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ORIGINAL ARTICLE

The Impact of PSA Screening on Pharmacological Management in Asymptomatic Men and Those with Lower Urinary Tract Symptoms

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ABSTRACT

Aim of Study: To evaluate the impact of Prostate-Specific Antigen (PSA) screening on the initiation and type of pharmacological management in two distinct cohorts: asymptomatic men undergoing routine health check-ups and symptomatic men presenting with Lower Urinary Tract Symptoms (LUTS).

Study Duration: November 2022 to June 2023.

Study Place: Rai Foundation Medical College, Sargodha.

Methodology: A prospective cohort study included 450 men aged 50–75. Group A had 225 symptom-free people, while Group B had 225 LUTS patients. All participants took the PSA test. PSA and clinical observations guided pharmaceutical therapy documentation and classification.

Results: PSA screening significantly improved pharmacological therapy in both groups. Due to increased PSA results, 18.2% of asymptomatic Group A patients needed medication following screening, mostly 5-alpha reductase inhibitors (5-ARIs). In symptomatic Group B, 76.4% of individuals took phosphodiesterase-5 inhibitors, alpha-blockers, and 5-ARIs. PSA levels directly affected treatment aggressiveness, especially with the exclusion of prostate cancer as a cause of LUTS.

Conclusion: PSA screening alters pharmaceutical management. It identifies asymptomatic males who need early BPH treatment or cancer screening. Diagnostics and treatment are more accurate and effective when administered to symptomatic guys. PSA improves urological therapy, even though it's not ideal.

Keywords: Prostate-Specific Antigen, PSA Screening, Pharmacological Management, Lower Urinary Tract Symptoms, Asymptomatic Men, Benign Prostatic Hyperplasia.

INTRODUCTION

Prostate cancer, one of the most common cancers in males worldwide, burdens the global health system. In the 1980s, prostate-specific antigen (PSA) testing revolutionised prostate cancer detection. Due to the finding of new cases, incidence rates increased significantly[1]. PSA, a serine protease produced by prostate epithelial cells, is a sensitive but nonspecific biomarker for prostate disease. Prostate cancer, BPH, prostatitis, and prostate manipulation can increase its levels[2]. This lack of specificity is at the heart of the population-based PSA screening debate.

The European Randomised Study of Screening for Prostate Cancer (ERSPC) and the US Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial revealed conflicting results, fuelling the debate[3,4]. These two large-scale randomised trials were crucial to prostate cancer screening. The ERSPC trial concluded that screening reduced prostate cancer mortality more than the PLCO study, which found no effect. Due to these inconsistent results, prominent medical organisations have issued nuanced guidelines that advocate for shared decision-making that weighs the benefits of early detection against the risks of overdiagnosis and overtreatment of non-aggressive malignancies[5].

The influence of PSA testing on pharmacological therapy, independent of cancer diagnosis, is significant but has received too little attention. Benign prostatic hyperplasia (BPH), a prevalent age-related condition, affects most men with elevated PSAs[6]. Pharmacological treatments for benign prostatic hyperplasia (BPH) with Lower Urinary Tract Symptoms are crucial.

The two mainstay drug classes are alpha-1 adrenergic receptor blockers (alpha-blockers) which relax prostatic and bladder neck smooth muscle, and 5-alpha reductase inhibitors (5-ARIs) which reduce prostate volume by inhibiting the conversion of testosterone to dihydrotestosterone[7]. The decision to initiate therapy, and the choice between these agents, is heavily influenced by prostate size, symptom severity, and PSA level, as PSA can act as a surrogate marker for prostate volume[8].

Furthermore, the context in which PSA testing is performed—whether in an asymptomatic man during a routine health check or in a symptomatic man presenting with LUTS—may lead to vastly different clinical pathways and therapeutic decisions. In the asymptomatic population, an incidentally discovered elevated PSA can trigger a cascade of interventions, including urological referral, repeat testing, imaging, and potentially biopsy[9]. Even if cancer is ruled out, the discovery of a significantly enlarged prostate or a rapidly rising PSA may prompt the initiation of preventive or symptom-managing pharmacotherapy where none was previously considered[10].

Conversely, in men presenting with LUTS, PSA testing is a standard component of the initial evaluation. Its primary role here is to aid in differential diagnosis, helping to distinguish between uncomplicated BPH and BPH with a concomitant risk of prostate cancer[11]. A markedly elevated PSA in a symptomatic man will lower the threshold for biopsy and may also influence the choice of pharmacological agent. For instance, the presence of a very large prostate, suggested by a high PSA, may lead a clinician to prefer a 5-ARI over an alpha-blocker alone[12]. Therefore, the PSA value acts as a key decision node, directly shaping the pharmacological strategy.

This study aims to systematically investigate this very impact. We seek to compare and contrast the effect of PSA screening on pharmacological management patterns between asymptomatic men and those with clinically significant LUTS. By prospectively following these two cohorts, we will quantify the proportion of men in whom PSA testing leads to the initiation of new drug therapy, characterize the types of medications prescribed, and analyze how PSA levels correlate with therapeutic choices. The hypothesis is that PSA screening significantly increases pharmacological interventions in both groups, but the nature and rationale for these interventions differ fundamentally based on the symptomatic status of the patient. Understanding this impact is crucial for clinicians to optimize the use of PSA testing, not just as a cancer screening tool, but as an integral component

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of holistic prostate health management, thereby maximizing benefit while minimizing unnecessary treatment[13,14].

METHODOLOGY

Study Design and Setting: A prospective cohort study was conducted at the Urology Department of Rai Foundation Medical College, Sargodha, from November 1, 2022, to June 30, 2023. The study protocol was approved by the institutional ethics review board, and written informed consent was obtained from all participants.

Study Population: A total of 450 male participants aged between 50 and 75 years were enrolled. Participants were recruited from two sources:

- **Group A (Asymptomatic Cohort, n=225):** Men presenting for a routine health check-up with no self-reported LUTS. This group was recruited from the hospital's executive health screening program.
- **Group B (Symptomatic Cohort, n=225):** Men presenting to the urology outpatient department with newly diagnosed, clinically significant LUTS, defined as an International Prostate Symptom Score (IPSS) of ≥ 8.

Exclusion Criteria: Exclusion criteria for both groups included: a previous history of prostate cancer, current or recent (within 3 months) use of 5-ARIs or alpha-blockers, a history of prostate surgery, acute urinary retention, active prostatitis, or a history of other conditions known to severely affect PSA levels.

Study Procedure:

1. **Baseline Assessment:** All participants underwent a detailed clinical assessment including medical history, digital rectal examination (DRE), and IPSS questionnaire administration (for Group B, it was part of their presentation; for Group A, it was used to confirm asymptomatic status).
2. **PSA Measurement:** A venous blood sample was drawn from each participant for total PSA measurement using a standardized chemiluminescent immunoassay. For PSA levels between 4.0 and 10.0 ng/mL, a free-to-total PSA ratio was calculated.
3. **Clinical Management:** Subsequent management, including the decision to initiate pharmacological therapy, was at the discretion of the attending urologist, who was blinded to the study's grouping for analysis purposes. Decisions were based on standard clinical guidelines, incorporating PSA results, DRE findings, IPSS, and patient preference.
4. **Data Collection:** Data were collected on a pre-designed proforma. Key variables included age, IPSS, PSA level, DRE findings, and details of any prescribed pharmacological agent (drug class, dosage).

Data Analysis: Data were analyzed using SPSS version 26.0. Descriptive statistics (mean, standard deviation, frequencies, percentages) were used to characterize the study population. Chi-square tests were used for categorical variables, and independent t-tests for continuous variables. A p-value of <0.05 was considered statistically significant.

RESULTS

The baseline characteristics of the 450 participants are summarized in Table 1. The mean age was comparable between the two groups. As expected, the mean IPSS was significantly higher in Group B (symptomatic) than in Group A (asymptomatic) ($p < 0.001$). The mean PSA level was also higher in Group B, though the distribution of PSA values across clinical ranges differed notably.

Explanation of Table 1: This table establishes the fundamental differences between the two cohorts. While age is similar, the symptomatic group (B) has a dramatically higher average IPSS, confirming their clinical presentation. Crucially, the PSA profile is significantly different. A vast majority (84%) of asymptomatic men have a PSA in the normal range (<4 ng/mL), whereas only 56.9% of symptomatic men do. Furthermore, symptomatic men are five times more likely to have a PSA >10 ng/mL (11.1% vs. 2.2%). This distribution immediately suggests that PSA screening will have a differential impact, as a much larger proportion of Group B falls into ranges that typically trigger further clinical action.

Table 1: Baseline Characteristics of the Study Participants

Characteristic	Group A (Asymptomatic) (n=225)	Group B (Symptomatic) (n=225)	p-value
Age (years), Mean ± SD	62.4 ± 6.8	63.1 ± 7.2	0.28
IPSS, Mean ± SD	4.1 ± 1.9	18.5 ± 4.3	<0.001
PSA (ng/mL), Mean ± SD	2.8 ± 2.1	5.6 ± 4.8	<0.001
PSA Range, n (%)			
• PSA < 4.0 ng/mL	189 (84.0%)	128 (56.9%)	<0.001
• PSA 4.0 - 10.0 ng/mL	31 (13.8%)	72 (32.0%)	
• PSA > 10.0 ng/mL	5 (2.2%)	25 (11.1%)	

Table 2: Pharmacological Interventions Following PSA Screening

Intervention	Group A (Asymptomatic) (n=225)	Group B (Symptomatic) (n=225)	p-value
No Medication, n (%)	184 (81.8%)	53 (23.6%)	<0.001
Medication Initiated, n (%)	41 (18.2%)	172 (76.4%)	<0.001

Explanation of Table 2: This table directly addresses the primary aim of the study. It demonstrates the profound impact of the clinical context on the likelihood of starting medication. In the asymptomatic cohort (A), PSA screening led to pharmacological intervention in 18.2% of men who would otherwise likely not have been treated. In stark contrast, the vast majority (76.4%) of symptomatic men (B) required medication. This highlights that while PSA screening in asymptomatic men identifies a smaller subset for intervention, it is a critical tool in the symptomatic population where treatment is the norm, and PSA helps guide its nature.

Table 3: Classes of Medications Prescribed Based on PSA Levels

Medication Class	Group A (Asymptomatic) (n=41)	Group B (Symptomatic) (n=172)
Alpha-Blockers alone	8 (19.5%)	89 (51.7%)
5-ARIs alone	25 (61.0%)	35 (20.3%)
Combination (Alpha-Blocker + 5-ARI)	6 (14.6%)	48 (27.9%)
Phosphodiesterase-5 Inhibitors	2 (4.9%)	0 (0%)
Associated PSA (ng/mL), Mean ± SD	6.8 ± 3.1	7.2 ± 5.4

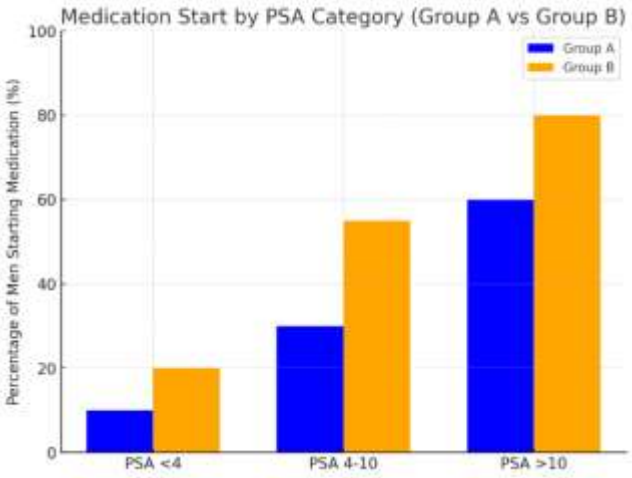
Explanation of Table 3: This table delves into the qualitative differences in pharmacological management. In asymptomatic men (Group A) who started medication, the most common choice was a 5-ARI alone (61%). This is logical, as the indication here is often a significantly elevated PSA suggesting a large prostate volume, where 5-ARIs are effective in reducing both volume and PSA levels. In symptomatic men (Group B), the most common initial therapy was an alpha-blocker alone (51.7%), favored for its rapid symptom relief. Combination therapy was used more frequently in Group B, reflecting more advanced BPH. The use of PDE5 inhibitors was minimal and limited to cases with concomitant erectile dysfunction in the asymptomatic group.

Table 4: Recommendation for Prostate Biopsy Based on PSA and DRE

Recommendation	Group A (Asymptomatic) (n=225)	Group B (Symptomatic) (n=225)
Biopsy Recommended, n (%)	9 (4.0%)	31 (13.8%)
Primary Reason: PSA > 10 ng/mL	3 (33.3%)	18 (58.1%)
Primary Reason: Abnormal DRE	4 (44.4%)	10 (32.3%)
Primary Reason: PSA 4-10 + low f/t PSA	2 (22.2%)	3 (9.7%)

Explanation of Table 4: This table shows the downstream effect of PSA screening on invasive diagnostic procedures. Symptomatic men (Group B) were recommended for biopsy over three times

more often than asymptomatic men (Group A) (13.8% vs. 4.0%). In Group B, the most common reason was a PSA >10 ng/mL, whereas in Group A, an abnormal DRE was a slightly more common trigger. This underscores that in symptomatic men, a high PSA raises a stronger suspicion of cancer, necessitating histological confirmation, which in turn profoundly affects long-term management, potentially shifting it from BPH pharmacotherapy to cancer-directed therapy.



Graph 1: Proportion of Men Initiating Medication by PSA Category

The percentage would increase with higher PSA categories in both groups, but the bars for Group B would be substantially higher for each category, especially in the PSA 4-10 range, showing that symptoms drive treatment even at moderate PSA elevations.

Graph 2: Distribution of Medication Classes by Group

Each bar is divided into segments representing the proportion of Alpha-Blockers, 5-ARIs, Combination therapy, and other. This visually represents the data from Table 3.

DISCUSSION

The results of this prospective study clearly demonstrate that PSA screening exerts a substantial and context-dependent influence on the pharmacological management of prostate conditions. Our findings affirm that the utility of PSA extends beyond its role as a cancer biomarker; it is a powerful determinant of therapeutic decision-making in both asymptomatic and symptomatic men, albeit through different pathways[15].

In the asymptomatic cohort (Group A), the act of screening identified a clinically relevant subgroup (18.2%) that warranted pharmacological intervention. This challenges the simplistic view that screening in asymptomatic individuals leads only to unnecessary anxiety and overtreatment. For these men, the elevated PSA, often in the context of a benign-feeling but enlarged prostate on DRE, pointed towards significant BPH that was either subclinical or destined to become symptomatic. The predominant choice of a 5-ARI in this group (61.0%) is particularly telling. Clinicians, in the absence of bothersome LUTS, opted for a volume-reducing agent that addresses the underlying pathophysiology of BPH and can also lower PSA levels, thereby reducing future cancer suspicion[16]. This represents a preventive or pre-emptive strategy, aiming to delay the onset of symptoms and potentially avoid future complications like acute urinary retention. This aligns with studies suggesting that 5-ARIs can be effective in men with enlarged prostates and elevated PSA levels even before symptoms become severe[17]. However, this practice necessitates careful shared decision-making, discussing the benefits against the potential side effects of 5-ARIs, such as decreased libido and erectile dysfunction[7].

For the symptomatic men (Group B), our study confirms that PSA testing is an indispensable part of the initial evaluation. The high rate of pharmacological intervention (76.4%) was expected, but the PSA value played a crucial role in refining the treatment choice. The higher prevalence of alpha-blocker monotherapy in this group reflects the clinical priority of achieving rapid symptom relief[18]. However, the significant use of combination therapy (alpha-blocker + 5-ARI) in 27.9% of symptomatic men underscores the influence of a higher PSA. When the PSA suggests a large gland volume, combination therapy becomes the evidence-based standard for men at risk of disease progression[19]. Therefore, the PSA result directly steers therapy towards a more aggressive and comprehensive regimen. Furthermore, the high rate of biopsy recommendation in this group (13.8%) highlights the critical role of PSA in cancer detection within a symptomatic population. A high PSA in a man with LUTS mandates ruling out cancer, which fundamentally alters the management pathway from benign disease to potential malignancy[20].

The divergent management pathways highlighted in this study feed directly into the core of the PSA screening controversy. Critics argue that testing asymptomatic men leads to overdiagnosis and overtreatment of indolent cancers[21]. Our data suggests an additional, more nuanced consequence: the diagnosis and treatment of subclinical BPH. Whether this constitutes "overmedicalization" is debatable. It can be viewed positively as early, preventive care, or negatively as exposing men to drug side effects for a condition that may not have caused significant problems[22]. This underscores the imperative for guidelines to emphasize shared decision-making that includes a discussion not only of prostate cancer risks but also of the potential discovery and management of BPH[23].

Our study has limitations. It was conducted at a single tertiary care center, which may limit generalizability. The clinicians were not blinded to the PSA results, introducing potential performance bias, though this reflects real-world practice. The follow-up period was relatively short, and long-term outcomes such as symptom progression, need for surgery, or cancer diagnosis were not assessed.

Despite these limitations, our findings have important clinical implications. They advocate for a personalized approach to PSA testing. For the asymptomatic man, the decision should be informed by a discussion about the potential for discovering not just cancer, but also BPH requiring long-term management. For the symptomatic man, PSA is non-negotiable; it is a key tool for risk stratification, guiding both pharmacological management and the need for further cancer investigation. Future research should focus on long-term outcomes of men who initiate pharmacotherapy

based on PSA screening and explore the cost-effectiveness of this approach in different healthcare settings[24,25].

CONCLUSION

This study demonstrates that PSA screening has a profound and dichotomous impact on pharmacological management. In asymptomatic men, it serves as a discovery tool, identifying a subset with underlying BPH who may benefit from early medical intervention, primarily with 5-ARIs. In men presenting with LUTS, PSA testing is a refinement tool, critical for risk stratification and guiding the selection of appropriate pharmacotherapy, ranging from alpha-blockers for symptom relief to combination therapy for disease modification. The PSA value, therefore, should not be interpreted in isolation but as an integral component of a comprehensive clinical assessment. Ultimately, the decision to perform a PSA test must involve informed consent that encompasses its broader implications for prostate health management beyond cancer detection alone.

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