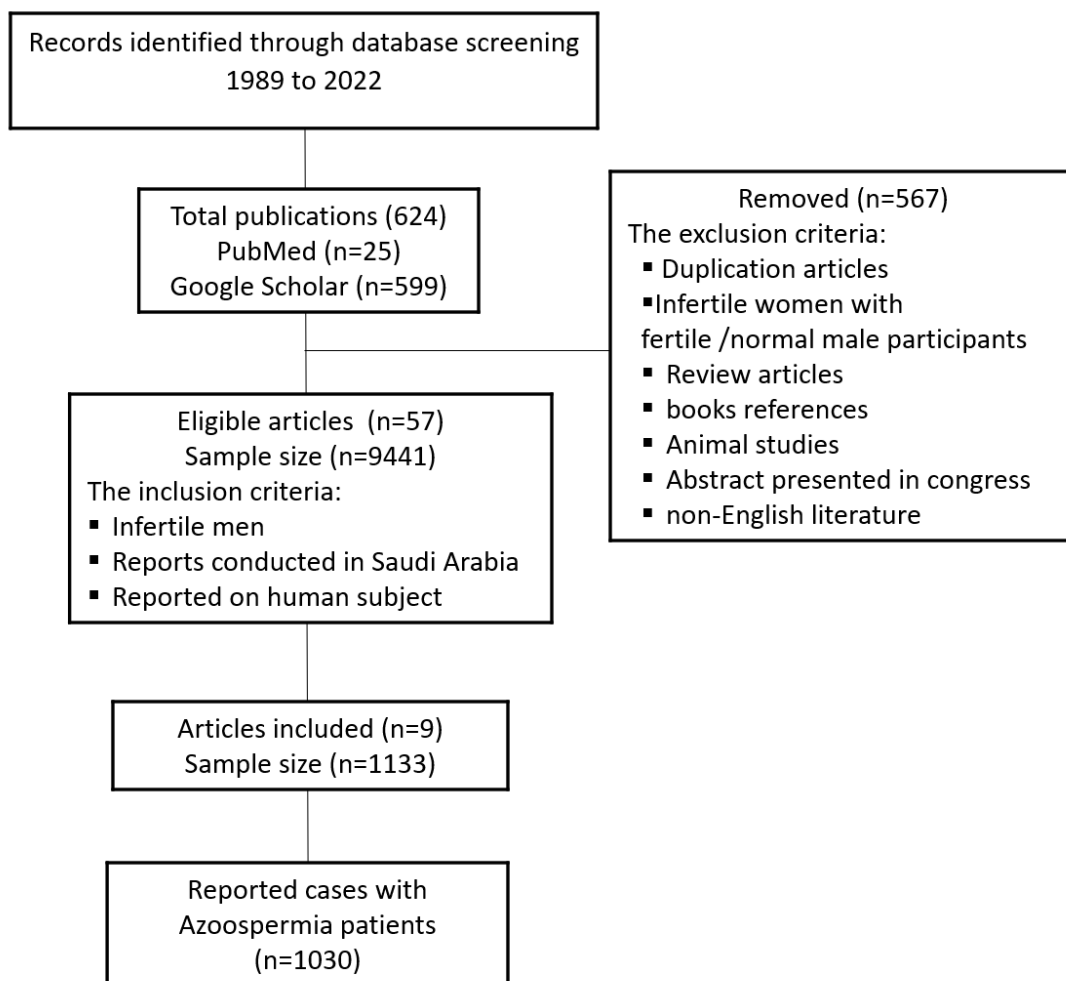
No such studies have been conducted in Saudi Arabia regarding the prevalence of Azoospermia, although it is a large country with considerable regional variation in its dietary habits and occupations. This review aimed to assess the current status of Azoospermia in the Kingdom of Saudi Arabia.

## **2. Methods**

This narrative review was conducted using a pre-defined protocol. A Medline PubMed and Google Scholar search were used to identify articles about male infertility published in English. The following terms were used for searching articles: "Male Infertility" AND "Azoospermia" AND "Saudi Arabia". The search was conducted from the date of inception of the mentioned databases to 15 January 2023. We include studies from Saudi Arabia that reported cases on the human subject, male infertility, and Azoospermia; we exclude studies from non-English literature, abstract-only reports, duplicated reports, review articles, animal studies, and studies not reported cases of male infertility, books references, and studies outside Saudi Arabia.

Based on our predefined inclusion and exclusion criteria, two authors screened these articles independently to collect the relevant information, including the title and abstract by the first author, written in English, peer-reviewed articles having a clear relation or relevance to the topics of male infertility and Azoospermia. Studies were eligible if they provided and reported male infertility cases in Saudi Arabia. The Joanna Briggs Institute Quality Assessment Tool [10] was used to evaluate each study. Two reviewers independently extracted data using a pre-designed table to summarize study results, including data related to the author, year, study design, and outcome measure. The following measures were extracted from each article: The number of male patients and patients diagnosed with primary infertility, secondary infertility, Non-obstructive Azoospermia (NOA), and obstructive Azoospermia (OA). Because the collection of the results has no impact or responsibility

on the patients, neither institutional review board approval nor informed consent was required— flow chart for selected studies in (Figure 1).



**Figure 1** Flow chart for selected studies.

### 3. Results

A total of 623 studies were reviewed. Based on our study selection, 57 articles reporting cases diagnosed with male infertility in Saudi Arabia were eligible for review, with a sample size of (n = 9441) (Figure 1).

Only 9 studies reported infertile male patients diagnosed with Azoospermia (n = 1030); most of the centers reported cases with Azoospermia from Riyadh city, Saudi Arabia's capital. Most of the study designs were Retrospective; 3 articles reported the type of infertility, 217 were primary infertility, and 63 were secondary infertility; the total number of patients with Azoospermia reported was (n = 1030) between 1989 and 2022 (Table 1).

**Table 1** Studies reported cases of Azoospermia in Saudi Arabia (n = 1030).

Author, year	City	Study design	Sample size	Age	Type of infertility (n)		Reported Azoospermia
					Primary	Secondary	
Jamal, 1989 [11]	Riyadh	Retrospective	155	Range 18-50	129	26	113
Mansi, 1995 [12]	Riyadh	Retrospective	123	Mean SD 37.6 ± 6.4	86	37	123
Binsaleh, 2014 [13]	Riyadh	Prospective	22	Mean 31	NR	NR	22
Binsaleh, 2017 [14]	Riyadh	Retrospective	255	Mean SD 35.8 ± 7.2	NR	NR	255
Beg, 2018 [15]	Jeddah	Prospective study	88	NR	NR	NR	49
Almesned, 2020 [16]	Riyadh	Case report	2	35-year-old	2	-	1
Alhathal, 2020 [17]	Riyadh	Chromosomal analysis	285	Range 24-63	NR	NR	237
Alrabeeah, 2021 [18]	Riyadh	Retrospective	122	Mean SD 37 ± 8.84	NR	NR	122
Aljubran, 2022 [19]	Asser	Retrospective	108	Mean SD 36.8 ± 10	NR	NR	108

*Abbreviations: NR; not reported.*

Among azoospermic men, NOA was highly prevalent, with 843 cases, whereas 187 patients were diagnosed with OA (Table 2). The Klinefelter syndrome was reported in 46 cases, and only 9 were reported with Y-chromosome microdeletion (YCM). Among NOA cases, three studies reported SRR of 43.9%, 44.3%, and 47.2%, respectively, and 4 studies reported histopathology pattern; the most common histology pattern was Sertoli cell only (SCO) in 120 cases (Figure 2), only one study reported pregnancy rate and live birth rate among NOA cases. Ninety cases of OA were documented in three studies, with the most common cause of OA being a history of genitourinary tract infections. After the microsurgical intervention, two studies reported an overall patency rate of 37.3% and 59%, respectively, and three researches reported an overall paternity rate of 6%, 10.4 and 36%, respectively (Table 2).

**Table 2** Patient characteristics with Azoospermia were reported from Saudi Arabia (n = 1030).

Author, year	Reported Azoospermic patient	NOA (n)	OA (n)	Karyotyping/Genetic testing n (%)	Etiology n (%)	Outcome n (%)
Jamal, 1989 [11]	113	71	42	NR	<b>Surgical technique:</b> Testicular biopsy <hr/> <b>Histopathology pattern:</b> - Hypospermatogenesis 7 (10) - Maturation arrest 11 (15) - SCO 19 (26) - Fibrosis & atrophy 34 (48) <hr/> <b>Cause of OA:</b> - Not reported 34 (81) - Complete vas deferens Block 5 (12) - Congenital absence of the vas deferens 1 (2) - Congenital atresia of the vas deferens 1 (2) - Partial aplasia of the vas deferens 1 (2) <hr/> <b>Surgical technique for OA:</b> - Vasoepididymostomy (VE)	† Overall pregnancy rate 2 (6)
Mansi, 1995 [12]	123	NR	123	NA	<b>Histopathology pattern:</b> - Normal spermatogenesis 7 (30.4) - Spermatogenic arrest 5 (21.7) - Mild to moderate hypospermatogenesis 9 (39.2) - Moderate to severe hypospermatogenesis 2 (8.7) <hr/> <b>Cause of OA:</b> - Empty epididymis 23 (18.7)	† Overall patency rate 25 (37.3)  † Overall pregnancy rate 7 (10.4)

					<ul style="list-style-type: none"> <li>- Congenital anomaly of the epididymis 4 (3.2)</li> <li>- Bilateral absent vas 11 (9)</li> <li>- Unilateral absent vas 2 (1.6)</li> <li>- Vasal block 5 (4.1)</li> <li>- Ejaculatory duct obstruction 2 (1.6)</li> <li>- Post-inflammatory epididymal obstruction 76 (61.8)</li> </ul>	† Overall Living birth 4 (6)
					<p><b>Surgical technique for OA:</b></p> <ul style="list-style-type: none"> <li>- VE 83 (67.5%):</li> <li>- Microsurgical VE (end-to-side single tubule anastomosis) 49 (59)</li> <li>- Conventional fistula technique VE 26 (31.3)</li> </ul>	
Binsaleh, 2014 [13]	22	NR	22	NA	<p><b>Cause of OA</b></p> <ul style="list-style-type: none"> <li>- previous genital infection (epididymitis, gonococcal or non-gonococcal urethritis) 14 (64)</li> <li>- post hydrocelectomy 2 (9)</li> <li>- idiopathic 6 (27)</li> </ul> <p><b>Surgical technique for OA:</b> Two-suture single-armed longitudinal intussusception vasoepididymostomy</p>	† Overall patency rate 13 (59)  † Overall paternity rate 8 (36)
Binsaleh, 2017 [14]	255	255	NR	KS 11 (4.3%)	<p><b>Surgical technique:</b></p> <ul style="list-style-type: none"> <li>- Microscopic testicular sperm extraction (micro-TESE)</li> </ul> <p><b>Histopathology pattern (n)</b></p> <ul style="list-style-type: none"> <li>- Hypospermatogenesis (n = 10)</li> <li>- Maturation arrest (n = 9)</li> <li>- SCO (n = 74)</li> </ul>	*Overall SRR 112 (43.9)  *KS SRR 6 (54.5)

					- Tubular atrophy (n = 2)	
					<b>Predictors of successful Micro-TESE:</b>	
					- Histological diagnosis (Hypospermatogenesis)	
Beg, 2018 [15]	49	49	NR	Abnormal Karyotype n = 10: 47, XXY n = 5 46,X,del[Y],(q11.22q12) n = 1 48,XXXY(3)/47,XXY(47) n = 1 47,XYY(34)/46,XY(16) n = 1 47,XYY(2)/46,XY(48) n = 1 46,XYdel(Y)(q11.2)(41)46,XY(9) n = 1 YCM n = 2 (AZF b,c) KS n = 6	<b>Surgical technique:</b> - Testicular biopsy followed by micro-TESE (n = 25)	NR
					<b>Histopathology pattern (n)</b>	
					- SCO (n = 1) - atrophy (n = 1)	
Almesned, 2020 [16]	1	1	NR	ROB translocation. 45, XY, der (13;14) (q10;q10)	NR	NR
Alhathal, 2020 [17]	237	237	NR	chromosomal aberrations 30 (10.5%) SCA n = 19 KS n = 18 YCM n = 4	NR	NR
Alrabeeah, 2021 [18]	122	122	NR	KS 11 (9%) YCM 3 (2.5%)	NR	*Overall SRR 54 (44.3)
Aljubran, 2022 [19]	108	108	NR	NR	<b>Surgical technique:</b> - micro-TESE	*Overall SRR 51 (47.2)
					<b>Histopathology pattern (n)</b>	
					- Hypospermatogenesis (n = 4) - Maturation arrest (n = 15)	

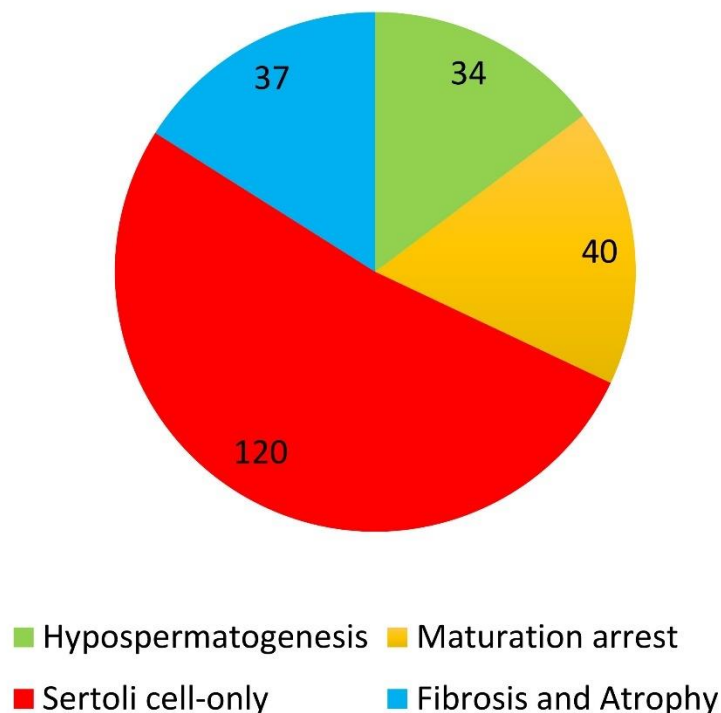


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- SCO (n = 26)	*Pregnancy
<b>Predictors of successful micro-TESE:</b>	rate 14
- Age	(13.7)
- FSH	
	*Living birth
	4 (28.6)

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*Abbreviations: NR; not reported, NA; not applicable, NOA; Non-obstructive Azoospermia, OA; Obstructive Azoospermia, SRR; sperm retrieval rate, ROB; Robertsonian, KS; Klinefelter syndrome, YCM; Y-chromosome microdeletion, SCA; sex chromosome aneuploidy. Micro-TESE; Microdissection testicular sperm extraction, SCO; Sertoli cell only. \*NOA cases, † OA cases.*



**Figure 2** The testicular histopathology pattern reported cases in men with non-obstructive Azoospermia in Saudi Arabia (n = 231/843).

#### 4. Discussion

Typically, Infertility cases are treated in doctors' offices and are probably underreported in developing countries where advanced treatment is either too expensive or unavailable [20]. As infertility is not a reportable disease, the exact incidence is unknown [20]. There are roughly 600,000 azoospermic men of reproductive age in the US at any given time, and the majority of them have NOA [21]. From our study, out of 57 articles with a sample size (n = 9441) identified in Saudi Arabia were eligible for review (Figure 1), only nine studies diagnosed with male infertility reported cases with Azoospermia, the total patients with Azoospermia reported were (n = 1303) between 1989-2022 (Table 1).

Cytogenetic abnormalities exist in about 5% of males with NOA [22]. The most common sex chromosomal abnormality is Klinefelter syndrome (KS), characterized by an extra X chromosome (47, XXY). One-half of patients are thought never to be diagnosed. The overall incidence affects one in 500 to 800 males, or around 3% of all infertile men [23]. From our review, the KS in 46 cases reported among azoospermic men.

It is becoming more and more evident that male reproductive and general health are related, with infertile men having more comorbidities than fertile controls [24]. Men with abnormal semen parameters have a higher risk of testicular cancer [25], and men with Azoospermia had higher total cancer occurrences than fertile men [26-29]. Azoospermia in men with testicular germ cell tumor (TGCT) has been observed in 5–8% [30] and oligospermia in 50% [31]. From our data, 120 patients with NOA have SCO testicular histology patterns (Table 2). Incomplete Sertoli cell-only syndrome (SCOS) patients have a higher prevalence of testicular nodules and cancer, according to Mancini et

al. This finding suggests that azoospermic men should have a complete testicular diagnosis before considering ART. The Sertoli cell-only syndrome (SCOS) may be strictly linked to risk factors for testicular neoplasm [29]. Therefore, the significant prevalence of testicular nodules in infertile men who are azoospermic but otherwise healthy should point to the need for routine clinical screening by a clinician [29].

Another genetic abnormality in male infertility is YCM; it is recommended that all men with primary testicular failure undergo karyotype and Y chromosome microdeletion testing. Approximately 6% of men with non-obstructive Azoospermia (NOA) will have YCM involving the AZFa and AZFb subregions. Around 4% will have a microdeletion of the AZFc subregion, which is less severe in infertility but can be inherited by male offspring [23]. The histopathology reveals about 46% of men with AZFc microdeletions will demonstrate SCOS, and 38% of the men will have a maturational arrest. Men with such microdeletions typically have extremely poor SRR and should be counseled to consider using donor sperm for ICSI or adoption [23].

From our data, YCM was reported only in 9 cases (Table 2) and is considered a low-reported condition. There is a need to establish better indicators describing suitable patients for molecular screening because the YCM has been reported in the literature so infrequently [32]. The most common molecular genetic cause of oligo/azoospermia is the YCM deleting the AZoospermia Factor (AZF) regions [33]. Azoospermic men (8–12%) and oligozoospermic (3–7%) had the highest rates of YCM, respectively [34, 35]. For testicular sperm retrieval, the YCM analysis has both diagnostic and prognostic utility [33]. In previous studies of infertile German men, AZFb,c deletions were not common [36]. However, in a recent investigation, AZFb,c deletions were the second most frequently identified among 1,473 multi-ethnic infertile men, with 58 YCM found [37]. In an earlier study from Saudi Arabia, eight patients with YCM were identified out of 257 infertile men (3%), but none of these were AZFb,c deletions [38]. This prevalence is similar to our findings and suggests that regional differences in microdeletion patterns may exist within the same ethnic population, as the patients in the Saudi study were mainly recruited from central Saudi Arabia, as evident in a previous report [15]. This contrasts with countries such as Egypt, Tunisia, and Iran, where YCM was found in about 12% of severely oligozoospermic or azoospermic men. Among 880 NOA patients from the Middle East, AZF deletions were detected in 66 cases (7.5%), with AZFb deletions being the most frequent (33.3%), followed by AZFbc deletions (17%) [39]. A lower incidence of AZF deletions (5%) was found in 142 Jordanian patients with NOA [40]. The highest reported incidence, at 24%, was among 99 infertile men in West Azerbaijan [41]. It is challenging to determine whether the varying prevalence of AZF deletions reflects ethnic differences or is influenced by patient selection and technical factors [15].

Other causes of Azoospermia include XYY syndrome, myotonic dystrophy, Noonan syndrome, 5-alpha reductase deficiency, androgen insensitivity syndrome, and vanishing testis syndrome [23].

Urologists specializing in andrology must understand common genetic abnormalities linked to infertility to advise couples seeking fertility treatment. Men with low sperm counts can achieve paternity through IVF, ICSI, and sperm extraction in azoospermia cases. However, infertile men's sperm shows higher rates of aneuploidy, chromosomal abnormalities, and DNA damage, risking genetic issues in offspring. Routine practice screens genomic DNA from blood samples, but screening for sperm aneuploidy is also feasible in selected cases, such as recurrent miscarriage [42-44].

Recent guidelines emphasize the recommendations for diagnostic and genetic testing for male infertility. According to the European Association of Urology (EAU), YCM testing may be offered to males with sperm concentrations below 5 million and is required for those with sperm counts below 1 million (strong recommendation) [45]. Meanwhile, the American Urological Association (AUA) recommends that men with primary infertility, Azoospermia, or severe oligozoospermia (sperm count below 5 million/mL), elevated follicle-stimulating hormone (FSH), testicular atrophy, or a presumed diagnosis of impaired sperm production as the cause of Azoospermia should undergo YCM analysis and karyotype testing (expert opinion) [46].

In the present review, the most common method of surgical SRR was microdissection testicular sperm extraction (Micro-TESE). A systematic review of sperm retrieval techniques has demonstrated that conventional TESE is twofold as effective at retrieving sperm compared to testicular sperm aspiration (TESA), and micro-TESE is 1.5 times more effective than traditional TESE. Micro-TESE is widely regarded as the current gold standard for surgical sperm retrieval [47].

Three studies reported a rate of SRR of viable spermatozoa of 43.9%, 44.3%, and 47.2%, respectively. A similar SRR (50%) was previously reported in the literature [48, 49]. In approximately 50% of cases of NOA, micro-TESE may enable retrieval of sperm.

This review's most common histopathological pattern was SCO (n = 120) (Figure 2). Key signs that predict successful sperm retrieval with micro-TESE in nonobstructive azoospermic men are focal type SCOS, late-stage maturation arrest (rather than early maturation arrest), hypospermatogenesis (as opposed to maturation arrest or SCOS), and the presence of viable sperm in the seminiferous tubules on testis biopsy. The successful SRR with micro-TESE is approximately 50%, similar to the success rate of ICSI, which also stands at about 50%. However, the combined pregnancy rate is only 25% [23].

In men with NOA, the sperm retrieval of those patients with YCM of the AZFa or AZFb subregions is reported to be zero, and about 46% of men with AZFc microdeletions will exhibit SCOS, and 38% will have a maturational arrest [23].

The most frequent cause of OA, which affects 30-67% of azoospermic males, is epididymal obstruction [50-52]. Congenital bilateral absence of the vas deferens (CBAVD), the typical manifestation of congenital epididymal obstruction, is 82% associated with at least one cystic fibrosis gene mutation [53]. Other congenital types of epididymal obstruction include Young's syndrome and persistent sinus-pulmonary infections [54]. The most typical cause of acquired secondary to acute (e.g., gonococcal) and subclinical (e.g., Chlamydial) epididymitis is infection [55, 56]. Other causes may be trauma or surgical intervention [57, 58].

From our review, a history of genitourinary infection, such as epididymitis, gonococcal, or non-gonococcal urethritis, was the leading cause of OA in 90 reported cases (Table 2). While data from the Western literature showed that vasectomy is the most common etiology of OA [59, 60], Schiff et al. [61] observed that a history of infection was not related to worse results following microsurgical vasoepididymostomy. Data reported from Saudi Arabia by Binsaleh et al. showed that prior infection and postoperative causes are associated with adhesions, as seen during scrotal exploration, making later reconstructive intervention more complex [13].

Most cases of Azoospermia were reported from centers in Riyadh, Saudi Arabia's capital city (Table 1). Health facilities in Saudi Arabia, including medical cities, specialized hospitals, university and military hospitals, and primary care centers, serve more than 31 million citizens and residents. The Saudi MOH aims to establish health clusters in all regions of the Kingdom to facilitate access to

health services and smooth transfers between different types of care. These clusters enable the movement of medical competencies and provide beneficiaries with an integrated and interconnected network of healthcare service providers governed by a single administrative structure. Two examples are the Riyadh First Health Cluster and the Riyadh Second Health Cluster. On behalf of the state, the Saudi MOH offers reproductive health care services, including preconception, pregnancy, childbirth, and postpartum care. Acknowledging the need to address infertility issues, the State enacted the Fertilization, Embryo, and Infertility Treatment Units Law, ensuring that infertility clinics provide services safely, fairly, and in an Islamic manner [62]. This regulation guarantees that clinics meet high standards of care, enhancing patient trust and outcomes. The presence of specialized hospitals and medical cities means that patients can receive advanced and focused infertility treatments. These facilities will likely have the latest technology and highly trained specialists dedicated to reproductive health. By providing an interactive map of all government medical facilities, the MOH makes it easier for individuals to locate and access infertility clinics and related services. This transparency helps patients find the most convenient and appropriate facilities.

The first step in the diagnosis and management of infertile male patients with Azoospermia is to differentiate between OA and NOA. It includes a thorough, detailed medical history and physical examination, as well as sperm analysis, hormonal, genetic testing, and imaging studies. Because the KS and 47, XYY syndromes, as well as transmembrane conductance regulator (CFTR) gene mutations, are mostly discovered late in life, during an infertility investigation, the sex chromosome aneuploidies and gene mutations require earlier medical attention [2]. To give infertility patients with Azoospermia the best opportunity of becoming parents, a coordinated multidisciplinary approach combining reproductive urologists/andrologists, reproductive gynecologists, geneticists, and embryologists is essential [2].

Reporting syndrome-related Azoospermia in a region with a high prevalence of consanguinity is vital. Establishing a nationwide azoospermia registry in Saudi Arabia is recommended. This is the first comprehensive review summarizing available evidence to determine the current status of Azoospermia, its types, and etiology in Saudi Arabia.

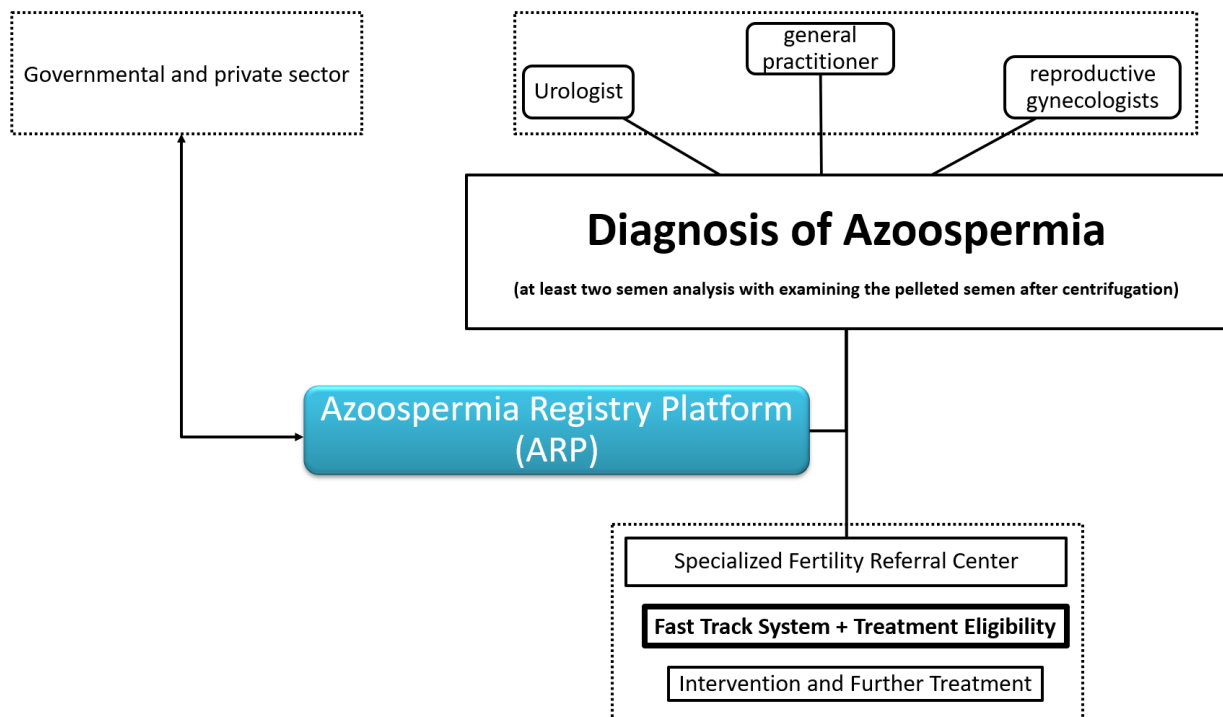
By implementing these measures, the current healthcare system enhances the accessibility and effectiveness of infertility services, specifically for men diagnosed with Azoospermia, ultimately improving outcomes for individuals and couples facing infertility challenges.

## **5. Recommendation and Future Direction**

Male factor infertility can be caused by an underlying medical problem that is often treatable but can be life-threatening. Due to a comprehensive evaluation of reproductive male function and improved diagnostic tools, the role of the malefactor in couple infertility has increased exponentially in recent decades. Despite these advancements in diagnosis, the most challenging aspect of treating infertility is usually Azoospermia. Several disorders that disrupt spermatogenesis and decrease sperm quantity and quality can cause Azoospermia. As a result, the urologist, even if they are not a specialist in the infertility field, is responsible for adequately evaluating, diagnosing, and treating the underlying condition, such as Azoospermia, whenever possible.

It is important to note that the number of reported cases of Azoospermia in Saudi Arabia is low. Because Saudi Arabia is a large country and a pluralistic society with significant regional variation in

its unique ethnicity and occupational and nutritional habits, there is a need for increased observation of Azoospermia among infertile male patients. As a result of this review, we proposed a scheme [Azoospermia Registry Platform (ARP)] (Figure 3) for future direction in the early detection and management of azoospermia infertile men. The ARP will help and guide and facilitate easy, fast-track access for patients with Azoospermia to develop a fast intervention and further management in high-volume centers treating such conditions.



**Figure 3** Proposed scheme for future direction in early detection and management of azoospermia cases in Saudi Arabia.

Because of the specific demographic, cultural, and healthcare infrastructure factors that affect azoospermia management in the region, this scheme is designed specifically for Saudi Arabia. Our review focuses on the resources, patient population, and healthcare legislation unique to Saudi Arabia, which explains why this idea is so pertinent to the nation. Furthermore, the suggested scheme is consistent with the strategic plans and healthcare reforms that the Saudi Ministry of Health is presently putting into practice, including the Fertilization, Embryo, and Infertility Treatment Units Law and the creation of health clusters as well as other specialized governmental and private sector provide fertility care. The scheme may contain more widely applicable components, but what makes it essential to this study is how it has been specifically implemented and tailored to Saudi Arabia's healthcare system. We recognize that more thorough study designs and data are required to support the generalization of this approach outside of Saudi Arabia, which may be a topic for future investigation.

The underutilization of urologists' services in addressing male infertility stems from both insufficient understanding and knowledge about their role among healthcare practitioners and the public [63]. To provide patient-centered care and maximize results, healthcare professionals must work collaboratively [23]. Governmental and private sectors are encouraged to adopt a program for

treating Azoospermia. Furthermore, financial obstacles, such as the lack of insurance support for infertility diagnosis and treatment, further hinder couples from seeking the care they need [64].

## 6. Conclusion

Estimates of male infertility are crucial in helping governments and healthcare decision-makers implement the right social and economic policies. The data on Azoospermia from Saudi Arabia is considered low. We encourage Urologists working with male infertility cases, specifically azoospermia patients, to do more reporting for such conditions, as they impact individuals and require advanced treatment, which is considered costly or unavailable.

## Abbreviations & Acronyms

NOA	Non-obstructive Azoospermia
OA	Obstructive Azoospermia
KS	Klinefelter syndrome
YCM	Y chromosome deletion

## Author Contributions

The author did all the research work for this study.

## Funding

This work does not receive specific funding.

## Competing Interests

The authors have declared that no competing interests exist.

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