



## A COMPREHENSIVE REVIEW OF THE PROSTATE GLAND AND BENIGN PROSTATIC HYPERPLASIA: HISTORICAL PERSPECTIVES AND THEIR ACKNOWLEDGMENT IN THE UNANI SYSTEM OF MEDICINE

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<p><b>Article Info</b></p> <p><b>Article Received:</b> 30 April 2026, <b>Article Revised:</b> 20 May 2026, <b>Article Accepted:</b> 10 June 2026.</p>	<p><b>ABSTRACT</b></p> <p>The historical understanding and clinical management of the prostate gland and its disorders have witnessed a remarkable evolution, from ancient misconceptions to the evidence-based practices of modern medicine. In antiquity, anatomists such as Herophilus and Galen referred vaguely to “c,” likely the seminal vesicles, as the prostate gland had not yet been recognized due to limitations in human dissection and reliance on animal models. The Renaissance marked a turning point when Niccolò Massa and Andreas Vesalius accurately described and illustrated the prostate, establishing the anatomical foundation for subsequent advances in urology. Today, Benign Prostatic Hyperplasia (BPH) is understood as a non-malignant enlargement of the prostate gland, predominantly affecting elderly men. Clinically, it is characterized by lower urinary tract symptoms (LUTS) and bladder outlet obstruction (BOO), significantly impairing quality of life. Current treatment options include pharmacological therapies such as <math>\alpha</math>-adrenergic blockers and 5<math>\alpha</math>-reductase inhibitors, alongside surgical interventions like transurethral resection of the prostate (TURP). Although effective, these approaches are frequently associated with adverse outcomes, including sexual dysfunction, cardiovascular complications, and perioperative risks, underscoring the need for safer and more holistic alternatives. Interestingly, classical Unani medicine, rooted in Greco-Arabic medical thought, described conditions resembling BPH centuries before the condition was anatomically recognized. Disorders such as <i>Waram-e-Unq-al-Mathana</i> (inflammation of the bladder neck) and <i>Insidad Majra-i-Mathana</i> (urinary passage obstruction) reflect clinical awareness of urinary difficulties aligned with modern BPH symptomatology. Unani scholars, including Hippocrates, Galen, and Avicenna, emphasized humoral imbalance (Sue Mizaj) as a central pathology, recommending herbal formulations, dietary regulation, and lifestyle modifications as therapeutic measures. This review explores the convergence of historical insights and modern biomedical understanding of BPH. By integrating contemporary clinical knowledge with Unani principles, it highlights the potential of traditional therapies as complementary strategies for symptom control, improved quality of life, and reduced adverse effects in the management of BPH.</p> <p><b>KEYWORDS:</b> Greco-Arabic, Prostate Gland, Urological History, Niccolò Massa, Herophilus, Galen &amp; BPH Review.</p>
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## INTRODUCTION

One of the most surprising realizations for modern urologists is the complete absence of any reference to the prostate gland in ancient, Byzantine, or Islamic medical texts, regardless of the terminological confusion surrounding the organ.<sup>[1]</sup> This historical omission can be attributed to the limitations of anatomical study during those eras. Until the 14th century, anatomical dissections—when permitted at all—were almost exclusively performed on animals. However, significant anatomical variations between species complicated the understanding of human structures. For instance, in animals like dogs, cats, cattle, and horses, the prostate is typically bilobed, while in sheep and goats, it is absent. Moreover, unlike herbivores, carnivores do not possess seminal vesicles, making cross-species comparisons unproductive for identifying the prostate.<sup>[2]</sup> During a brief period in Alexandria around 300 BCE, human dissection was permitted, positioning the city as a hub of Hellenistic scientific inquiry. Among the prominent figures of this era was **Herophilus**—often called "**the first anatomist**"—who made groundbreaking descriptions of male reproductive organs. He may have come close to identifying the prostate, as suggested by a passage in Galen's later anatomical summaries. Galen recounted that "glandular bodies" (likely referring to the seminal vesicles) secrete fluids that enter the male urinary tract, enhancing sexual pleasure and lubrication. Herophilus, according to Galen, labeled these structures "glandular assistants" (*parastatai adenoides*) and other nearby anatomical features as "varicose assistants" (*parastatai kirsoeides*), referring to what we now identify as the ampullae of the vas deferens. However, the most compelling argument against interpreting Herophilus's "glandular assistants" as references to the prostate lies in his consistent use of plural terminology, implying bilateral structures, like the seminal vesicles and ducts, rather than a singular organ like the prostate. By the 2nd century CE, **Galen**, working within the Alexandrian anatomical tradition, referred to certain glandular structures as "semen-containing assistants." However, he did not specifically identify the prostate gland. Consequently, by the end of the classical era, although the seminal vesicles and ducts had been differentiated both anatomically and terminologically, the prostate remained unrecognized. More accurate identification of the prostate only became possible with the revival of human dissection in later medical history, representing a pivotal advancement in the development of urology. Concerning this subject, Latin anatomical literature of the 16th century can be categorized into three distinct phases: the pre-Vesalian phase, which largely repeated ancient understandings and perpetuated Herophilean-Galenic terminology; the Vesalian phase, marked by Vesalius's anatomical depictions and descriptions in 1538 and 1543; and the post-Vesalian phase, characterized by varying linguistic practices and ongoing speculation regarding the function of the organ. The challenges faced in identifying the prostate during early dissections are evident in Leonardo da Vinci's

anatomical sketches. Despite his detailed and artistically rendered illustrations of the male genital system, based on his autopsies, the prostate is notably absent. This omission may reflect the influence of classical medical texts, which did not mention the organ. Leonardo's work highlights how early modern anatomical understanding was heavily influenced by prevailing theoretical frameworks. Similarly, Jacopo Berengario da Carpi, a pre-Vesalian anatomist and professor in Pavia and Bologna, referred only to the seminal vesicles in 1520, writing: "Galen, following Heracleus (i.e., Herophilus), refers to them as parastata adeniformia because they are surrounded by gland-like tissue." The earliest known reference to the prostate appears in 1536, when Venetian physician Niccolò Massa briefly mentioned it in his *Introductory Book of Anatomy*: "you will find a glandular flesh upon which the neck of the bladder and the ends of the previously mentioned seminal vessels rest... The seminal vessels also pass through these carunculae."

However, it was Andreas Vesalius, the central figure in the reform of anatomy, who first accurately illustrated and described the prostate gland. His 1538 work includes the earliest known image of the prostate. In 1543, Vesalius distinguished the vasa deferentia and the prostate from each other, though he did not yet distinguish the seminal vesicles. He located the prostate between the bladder and the surrounding sphincter, referring to it in the text and illustrations as a "glandulous body" (*corpus glandulosum*) and a "glandulous bystander." In doing so, Vesalius reinterpreted the Galenic term "glandular bodies," transferring it from the familiar seminal vesicles to the newly identified prostate. He described it as follows: "The glandulous body into which the vessels transporting semen converge after joining lies at the base of the bladder and its neck. It is a singular body, often larger than the testicles. It was not perfectly round but had indentations in the front and back, while being spherical on the sides. The vesical canal runs through its center." Scholars in the post-Vesalian era acknowledged the prostate as a distinct anatomical structure, although debate persisted regarding whether it was a paired or singular organ. Four principal theories emerged concerning its function: one suggested the prostate refined semen from the testes; another proposed it secreted a pungent, whey-like fluid to enhance sexual pleasure; a third claimed it produced a substance to moisten and protect the urethra; and a fourth maintained that semen itself originated in the prostate.<sup>[3]</sup> Over time, attention shifted from theoretical speculation to clinical implications, particularly about **BPH**, a condition associated with the prostate gland that has troubled men since antiquity. BPH is a prevalent non-malignant urological condition commonly affecting elderly men. Histologically, it is classified as *Benign Prostatic Enlargement* and is marked by the proliferation of both epithelial and stromal cells within the peri-urethral zone of the prostate, thus justifying the designation

*hyperplasia*.<sup>[4]</sup> Approximately 50% of men in their sixth decade report experiencing *Lower Urinary Tract Symptoms (LUTS)* associated with *Bladder Outlet Obstruction (BOO)*. The incidence of BPH increases with age, as demonstrated by autopsy studies that reveal histological evidence of BPH in 8% of men in their 40s, 50% in their 60s, and up to 80% by the ninth decade of life.<sup>[5-7]</sup> It is generally recognized that, given sufficient lifespan, most men will develop histological signs of BPH. Although a strong correlation exists between BPH and LUTS, the presence of histological BPH does not always coincide with significant urinary symptoms. Conversely, not all individuals presenting with LUTS or BPH exhibit noticeable prostate enlargement.<sup>[8,9]</sup> *Clinical BPH* is diagnosed when at least two of the following criteria are met: (A) moderate to severe LUTS, indicated by an *International Prostate Symptom Score (IPSS)* greater than 8; (B) an enlarged prostate, defined as a total prostatic volume exceeding 30 mL; and (C) a maximum urinary flow rate under 15 mL/s.<sup>[10]</sup> Furthermore, the impact of LUTS on an individual's *quality of life (QoL)* varies significantly, underscoring the need for personalized approaches to assessment and management.<sup>[11]</sup>

#### Tracing the Historical Roots of BPH: The Prostate Gland in Unani Medical Tradition

In Classical Unani literature, while not explicitly naming BPH as a distinct disease entity, reflects an awareness of prostate enlargement and its associated symptoms. Traditional Unani physicians managed such conditions using various medicinal preparations and minor surgical techniques, including puncturing, incisions, and punching. Although the term "Benign Prostatic Hyperplasia" does not appear in early texts, the phrase "*Izm-i-Gudda-i-Mazi*" is employed as a literal translation of the modern term. In Unani medicine, conditions associated with prostate enlargement are described using various terms, such as *Sala'a Gudda-i-Mazi*, *Warm-i-Gudda-i-Mazi*, and *Warm-i-Unq-i-Mathāna*. Symptomatic treatments for *Izm-i-Gudda-i-Mazi* are categorized under related urological complaints, including *Ihtibas al-Bawl* (urinary retention), *Taqīr al-Bawl* (dribbling of urine), *Usr al-Bawl* (difficulty in urination), *Hurqat-al-Bawl* (burning urination), *Kasrate-e-Bawl* (frequent urination), and *Salasul Bawl* (urinary incontinence). These references underscore the historical depth of clinical observations in Unani medicine, reflecting a systematized approach to the diagnosis and management of symptoms now associated with BPH.

**Greco-Arabic scholars** were well aware of the causes of *Ihtibās al-Bawl* (Retention of urine), *'Usr-al-Bawl* (Dysuria), *Taqīr al-Bawl* (Dribbling of urine), *Salasul bawl* (Incontinence of urine), etc.<sup>[12]</sup> Classical Unani texts described that *Waram-i-aza-i-mujawira* (inflammation or swelling of neighboring organs) of the urethra may compress the urethra and obstruct the urine flow. Such problems could be related to benign prostatic hyperplasia (BPH), a condition in which an enlarged prostate

compresses the prostatic urethra and produces symptoms like hesitancy, intermittent urination, a lower urine stream, incomplete emptying, and post-void dribbling. The main cause of swelling (*waram*) or inflammation of any *Uzuw-e-Gudadi* (Gland) in the body has been identified as an abnormal accumulation of thick phlegm, known as *Balgham-i- Ghalīz* or *Mawād -i- Ghalīz*.<sup>[13]</sup>

**Hippocrates, Father of Medicine** (460-370 BCE), described "*Auram*" (swellings) as abnormal growths due to imbalances in the four humours (*Akhlat-e-Arba*). A soft swelling is caused by "*Khilt-e-Balgham*," while a hard swelling is due to "*Waram-i-Šulb*" or "*Sala'a*" from an excess of black humour. "*Khilt-e-Sawdā'*" Unani physicians classify "*Sala'a*" (tumor) as a type of abnormal growth or swelling. *Maseehi* described "*Sala'a*" as an enlargement or overgrowth caused by "*Balgham*" or "*Mawād-i-Ghalīz*".<sup>[14]</sup>

**Abu Mansur al-Hasan Ibn Nuh al-Qumri** (Mid-10th century) writes in his treatise "*Ghina Muna*" (Book of Wealth and Wishes) that urine retention or dribbling can be attributed to the inflammation of the kidney and urinary bladder (*waram-i-Gurda-wa-Mathāna*), *sudda* (Obstruction), or growth in the urinary tract.<sup>[15]</sup>

The Persian physician **Razi** (854–925 CE) also observed that urinary dribbling is more commonly seen in the elderly, attributing it primarily to a cold temperament imbalance (*Su'-i-Mizaj Barid*).<sup>[16]</sup>

The renowned medical text, **the Canon of Medicine by Avicenna** (980–1037 AD), outlines the causes of urinary symptoms, including retention, dysuria, dribbling, and incontinence. These include *Waram-i-Šulb*, *Sudda Majārī al-Bawl*, *Istirkhā' al-Mathāna* (laxity of the bladder), an abnormally hot temperament of the bladder, inflammation in nearby structures, and displacement of the bladder. Avicenna described two types of swelling: hot (*Waram-i Hārr*) and hard (*Waram-i Šulb*). Hot swelling, also called inflammation (*İltihāb*), leads to symptoms of hot temperament (*Sū'-i-Mizāj Hār*) like burning urination, increased thirst, and fever. Hard swelling, often caused by infection or wear and tear, can obstruct urine and bowel flow, resulting in symptoms such as dribbling, dysuria, anuria, and constipation. Avicenna also noted that this type of swelling can invade the bladder and block urine flow, leading to *Ihtibās al-Bawl* (urinary retention) and a weak, intermittent urine stream due to hypertrophy and flaccidity of the bladder muscles.<sup>[12]</sup>

**Ismail Gorgani** (1041-1136 CE) wrote the Persian medical encyclopedia, "*Thesaurus of the Shah of Khwarazm*" has discussed the causes of dysuria, dribbling of urine, incontinence, or burning micturition as any growth in the urinary tract resulting in obstruction (*sudda*), abnormally cold temperament (*Sū'-i-Mizāj Bārid*), weakness of the bladder muscles (*Du'f-i Ađala-al-Mathāna*), alcohol intake, use of diuretics,

excessive fluid intake, dislocation of vertebrae, musculoskeletal injuries affecting the bladder the, and diseases of the surrounding structures. They classified the swelling at the bladder neck into two types: hot swelling (*Waram-i-Harr*) and cold swelling (*Waram-i-Barid*). He suggested that hot swelling is caused by blood or yellow bile (bilious), while cold swelling is caused by phlegm or black bile. Furthermore, he noted that urinary symptoms and constipation are associated with cold swelling (*Waram-i-barid*).<sup>[17]</sup>

According to reputed Unani texts such as "*The Canon of Medicine* and *Treasure of Khwarzamsahi*," a type of constrictive swelling (*Waram-i-zaghit*) can be obstructed by palpating over the urethra or neck of the bladder. This can lead to symptoms such as dysuria (*Usr al-Bawl*), dribbling of urine (*Taqfir al-Bawl*), and retention of urine (*Ihtibas al-Bawl*).

**Avenzor (1094-1162)**, in his famous book "*Kitab-Al-Taiseer*", attributed the inflammation at the neck of the urinary bladder as the reason for urinary retention.<sup>[18]</sup>

**Muhaddhab Al-Deen Al-Baghdadi** (1117-1213 AD) wrote a book, "*Mukhtarat-fit-Tibb*" (Choice Book on Medicine), which discusses the presence of *waram*, *sudda*, *warts*, accumulated blood, and pus. He also outlined various causes of urinary retention, dribbling, dysuria, and incontinence, such as healed ulcers, pressure from surrounding structures, inflammation in surrounding structures, excessive cold or heat in the bladder, weak bladder muscles, vertebral disc dislocation, and diabetes.<sup>[19]</sup>

**Ibn-al-Quff** (1233-1286) in his book *Kitab-al-Umdah Fi-A-Jarahat* (Basics in Art of Surgery), described that *Waram-e-Ghudad is Waram-e-Balghami*.<sup>[20]</sup>

The Mughal physician **Muhammad Akbar Arzani** (1772 CE), in his renowned treatise *Tibb Akbar*, discussed the causes of urinary retention, dribbling, incontinence, and burning urination. He attributed these symptoms to *waram* (swelling), abnormal growths within the urinary tract, weakness of the bladder muscles (*Du'f-i Adala al-Mathāna*), and vertebral dislocation.<sup>[21]</sup>

The book "**Akseer e Azam**" by Azam Khan comprehensively addresses the causes of urinary retention. These causes encompass urinary tract growth, weakened bladder muscles (*Du'f-i Adala-al-Mathāna*), and damage to the bladder musculature.<sup>[22]</sup>

In the modern era, Venetian anatomist Nicolo Massa described the prostate gland in the 16th century. The earliest operations performed on the prostate were in 1639 when French urologist Joseph Covillard described the trans-perineal incision to remove the prostate tissue in a lithotomy position. However, the pathological understanding of the condition remained unclear. Jean Riolan the Younger (1577–1657) was the first to propose

that an enlarged prostate could lead to urine retention. Despite this discovery, prostate enlargement was largely overlooked by scientists for a significant period. By the late 18th century, specialized surgical instruments for addressing the condition were developed. In the early 19th century, it became evident that removing the obstruction alone, without addressing the prostate gland itself, could be life-threatening for patients. This realization brought greater scientific attention to prostate enlargement, leading to the development of various medical and surgical treatments over time. Additionally, the increase in average life expectancy further drove the demand for effective treatments. Notably, the term "prostatism," previously used to describe symptoms of BPH, was deemed obsolete during the 4th International Consultation on BPH and was replaced by "LUTS."<sup>[23]</sup>

### Incidence and prevalence

BPH is increasingly recognized as a significant health concern associated with aging. Once primarily assessed through autopsy studies, it was found in approximately 50% of men in their sixth decade and nearly 90% by their ninth decade of life.<sup>[24]</sup> For instance, the prevalence is estimated at 104 per 1,000 men in their 50s, rising to 429 per 1,000 in their 80s.<sup>[25,26]</sup> Autopsy data further support this trend, revealing histological BPH in about 10% of men in their 30s, 20% in their 40s, increasing to 50–60% in their 60s, and reaching 80–90% in men aged 70 and above.<sup>[27]</sup>

Globally, the prevalence among men over 50 ranges between 20% and 62%. From a healthcare economics standpoint, the burden is considerable. In the United States alone, it accounted for 4.4 million outpatient visits, over 105,000 hospitalizations, and an estimated loss of 21 to 38 million work hours in 2003.<sup>[25,28]</sup>

In India, prevalence rates are similarly significant, recorded at 25%, 37%, 37%, and 50% for age groups 40–49, 50–59, 60–69, and 70–79, respectively. A large-scale multinational survey on aging men reported moderate to severe *Lower Urinary Tract Symptoms (LUTS)* in 34% of American men, 29% of European men, and 18% of Asian men aged 50–80 years.<sup>[29]</sup>

In the United States, both the prevalence and incidence of BPH and LUTS rose steadily between 1994 and 2000, continuing upward through 2007. These increases align with the global trend of population aging. By 2030, it is projected that 20% of the U.S. population will be aged 65 or older, including over 20 million men. Notably, the most rapidly expanding demographic is the oldest old—those over 85 years. The number of Americans aged 80 and above is expected to grow from 9.3 million in 2000 to 19.5 million by 2030, more than doubling within three decades.<sup>[30]</sup>

### Risk factors

Factors at the population level associated with BPH can be divided into two main categories: i) non-modifiable

factors, such as age, geography, and genetics, and ii) modifiable factors, including metabolic syndrome, obesity, physical activity, nutrition, and inflammation.

### Non-modifiable factors

#### Age

As men get older, their prostates tend to enlarge. Findings from the Krimpen and Baltimore Longitudinal Study of Aging indicate that the prostate grows annually by approximately 2.0% to 2.5% in older males.<sup>[31]</sup>

#### Genetic predisposition

The researchers also estimated that half of the men under 60 who underwent surgery for BPH had a hereditary form of the condition. In a subsequent study, they found that hereditary BPH was associated with larger prostate sizes and an earlier onset than non-hereditary cases. These results, along with other data, point to an autosomal dominant inheritance pattern. Additionally, a large-scale study by Ganpule et al. on the Indian population showed that the IPSS tends to be higher even at smaller prostate volumes when compared to Western populations.<sup>[32]</sup>

#### Geography

International studies have also highlighted geographic differences in prostate volume and the prevalence of LUTS. Men from Southeast Asia generally have notably smaller prostate volumes compared to their counterparts in Western countries.<sup>[33]</sup>

### Modifiable Risk Factors

#### Sex steroid hormones

Numerous studies have investigated the relationship between naturally occurring sex hormones, particularly testosterone, DHT, and estrogen, and the development of BPH and LUTS. Several have identified a higher risk of BPH in individuals with elevated serum levels of DHT and its metabolites. One prospective community-based study found that men with the highest midlife DHT levels had almost three times the risk of developing BPH compared to those with the lowest levels. However, other observational studies have reported either no link or even an inverse association between hormone levels and BPH or LUTS. Prior research has shown varying results regarding natural estrogen levels, with studies indicating positive, negative, or no correlation with BPH and LUTS.<sup>[34,35]</sup>

#### Metabolic syndrome

Metabolic syndrome refers to a cluster of metabolic disorders primarily resulting from modifiable lifestyle factors, such as poor diet and physical inactivity, habits commonly seen in Western cultures. It encompasses conditions like obesity, glucose intolerance, dyslipidemia, and hypertension, all of which elevate the risk of cardiovascular disease. Research indicates a strong association between metabolic syndrome and an increased risk of BPH as well as LUTS. For instance, a study involving 2,372 men found that those with at least

three components of metabolic syndrome faced an 80% higher risk of developing LUTS compared to men without any components. Additionally, individual elements of metabolic syndrome have been specifically linked to both BPH and LUTS.<sup>[36,37]</sup>

#### Obesity

Different definitions of metabolic syndrome don't agree on which measures should be used to define obesity, such as BMI, waist circumference, or waist-to-hip ratio. However, there is considerable evidence suggesting a strong, positive correlation between most measures of body size and prostate size. Body weight, BMI, and waist circumference are positively linked to prostate volume. This means that the greater the weight, BMI, or waist circumference, the greater the prostate volume.<sup>[38]</sup>

#### Dyslipidemia

Formal criteria for metabolic syndrome also include low HDL cholesterol, defined as less than 40 mg/dL in men, and high serum triglycerides, defined as 150 mg/dL or higher.<sup>[36]</sup> Another potential manifestation of dyslipidemia is an increase in serum LDL cholesterol levels, but the LDL level is not considered a component of the metabolic syndrome. There is limited data available on the relationship between dyslipidemia, benign prostatic hyperplasia (BPH), and lower urinary tract symptoms (LUTS). Four studies have been conducted on this topic, with two showing positive associations and two showing no associations. In a Swedish cohort, low HDL cholesterol was linked to increased prostate volume.<sup>[39]</sup> However, a cohort study of Turkish men living in the community did not find significant associations between serum lipids and BPH or LUTS.<sup>[40]</sup> Similarly, a case-control study by Zucchetto et al found no connections between serum lipids and BPH.<sup>[41]</sup>

#### Diabetes and disruptions in glucose homeostasis

There is a correlation between an increased risk of BPH (benign prostatic hyperplasia), LUTS (lower urinary tract symptoms), and disruptions in glucose homeostasis at various levels. These disruptions can range from changes in serum insulin-like growth factor (IGF) concentrations to the diagnosis of clinical diabetes. Research has found that elevated serum concentrations of IGF-1 and insulin-like growth factor binding protein 3 are linked to an increased risk of both clinical BPH and BPH surgery.<sup>[42]</sup> In several studies, it has been found that higher serum insulin, elevated fasting plasma glucose, and physician-diagnosed diabetes are associated with larger prostates and an increased risk of prostate enlargement, clinical BPH, BPH surgery, and LUTS.<sup>[43]</sup>

#### Diet

Though the trends are mixed, there are some signs that both macronutrients and micronutrients may influence the risk of BPH and LUTS. In terms of macronutrients, the risks of symptomatic BPH and BPH surgery may be increased by higher total energy intake, energy-adjusted

total protein intake, and consumption of red meat, fat, milk and dairy products, cereals, bread, poultry, and starch. Whereas, Vegetables (especially carotenoids), fruits, polyunsaturated fatty acids, linoleic acid, Vitamin A, and Vitamin D may decrease the risks of symptomatic BPH and LUTS.<sup>[44,45]</sup> Higher levels of circulating vitamin E, lycopene, selenium, and carotene have been inversely linked to BPH and LUTS in terms of micronutrients; zinc and vitamin C have been linked to both increased and decreased risk.<sup>[46,47]</sup>

### Inflammation

Most observational research implies a connection between inflammation and the onset of LUTS and BPH. It's unknown what mechanisms underlie this link. A plausible rationale is that the association is mediated by the metabolic syndrome, which stimulates oxidative stress and systemic inflammation. Prostate carcinogenesis has been linked to inflammation as a major trigger, and BPH may be a non-malignant proliferative route aided by oxidative stress and inflammatory mediators.<sup>[48]</sup> Men with LUTS are more likely to have higher serum C-reactive protein, a marker of systemic inflammation. At the same time, prior gonorrheal infection or prostatitis increases the likelihood of BPH surgery and LUTS. A history of infection with gonorrhea, chlamydia, or trichomoniasis increases the risk of elevated PSA, and high serum IgG antibody titers to cytomegalovirus, herpes virus, human papillomavirus, and hepatitis are associated with LUTS.<sup>[49]</sup>

### Smoking

Several studies also support the existence of an inverse, protective effect of smoking on the risk of BPH and LUTS. In the Massachusetts cohort, current cigarette smokers were half as likely to have clinical BPH as nonsmokers. Heavy smoking was also associated with a decreased risk in the Zurich study and in an Italian study, each of which showed a 50% decreased risk of BPH surgery or clinical BPH in heavy smokers compared to nonsmokers.<sup>[50]</sup>

### Alcohol

Interestingly, several large studies have consistently shown an inverse association, or protective effect, between alcohol intake and both BPH and LUTS. Men who consumed moderate alcohol in the PLCO were 30% less likely to have clinical BPH, 40% less likely to undergo TURP, and 20% less likely to have nocturia. Community-dwelling men in Zurich who drank alcohol had a significantly lower risk of BPH surgery or diagnosis than non-drinkers. Given its strong diuretic effects, the idea that alcohol use in any amount may prevent the development of BPH and LUTS would appear illogical. However, since a modest amount of alcohol consumption has been associated with a lower risk of coronary artery disease, one possible reason is that alcohol has positive effects on the cardiovascular system, which lowers BPH and LUTS.<sup>[51,52]</sup>

### Physical activity

Higher levels of physical activity have been linked to a reduced risk of BPH and LUTS in several large studies, indicating that exercise may act as a protective factor. Compared to a sedentary lifestyle, moderate to vigorous physical activity reduced the incidence of BPH or LUTS by up to 25%, according to a meta-analysis of 11 studies (n = 43,083 males), with the protective effect increasing as activity levels rose.

### Etiopathogenesis

The exact cause of BPH remains unknown, but two main theories have been proposed to explain its development. Various researchers have expressed differing opinions regarding the development of BPH, which are summarized below.

### Hormonal theory (Role of Androgens)

#### Testosterone

In older men, testosterone is considered a key contributor to the development of benign prostatic hyperplasia (BPH), largely due to the disrupted balance between testosterone and dihydrotestosterone (DHT). Around 90% of the androgens present in the prostate exist in the form of DHT. This more potent androgen, estimated to be 2–3 times stronger than testosterone, is produced from testosterone by the action of the enzyme steroid 5 $\alpha$ -reductase within the prostate. DHT is a major driver of stromal and glandular cell growth. Upon binding to hormone receptors, DHT interacts with specific DNA-binding sites in the nucleus, triggering the transcription of androgen-responsive genes and promoting protein synthesis, which leads to glandular hyperplasia.<sup>[53]</sup>

Testosterone and DHT affect the prostate through both direct and indirect pathways. While a consistent link between circulating androgen levels and prostate enlargement has not been established, the concentration of androgens and androgen receptors within the prostate itself is thought to be crucial to BPH development. Early research showed that DHT concentrations in hyperplastic prostate tissue were 3–4 times higher than in normal tissue, as demonstrated in studies by Meikle et al., Geller et al., Hammond, and Krieg. However, later research has not consistently confirmed these differences. In the adult prostate, androgen receptors are predominantly located in luminal epithelial cells rather than stromal cells. Castration at any age reduces testosterone levels, leads to the loss of secretory luminal epithelial cells, and results in a decrease in prostate size.<sup>[54]</sup>

#### Estrogen

While the prostate is typically recognized as a target for androgens, it is also significantly influenced by estrogen. Estradiol—the most active form of estrogen—is found in higher concentrations within the prostate than in the plasma. Research has demonstrated that castrated dogs injected with both 3 $\alpha$ -androstane diol and 17 $\beta$ -estradiol exhibited substantially greater prostate growth than with either compound alone, emphasizing the synergistic

effect of androgens and estrogens in driving prostatic hyperplasia. Although the precise mechanisms by which estrogen affects the prostate are not fully understood, a higher estradiol-to-DHT ratio has been closely linked to stromal hypertrophy. Additionally, dietary estrogens like phytoestrogens, lignans, and flavonoids have been found effective in preventing and alleviating prostate conditions. Estrogen's dual action in the prostate is thought to be regulated through two distinct estrogen receptor subtypes: ER $\alpha$ , which stimulates prostate cell proliferation, and ER $\beta$ , which promotes apoptosis.<sup>[55]</sup>

**The Role of growth factors (Neoplastic theory)**

Growth factors are small peptide molecules that stimulate, or in some cases inhibit, the cell division and differentiation processes.<sup>[114]</sup> Cells that respond to the growth factors have specific receptors on their surface for that growth factor. These receptors are linked to a variety of transmembrane and intracellular signaling mechanisms." The interaction between growth factors and steroid hormones can change the balance between cell proliferation and cell death, leading to the

development of BPH.<sup>[115]</sup> After Story initially described the basic fibroblast growth factor in BPH, a range of growth factors have been identified in normal, hyperplastic, and neoplastic prostatic tissue. In addition to b-FGF (FGF-2), other factors such as acidic FGF (FGF-1), Int-2 (FGF-3), keratinocyte growth factor (FGF-7), transforming growth factor (TGF- $\beta$ ), and epidermal growth factor have also been linked to prostate growth. TGF- $\beta$  is known to strongly inhibit proliferation in normal epithelial cells across various tissues. Growth factors likely play a role in the development of BPH.<sup>[55]</sup>

**Pathophysiology**

In benign prostatic hyperplasia (BPH), blockage of the prostatic urethra or bladder neck leads to lower urinary tract symptoms (LUTS), which can range from mild to severe. Microscopic BPH in the prostate's transitional zone may result in prostate enlargement or increased smooth muscle growth, both of which contribute to bladder outlet obstruction, symptomatic BPH, and LUTS.<sup>[56]</sup>

**PATHOPHYSIOLOGY OF BENIGN PROSTATIC HYPERPLASIA**

**1. Hormonal changes**

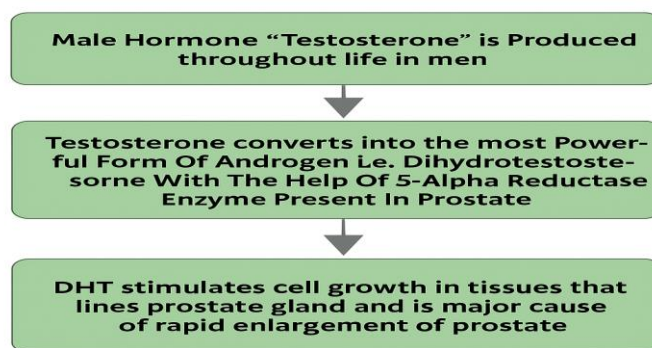


Figure No. 1: Hormonal changes in BPH.

**2. Inflammation**

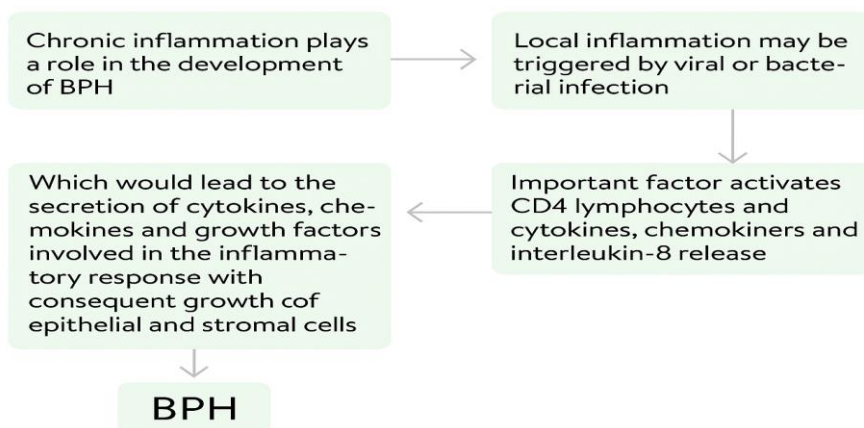


Figure. No. 2: Inflammation in BPH.

### 3. Age-related tissue remodeling

#### Prostate tissue remodeling in the transition zone is characterized

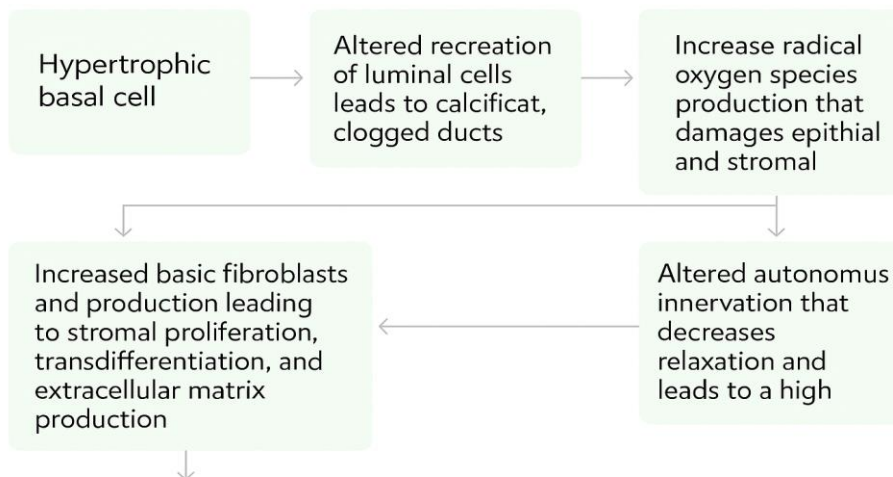


Figure. No. 3: Age-related Tissue Remolding BPH.

#### Morphological features

Benign prostatic hyperplasia (BPH) is fundamentally a true hyperplastic condition.<sup>[57]</sup> According to McNeal's research, most early nodules found around the urethra are mainly stromal. In contrast, initial nodules in the transition zone show glandular proliferation, which may be linked to a relative decrease in stromal content. An enlarged prostate typically appears smooth, nodular, and firm, weighing between two to four times the normal, reaching around 40–80 grams. The internal appearance of the gland depends on whether the hyperplasia is primarily glandular or fibromuscular. In cases of mainly glandular benign prostatic enlargement (BEP), the tissue is yellow-pink, soft, honeycombed, and secretes a milky fluid. On the other hand, predominantly fibromuscular BEP presents a firm, uniform cut surface without milky discharge. Hyperplastic nodules form masses chiefly in the inner periurethral zone of the prostate, pushing adjacent prostatic tissue into a pseudo-capsule, which helps surgeons remove these nodules more easily. Remaining peripheral prostate tissue may later develop new nodules or even progress to carcinoma.<sup>[58]</sup>

**Microscopically,** benign prostatic hyperplasia consistently shows an overgrowth of all three tissue types—glandular, fibrous, and muscular—in varying proportions. Glandular hyperplasia is the most common and is marked by prominent papillary projections within the glandular acini, supported by thin fibrovascular cores. The glandular lining features two layers: an inner layer of tall columnar cells that secrete mucus and have indistinct cell borders, and an outer layer composed of cuboidal to flattened cells with nuclei located at the base. When fibromuscular hyperplasia predominates, it appears as groups of spindle-shaped cells, closely resembling uterine fibromyoma. In addition to glandular

and/or fibromuscular hyperplasia, typical histologic findings include lymphocytic aggregates, small areas of infarction, corpora amylacea, and regions of squamous metaplasia.<sup>[58]</sup>

#### Clinical features

Benign Prostatic Hyperplasia (BPH) typically presents with Lower Urinary Tract Symptoms (LUTS), which may include hesitancy, urgency, frequent urination, dribbling, a weak urine stream, painful straining to urinate (strangury), nocturia, urge incontinence, and bedwetting (enuresis). In addition, symptoms related to Bladder Outlet Obstruction (BOO) may be present, such as urinary retention, a sensation of incomplete bladder emptying, painful urination, and occasionally, blood in the urine (hematuria).<sup>[5,6,59]</sup>

#### Complications of BPH

- ✓ Recurrent urinary tract infections,
- ✓ Urinary stones,
- ✓ Hematuria,
- ✓ Diverticulae of the Urinary bladder,
- ✓ Hydroureter,
- ✓ Hydronephrosis,
- ✓ Renal failure,
- ✓ Malignancy.

#### Diagnosis and evaluation

At first, the assessment of patients with BPH or LUTS involved only a medical history review and physical examination, including a digital rectal exam (DRE) and urinalysis. Basic blood tests and imaging were primarily used to detect urinary tract damage or rule out other conditions. As technology advanced, new diagnostic and therapeutic tools were introduced. These included ultrasonography, computed tomography (CT),

transurethral ultrasonography, and urodynamic studies. Ultrasound became particularly useful for measuring post-void residual urine and estimating prostate volume. Serum prostate-specific antigen (PSA) testing also became a standard component in evaluating men with urinary symptoms.<sup>[9]</sup>

The American Urological Association Symptom Index (AUA-SI), also known as the International Prostate Symptom Score (IPSS), is now considered the most reliable tool for assessing the severity of BPH and planning treatment. This index is recommended by the American Urological Association, European Association of Urology, and the World Health Organization for routine evaluation of patients suspected of having BPH. According to their guidelines, mild symptoms (low IPSS) are managed through observation or "watchful waiting," while moderate to severe symptoms (IPSS ≥ 8) call for a formal treatment approach. Surgery is reserved for cases with complications.<sup>[60]</sup>

Despite its limitations, the DRE still plays a role in assessing the prostate's size, firmness, symmetry, and presence of nodules. Invasive diagnostics like pressure-flow studies and full urodynamic assessments can help identify bladder neck obstruction, though these are generally reserved for more severe cases or when surgical treatment is being considered. Imaging of the upper urinary tract through intravenous urography or CT is rarely recommended, as these patients usually do not show a higher rate of upper tract abnormalities.<sup>[61]</sup>

**Management<sup>[60]</sup>**

When BPH symptoms are mild to moderate and not particularly troublesome, a strategy of "watchful waiting" is often employed. However, once symptoms become moderate to severe and begin to significantly affect daily life, active treatment becomes necessary. BPH treatment generally falls into two main categories: medical and surgical. Before the 1990s, surgical procedures like prostatectomy were the standard treatment. Over time, the transurethral incision of the prostate (TUIP), followed by the more commonly adopted transurethral resection of the prostate (TURP), became the preferred surgical methods. In recent years, medical management has gained prominence, revolutionizing BPH care. Current pharmacological options include alpha-adrenergic antagonists, 5-alpha-reductase inhibitors, antimuscarinics, beta-adrenergic agonists, phosphodiesterase type 5 inhibitors,

vasopressin analogs, and phytotherapies.<sup>[62]</sup> Among these, alpha-blockers are most frequently prescribed for relieving lower urinary tract symptoms (LUTS) associated with BPH, followed by 5-alpha-reductase inhibitors. Despite the shift toward medical therapy, TURP remains the most commonly performed surgical procedure for managing bothersome symptoms. While these treatments are generally effective in improving symptoms and quality of life, they may also cause side effects, most notably erectile dysfunction, reduced libido, and ejaculatory issues, which can be particularly concerning for patients. Beyond conventional treatments, various minimally invasive techniques have been introduced for BPH management. These include transurethral microwave thermotherapy, transurethral needle ablation, transurethral vaporization of the prostate, interstitial laser coagulation, prostatic urethral lift, laser enucleation, Aqua-ablation, and water vapor thermal therapy.<sup>[9]</sup> Despite these innovations, surgery continues to play a crucial role in specific cases. Additionally, experimental methods such as absolute ethanol injection, temporary implantable nitinol devices, intraprostatic botulinum toxin injections, and histotripsy are being investigated but are not currently recommended as standard treatment options.

**Perspective of BPH in the Unani system of medicine**

The Unani (Greco-Arab) system of medicine, practiced extensively in the Indian subcontinent and Central Asia, traces its origins to the teachings of Hippocrates, the renowned Greek physician and "Father of Medicine." This system is rooted in the classical humoral theory, which posits that the human body contains a specific balance of four humors: blood (Dam), yellow bile (Safra), phlegm (Balgham), and black bile (Sawda). The unique combination of these humors determines an individual's temperament (Mizaj), and any imbalance among them results in a state of "distemperament" (Su'-i-Mizaj), leading to disease. According to Unani principles, a predominance of blood creates a Sanguine temperament, yellow bile results in a Bilious temperament, phlegm causes a Phlegmatic temperament, and black bile produces a Melancholic temperament. Sanguine and Bilious temperaments are characterized as hot, whereas Phlegmatic and Melancholic temperaments are cold. The Unani approach to treatment focuses on three core principles: eliminating the root cause of the disease (Izala Sabab), restoring humoral balance (Tadeele Akhlat), and normalizing the function of affected organs or tissues (Tadeele Aza).<sup>[63]</sup>

**Correlation Between Benign Prostatic Hyperplasia (BPH) in Modern Medicine and the Unani System of Medicine.<sup>[63]</sup>**

BPH (“ <i>Izm-i-Gudda-i-Mazi</i> ”)	Unani perspective	Modern perspective
<b>Etiopathology (Asbab-wa-mahiyat-e-marad)</b>	Unani theories closely align with the modern understanding of BPH pathogenesis: 1. <b>Hot Swelling (<i>Waram Hārr</i>):</b> Seen as inflammation ( <i>Iltihāb</i> ), this is linked to a hot temperament ( <i>Sū'-i-Mizāj Hār</i> ) and an excess of yellow bile ( <i>Khilt-i-Safra</i> ),	1. "Benign Prostatic Hyperplasia (BPH) is marked by an overgrowth of epithelial and stromal cells within the periurethral region of the prostate. Several theories have been proposed to explain its

	<p>causing symptoms like burning urination, fever, and thirst.</p> <ol style="list-style-type: none"> <li><b>Phlegmatic Swelling and Hormonal Factors:</b> Unani medicine associates hormones like testosterone and dihydrotestosterone with white humour (<i>Khilt-i-Balgham</i>), bridging traditional concepts with modern hormonal theories of BPH.</li> <li><b>Age and Temperament Shift:</b> Modern studies note that BPH's prevalence increases after the fifth decade. In the Unani system, aging shifts the body's temperament—<i>Barid Yabis</i> in middle age and <i>Barid Ratab</i> in old age—leading to <i>Sū'-i-Mizāj Bārid</i>, which predisposes individuals to conditions like BPH.</li> </ol>	<p>development:"</p> <ol style="list-style-type: none"> <li><b>Neoplastic theory:</b> Growth factors are small peptide molecules that stimulate, or in some cases inhibit, the cell division and differentiation processes.</li> <li><b>Hormonal theory:</b> Disturbed DHT and testosterone ratio (DHT: Testosterone)</li> <li><b>Age-Related Tissue Remodeling:</b> In the transition zone of the prostate, age-associated changes lead to structural remodeling of the tissue.</li> </ol>
<p><b>Clinical features (Alam'at)</b></p>	<ul style="list-style-type: none"> <li><i>Usr al-bawl</i> (dysuria),</li> <li><i>Ihtibas al-bawl</i> (anuria)</li> <li><i>Salas al-bawl</i> (urine incontinence)</li> <li><i>Taqṭīr al-bawl</i> (dribbling of urine)</li> <li><i>Kasrat-e-bawl</i> (increased frequency)</li> </ul>	<ul style="list-style-type: none"> <li>Partial or complete urine retention</li> <li>Increased frequency</li> <li>urge incontinence</li> <li>Dribbling of urine</li> </ul>
<p><b>Principles of management (Usool-e-ilaj)</b></p>	<ul style="list-style-type: none"> <li>In the Unani system of medicine, the management of Benign Prostatic Hyperplasia (<i>Izm-i-Gudda-i-Mazi</i>) involves the use of drugs possessing the following therapeutic properties:</li> <li><b>Muhallil-e-Auram-e-Ahshah</b> – Visceral anti-inflammatory agents</li> <li><b>Mudir-e-Bawl</b> – Diuretics that promote urine flow</li> <li><b>Musakkin-e-Alam</b> – Analgesics to relieve pain</li> <li><b>Mufatteh-e-Sudad</b> – Deobstruents that helps clear blockages</li> <li><b>Surgical Management:</b> In earlier times, bladder incision was a traditional method used to relieve complete urinary obstruction.</li> </ul>	<p>Medical Management:</p> <ul style="list-style-type: none"> <li>Aimed at relieving symptoms</li> <li>Helps in reducing the size of the prostate gland</li> </ul> <p>- <b>Surgical Management:</b></p> <ul style="list-style-type: none"> <li>Involves partial or complete removal of the gland</li> <li>Common procedures include open prostatectomy, transurethral resection of the prostate (TURP), and transurethral incision of the prostate (TUIP)</li> <li>Surgery becomes necessary in cases where complications arise.</li> </ul>

**Management**

**Single herbs in Unani medicine**

Numerous herbal remedies, such as *beekh-e-Kasni*, *Khar-e-Khasak*, *Tukhm-e-Khyarain*, *Maghz-e-Tukhm-e-Kaddu*, *Bhui Amla*, *Tukhm-e-Karafs*, and *Bisheri Booti*, have been effectively used as single drugs to alleviate various symptoms of BPH.

**Formulations in Unani medicine**

In addition to single drugs, several compound formulations have shown efficacy in managing BPH symptoms. These include *Sharbat-e-Bazoori*, *Bandiql Buzoor*, *Majoon Kundur*, *Jawarish Zarooni*, *Itrifal Ghududi*, *Majoon Rasheedi*, *Sharbat-e-Aloo-Baloo*, and

*Habb-e-Muqil*, which have proven to be beneficial in relieving associated discomforts.

**CONCLUSION**

The review of BPH in modern medicine and its appreciation in the Greco-Arab (Unani) system of medicine enlightens the disease. The discussion also reveals a close relationship between the disease perception in both systems of medicine. This encourages the discovery and validation of effective medicinal herbs and other natural ways of treatment for BPH and its associated symptoms. Unleashing natural remedies will prove beneficial to decrease the burden of conventional medicines and the need for surgery, with their different possible side effects.

**Conflicts of interest**

The authors have declared that there is no conflict of interest.

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