Review Article

DOI: 10.7860/JCDR/2026/84709.23401

Surgery Section

Clinical Features, Molecular Pathogenesis, Diagnosis, and Management Strategies of Zinner Syndrome: A Comprehensive Review

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ABSTRACT

Zinner syndrome is a rare congenital defect of the male reproductive organs, which is traditionally characterised by the presence of the triad of unilateral renal agenesis, ipsilateral seminal vesicle cyst, and obstruction of ejaculatory ducts. It is a result of malformed development of the mesonephric (Wolffian) duct during embryogenesis, commonly asymptomatic, and is discovered incidentally by imaging. Mass effect can cause symptomatic patients to present with lower urinary tract symptoms, lower abdominal or pelvic pain, reproductive dysfunction, and bowel symptoms, uncommonly. Magnetic Resonance Imaging (MRI) is the diagnostic gold standard, Computed Tomography (CT), Ultrasound (US) and emerging modalities can help in early detection. Individualised management includes conservative observation and minimal invasive, robotic-assisted or endoscopic intervention with new therapies emerging to help relieve the symptoms and preserve fertility. Genetic research, such as whole exome sequencing, has proposed a role of genetic factors such as GATA3 and PAX8, among others, in the pathogenesis. The present article is a review of clinical presentation, imaging, pathogenesis, and treatment.

Keywords: Congenital malformation, Ejaculatory duct obstruction, Genetic basis, Imaging modalities

INTRODUCTION

Zinner syndrome is a rare congenital malformation of the male genitourinary system, and is traditionally characterised by triad of unilateral renal agenesis, ipsilateral seminal vesicle cyst, and ipsilateral ejaculatory duct obstruction [1]. It is a result of the aberrant development of mesonephric (Wolffian) duct during embryogenesis and is most frequently diagnosed due to pelvic or lower-urinary symptoms or incidentally on imaging [2]. Radiological diagnosis is the rule, MRI as an imaging technique is crucial to outline the anatomy of the pelvis and seminal vesicle pathology, while CT/ultrasound is done to confirm renal agenesis [2,3]. The condition was first described by A. Zinner in 1914 and later summarised and popularised in the urological literature as Zinner syndrome [1]. Initial descriptions were limited due to the rarity of the condition and the tendency to remain silent clinically, but now with the widespread application of pelvic cross-sectional imaging (CT and particularly MRI), even more cases have been identified and characterised in the contemporary world [4]. Few hundred cases were described of Zinner Syndrome but exact prevalence in the general population is unknown as many patients are asymptomatic and not imaged [5]. The article aims to provide comprehensive overview of Zinner syndrome, its clinical presentation, pathogenesis. It evaluates the existing diagnostic modalities and new management strategies. Lastly, it identifies research gaps and directions to advance knowledge, diagnosis, and treatment of this rare disease.

Clinical Features and Symptomatology of Zinner Syndrome

Zinner syndrome is most typically identified in an incidental manner in adolescents and young adult males and is mostly asymptomatic; but, when symptomatic, the clinical picture is one of mass effect as a result of seminal vesicle cysts and ejaculatory duct obstruction [6].

Clinical manifestations and symptoms of Zinner Syndrome are mentioned in [Table/Fig-1] [6-10].

Category	Clinical features/Symptoms	References
General/usual presentation	Often incidental finding in adolescents or young adult males; mostly asymptomatic	[6]
Lower Urinary Tract Symptoms (LUTS)	- Urinary frequency - Urgency - Dysuria - Haematuria - Weak urinary stream (obstructive flow symptoms)	[6-8]
Pain symptoms	- Non-specific lower abdominal pain - Pelvic pain - Perineal pain - Radiating pain to medial thigh, groin, or ipsilateral testis - Backache or flank pain	[6,8,9]
Reproductive symptoms	- Pain during ejaculation - Haematospermia - Post-ejaculatory discomfort - Infertility or subfertility - Anejaculation - Nocturnal emissions	[9,10]
Mass-Effect Symptoms (Large seminal vesicle cysts)	- Bowel-related symptoms (e.g., incomplete evacuation) - Palpable pelvic fullness	[9]

[Table/Fig-1]: Clinical manifestations and symptoms of Zinner Syndrome [6-10].

Emerging and Under-recognised Clinical Manifestations of Zinner Syndrome

Less commonly identified symptoms inclusive of seminal-vesicle calculi, ectopic ureteric drainage, atypical irritative urinary symptoms, which are also being highlighted in recent literature, further expand the symptomatic spectrum of Zinner syndrome [11,12]. Seminal-vesicle calculi have been increasingly observed within cystic cavities, thereby producing episodic pelvic pain, recurrent microscopic or gross haematuria, which usually worsens obstructive symptoms [12]. These stones often cause complications of chronic inflammation within the cyst as well, and it can necessitate surgical removal when conservative management fails [12]. In some anatomical variants of Zinner syndrome, an ectopic ureter that drains into the seminal

vesicle introduces atypical urinary complaints, inclusive of recurrent urinary tract infections, persistent irritative voiding symptoms, along with unusual patterns of urine leakage [11].

Beyond of typical fertility issues, emerging reports also describe azoospermia which is a more severe reproductive manifestation that can result from compression of the ejaculatory ducts or associated ejaculatory-duct cysts [13]. Additionally, infected seminal vesicle cysts can also mimic chronic bacterial prostatitis, presenting with fever, perineal discomfort, as well as painful ejaculation unresponsive to routine prostatitis therapy [14]. Such clinical presentations may lead to delays in the proper diagnosis until clinicians maintain a high index of suspicion and for which they also pursue early imaging.

Another evolving clinical pattern, which is inclusive of exaggerated colorectal-type symptoms, where large cysts cause pelvic or anal pressure, tenesmus, or a sensation of incomplete evacuation, that often further prompts initial referral to colorectal specialists [13]. In rare cases involving adolescents and young adults, symptomatic patients can also develop acute urinary retention and obstructive uropathy, usually when cysts co-exist with ectopic or duplicated urogenital structures [15]. Unusual systemic manifestations, such as new-onset hypertension which get resolved following cyst excision is also observed, suggesting a possible but poorly understood neurohumoral mechanism [16]. Lastly, co-existing genitourinary pathologies, which include incidental prostate abnormalities, complex ureteric variations, can cause modification into both symptomatology and management strategies in affected patients [17]. These emerging clinical features points toward heterogeneous and evolving nature of Zinner syndrome, which further suggests need of proper individualised diagnosis and management methods [16,17].

Pathogenesis and Molecular Basis of Zinner Syndrome

Mesonephric (Wolffian) duct plays a role in the formation of male reproductive organs such as kidneys, seminal vesicles and ejaculatory ducts [18]. Mesonephric duct which is abnormally developed during 4th to 13th week of embryogenesis thus leading to characteristic features of Zinner syndrome [18]. Pathogenesis and Molecular Basis of Zinner Syndrome is described in [Table/Fig-2] [18-24].

Category	Details	References
Embryologic origin	Abnormal development of the mesonephric (Wolffian) duct during 4th-13th week of embryogenesis leading to seminal vesicle cysts, ejaculatory duct obstruction, and renal malformations.	[18,19]
Paediatric pathogenesis	Abnormal distal mesonephric duct development → ejaculatory duct atresia/stenosis → cystic seminal vesicle swelling → abnormal ureteral budding → renal malformations. Urinary reflux may cause infections like epididymo-orchitis or urinary tract infections.	[20-22]
Adult pathogenesis	Ejaculatory duct obstruction → infertility, perineal pain, possible lower urinary tract symptoms.	[23]
Genetic basis	Exact cause unclear. Whole Exome Sequencing (WES) has identified somatic mutations in genes related to urogenital development: GATA3 – critical for urogenital development PAX8 – involved in mesonephric duct differentiation Other genes: MYEOV, BAGE, NAALAD2 – potential contributors to pathogenesis	[24]
Clinical significance	Highlights the role of complex genetic and developmental studies in understanding pathogenesis and improving diagnostic accuracy.	[24]

[Table/Fig-2]: Pathogenesis and molecular basis of Zinner Syndrome [18-24].

Diagnostic Imaging and Emerging Modalities in Zinner Syndrome

The diagnosis is mostly done by imaging modalities since the clinical manifestations are typically not specific [25]. MRI is known to be the gold standard due to its superior soft-tissue contrast as well as multiplanar capability, which further allows precise visualisation of the seminal vesicles, prostate, ejaculatory ducts and the relationship of cystic lesions to adjacent pelvic structures [25,26]. On MRI, seminal vesicle cysts are characteristically hyperintense on T2-weighted images, with T1 signal varying according to proteinaceous or haemorrhagic contents [26]. MRI also clearly demonstrates associated abnormalities such as ipsilateral renal agenesis, atrophic/ectopic kidneys, ectopic ureteral insertion or a dilated ipsilateral vas deferens when present [26]. MRI, therefore, not only confirms cystic nature and origin of the pelvic lesion but also helps in mapping anatomy, which is very important for surgical planning [26].

The US typically, transabdominal sonography is used as an initial modality, which can detect the absence of a kidney as well as show a midline or paravesical cystic pelvic mass, but it has limited ability to define the organ of origin in complex cases [27]. Transrectal Ultrasound (TRUS) provides an excellent anatomic detail of the seminal vesicles, ejaculatory ducts which is very useful for demonstrating seminal vesicle dilatation, internal septations, calculi, and any communication with the ejaculatory duct [27,28]. TRUS an also serve interventional purposes, inclusive of aspiration, image-guided sampling, and cyst drainage when required [27,28]. TRUS is inexpensive, real-time also widely available, but its field of view, tissue characterisation are inferior to MRI [26,28].

The CT thereby remains valuable, usually when patients first present having non-specific abdominal or urinary complaints because it readily demonstrates renal agenesis or dysplastic multicystic kidneys and the presence of a pelvic cystic mass [29]. Modern CT urography using three-dimensional (3D) reconstructions improves anatomical correlation between the pelvic cyst-urinary tract, helps delineate mass effect on bladder or ureter, as well as it can more clearly show ectopic ureteral courses or an associated dysplastic kidney remnant [30]. however, CT has lower soft-tissue contrast than MRI and involves ionising radiation, which limits its use as the definitive problem-solving test [30].

Recent advances, inclusive of novel diagnostic technologies, which can help in improving detection and anatomical characterisation of Zinner syndrome beyond conventional MRI, CT, and TRUS [31]. Diffusion-Weighted MRI (DWI), MR spectroscopy further show importance in differentiating seminal vesicle cysts from other pelvic cystic lesions, which can be done through evaluation of tissue composition, internal septations, as well as possible haemorrhagic or proteinaceous content, all of these features can guide decisions between conservative management and minimally invasive treatment [31]. Additionally, Contrast-Enhanced Ultrasound (CEUS) is also being explored further for its ability to delineate cyst vascularity while it also helps to exclude solid or inflammatory components in pelvic cystic masses, thereby offering a radiation-free option having improved lesion characterisation as compared to standard ultrasound [30,32]. High-frequency micro-ultrasound (29-70 MHz), which provides near-histologic resolution of the prostate and seminal vesicles, can be helpful in Zinner syndrome diagnosis, as it allows more precise evaluation of the ejaculatory ducts and adjacent soft-tissues [30,33].

Management Strategies and Emerging Therapeutic Approaches in Zinner Syndrome

Zinner syndrome is managed in relation to the severity of the symptoms and the age of the patient. Conservative observation often helps in asymptomatic cases, where frequent imaging is done to keep track of the cyst size also to avoid possible complications [34]. Patients with symptoms, especially with the presence of pelvic pain, haematuria or infertility, might be subject to surgery [34]. Less invasive interventions e.g. laparoscopic excision of the seminal vesicle cyst would enable precise resection with small incisions, offering less postoperative pain and shorter days of hospitalisation, but could be technically difficult in complicated

anatomy [34]. Robotically-aided excision offers greater dexterity and visualisation, which improves accuracy and may minimise complications during the surgery, but it needs specialised equipment and expertise, which have already proved effective at minimising symptoms and maintaining fertility in selected cases [35]. Transurethral resection with methylene blue guidance has been mentioned in case of patients presenting with ejaculatory duct obstruction, as a less invasive treatment modality, whereby it is possible to identify and remove the obstruction with minimal effect to surrounding structures, however it may result in recurrence when the obstruction is extensive [36].

Emerging therapies in Zinner syndrome expand beyond traditional excision and transurethral resection and are aimed at less-invasive, fertility-sparing and image-guided therapies. Alpha-blockers (e.g., tamsulosin or silodosin) were reported to improve medical symptoms in several individual cases, and may be used as a first-line approach, or as an adjunct, when planning definitive medical treatment [37]. Endoscopic seminal vesiculoscopy (Transurethral Seminal Vesiculoscopy, TRU-SVS) using techniques that include holmium-laser incision, stone removal and internal drainage has become a less invasive procedure to directly treat intravesicular stones, re-establish ejaculatory duct patency and alleviate symptoms without major dissection of the pelvis [38,39]. Image-guided percutaneous techniques (transperineal, transgluteal or transvesical drainage) are becoming an increasingly popular option in cases of infected or symptomatic cysts or abscesses to achieve immediate decompression and source control [40]. Conventional and emerging management options in Zinner Syndrome are detailed in [Table/Fig-3] [36,41-48].

Prognosis, Research Gaps, and Future Perspectives in Zinner Syndrome

The overall prognosis of Zinner syndrome is positive because the majority of asymptomatic patients do not require treatment and those with symptoms generally get excellent relief after minimally invasive or surgical removal of seminal vesicle cysts laparoscopic, robotic, or endoscopic [5]. However, the long-term results are not clearly outlined, especially with regards to fertility recovery, cyst recurrence, and contralateral renal functioning because most of the evidence is based on case reports and limited series with little follow-up [49]. Research gaps that exist today are the lack of prospective multicenter data, inconsistency in reporting of reproductive outcomes, and insufficient molecular knowledge of the disorder [49]. New genomic studies about somatic or germline mutations in GATA3, PAX8, MYEOV, BAGE, NAALAD2, has indicated potential developmental pathways but needs to be validated in larger cohorts [24,50].

CONCLUSION(S)

Zinner syndrome is a rare congenital malformation of the male genitourinary tract, which is mainly due to abnormal development of mesonephric ducts. Although, it is commonly asymptomatic, occasionally it may have a urinary, reproductive, or mass-effective symptomology, which requires specific diagnostic and treatment approaches. MRI remains the gold standard for diagnosis, with management being either through simple observation or minimum invasive or robotic-assisted surgeries. New treatments are aimed at fertility conservation and symptom management. Regardless of positive results, there are still gaps in the prognosis of long-term reproduction and molecular insights, which should be utilised by multicentre research and genetic studies to streamline care.

Approach	Description	Advantages	Limitations/considerations	Evidence (studies/ case reports)
Conservative Observation	Regular follow-up and imaging in asymptomatic patients	Avoids unnecessary intervention; safe if stable	Risk of progression or complications; requires long-term surveillance	Conservative follow-up for asymptomatic seminal vesicle cysts described with stable outcomes in case reports (Almuhanna AM et al., 2021) and reviews recommending surveillance unless symptoms occur (Anwaar A et al., 2025) [41,42].
Laparoscopic excision	Minimally invasive removal of seminal vesicle cysts	Precise resection, less postoperative pain, shorter hospitalisation	Technically challenging in distorted anatomy	Successful laparoscopic excision reported in case with symptom resolution (Jarzemski P et al., 2014) [43]
Robotic-assisted excision	Robotically-aided cyst excision with enhanced visualisation.	Greater dexterity, accuracy, improved safety, fertility preservation.	Requires advanced expertise and specialised equipment	Case report documents safe removal of large cysts with excellent visualisation and functional outcomes through robotic-assisted excision (Carbin DD et al., 2022) [44]
Transurethral Resection (with Methylene Blue Guidance)	Endoscopic removal of ejaculatory duct obstruction.	Minimally invasive, preserves surrounding structures.	Risk of recurrence in extensive obstructions.	TURED supported by case report demonstrating improvement in semen parameters and ejaculatory symptoms using dye-guided localisation (Kardoust Parizi M et al., 2013) [36]
Alpha-blocker Therapy (e.g., Tamsulosin, Silodosin)	Medical management to relieve obstructive urinary/ejaculatory symptoms.	Non-invasive, symptom relief, may serve as first-line or adjunct therapy.	Symptomatic only, does not address structural cause.	Symptom improvement reported in case with silodosin for painful ejaculation (Uetani M et al., 2023) [45]
Endoscopic Seminal Vesiculoscopy (TRU-SVS)	Direct visualisation and treatment using holmium-laser incision, stone removal, or drainage.	Restores duct patency, minimally invasive, fertility-sparing.	Limited availability, requires expertise.	Holmium-laser SVS documented in case reports demonstrating restored drainage and symptom resolution (Andrade V et al., 2023; Zarli M et al., 2025) [46,47].
Image-Guided Percutaneous Drainage (Transperineal, Transgluteal, Transvesical)	Image-guided aspiration/drainage of infected or symptomatic cysts.	Immediate decompression, useful in acute infection/ abscess.	Temporary solution; may require definitive surgery later.	Image-guided drainage reported effective for seminal vesicle abscess/cyst decompression in acute settings (Hooshyari A et al., 2024) [48]

[Table/Fig-3]: Conventional and emerging management options in Zinner Syndrome [36,41-48].

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Oct 17, 2025
- Manual Googling: Jan 13, 2026
- iThenticate Software: Jan 16, 2026 (2%)

ETYMOLOGY: Author Origin

EMENDATIONS: 7

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? NA
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Oct 02, 2025**
Date of Peer Review: **Dec 06, 2025**
Date of Acceptance: **Jan 19, 2026**
Date of Publishing: **May 01, 2026**