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ORIGINAL ARTICLE

Age-Related Anatomical Variations in the Prostate Gland, Implications for Urological Health and Disease Progression

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ABSTRACT

Background: Lower urinary tract symptom (LUTS) due to benign prostatic hyperplasia (BPH) is the most common disorder of aging male that affects the overall quality of life. They are also important in early diagnosis and management of the anatomical and pathological changes with aging.

Objectives: The goal of this study was to determine how age-related prostate enlargement affects the clinical outcome parameters including prostate volume, LUTS severity, PSA levels, and pathologic changes. It also seeks to find correlations between these factors, and early intervention and therapeutic advancements in the areas of these factors.

Methods: The study was carried out cross sectionally by investigating n=60 male patients divided into three age groups: 40–50 years, 51–65 years and 66–80 years. International Prostate Symptom Score (IPSS), prostate specific antigen (PSA) levels and urinary flow rates were included in the clinical assessment. Imaging modalities as well as histopathological analysis were used to evaluate prostate volume, stromal proliferation, epithelial hyperplasia and fibrosis.

Results: There existed a strong correlation between prostate enlargement, increasing age, and worsening LUTS. PSA levels were elevated, urinary flow rates were lower and IPSS scores were increased in older patients. It progressed with enlargement of the transition zone, and urethral compression increased. Stromal proliferation, epithelial hyperplasia and fibrosis were confirmed histologically and the role of chronic inflammation in BPH progression was demonstrated.

Conclusion: Aging is concluded to be a major contributor to prostate enlargement and LUTS severity. Disease progression can be managed through early detection and intervention and improved patient outcomes. Future research should involve elucidation of molecular pathways involved in inflammation and the development of novel therapeutic approaches.

Keywords: Benign prostatic hyperplasia, aging, lower urinary tract symptoms, prostate volume, PSA, fibrosis, inflammation, histopathology.

INTRODUCTION

The prostate gland is subject to substantial structural and functional changes during life, aging being by far the principal determinant of its morphological and physiological modifications. Such age-related variations have been implicated in the pathogenesis of various urological disorders including benign prostatic hyperplasia (BPH), lower urinary tract symptoms (LUTS), and prostate cancer (PCa) [1]. As global life expectancy increases, it is of utmost importance to characterize the anatomical changes of the prostate in each age group to improve the disease detection, management and therapeutic intervention[2].

BPH is the most common age associated condition and among men it affects up to 90% of men over the age of 80. The typical findings are non-malignant hyperplasia of epithelial and stromal components that produce increased prostate volume and compression of the urethra, thereby causing LUTS[3]. While the anatomical alterations that contribute to progression of disease are much better known than the hormonal changes, particularly the decline in testosterone and the shift in the estrogen to androgen ratio, they are still an area of active research. Also, similar to prostate cancer, prostate cancer increases incidence with age, and chronic inflammation, genetic mutations and epigenetic modifications are key to its initiation and progression. Nevertheless, it is unclear how far these conditions are attributable to age-related changes in anatomical prostate[4, 5].

However, despite improvements in imaging, such as multiparametric magnetic resonance imaging (mpMRI) and transrectal ultrasound (TRUS), an ability to distinguish the pathological enlargement of the prostate from physiological aging has remained difficult. The structural and histological changes seen in the prostate with age are important for refining diagnostic criteria and improving clinical decision making[6,7].

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In this study, the aim was to systematically analyse age-related anatomical variation in the prostate gland and its implications in urologic health and disease progression. Histological assessments, imaging data and quantitative morphometric analysis were combined to characterize structural differences among various age groups and the potential relationship with clinical symptoms[8]. The finding of this study provides critical anatomical evolution of the prostate gland insights that may help in early disease detection, risk stratification and targeted therapeutic strategy development for age associated urological conditions[9].

MATERIALS AND METHODS

Study Design and Patient Selection: This was a cross-sectional study carried out at different tertiary care hospitals in Pakistan during June 2021 till November 2022. Sixty male patients, 40 to 80 years of age, were enrolled having LUTS or undergoing routine urological evaluation. Patients aged 40–50 years (Group A, n=20), 51–65 years (Group B, n=20) and 66–80 years (Group C, n=20) were made into three groups. Inclusion criteria included individuals without prior prostate surgery, malignancy or hormone therapy. Exclusion was if known to have prostate cancer, if severe urinary tract infection or neurogenic bladder disorder, if clinical data incomplete. All the participants gave informed consent and ethical approval was obtained from the Institutional Review Board.

Clinical and Laboratory Assessments: Medical history, physical examination, and scoring of the IPSS were performed in the participants as a comprehensive clinical evaluation. Digital rectal examination (DRE) was used to assess prostate size and consistency. Standard immunoassay techniques that we had available in the laboratory were used to measure serum prostate specific antigen (PSA) levels in blood samples. We assessed urinary flow rates by uroflowmetry and post void residual urine volume by trans abo medial ultrasound and they were done routinely available in our facility.

Imaging and Morphometric Analysis: Prostate imaging was performed using a commonly available modality in Pakistan, namely transabdominal ultrasound (TAUS). To estimate prostate volume, we used TAUS to measure the anterior-posterior, transverse and longitudinal dimensions and applied the ellipsoid formula: Volume = (π/6) × transverse diameter × anteroposterior diameter × longitudinal diameter. These measurements allowed age specific morphologic changes in the size and structure of the prostate to be assessed.

Histological Analysis: Tissue samples were collected for histopathological examination in cases when patients underwent transurethral resection of the prostate (TURP) for clinical indications. Formalin fixed specimens were embedded in paraffin, sectioned at 5 µm thickness and the sections were stained with haematoxylin and eosin stain. Glandular and stromal architecture was evaluated by H&E staining. Histological analysis was performed to look for such features as epithelial hyperplasia, stromal proliferation and fibrosis that are relevant to age related changes in the prostate.

Statistical Analysis: IBM SPSS Statistics version 29, a very common statistical software in Pakistan, was used to analyse data. The mean ± SD was used to express continuous variables and frequencies and percentages were used to express categorical variables. One way ANOVA was employed using continuous variables and Chi square tests for categorical variables to make comparisons between age groups. Associations between prostate volume, PSA levels and age-related anatomical changes were evaluated by Pearson correlation analysis. Statistically significance was taken as a p-value <0.05.

RESULTS

Patient Demographics: They included 60 male patients all of whom were equally distributed among three age groups: Group A (40–50 years, n=20), Group B (51–65 years, n=20), and Group C (66–80 years, n=20). Mean ages for each group were 45.2 ± 3.1, 58.7 ± 4.2 and 72.4 ± 3.6 years.

Characteristics at baseline including body mass index (BMI), prevalence of hypertension and diabetes increased with age. Patients in Group C had the highest rates of hypertension (55%) and diabetes (50%), while these conditions were significantly less prevalent in younger groups. Additionally, gender distribution was 100% male, as per the study inclusion criteria as shown in table 1.

Table 1: Patient Demographics and Baseline Characteristics

Age Group	Number of Patients	Mean Age (±SD)	BMI (±SD)	Hypertension (%)	Diabetes (%)	Gender
Group A (40-50 years)	20	45.2 ± 3.1	24.5 ± 2.3	30	20	Male
Group B (51-65 years)	20	58.7 ± 4.2	25.8 ± 2.7	40	35	Male
Group C (66-80 years)	20	72.4 ± 3.6	26.2 ± 3.1	55	50	Male

Clinical and Laboratory Findings: The International Prostate Symptom Score (IPSS) for severe LUTS increased markedly with age. Mean IPSS of Group A was 8.5 ± 2.3, Group B was 12.7 ± 3.1 ($p<0.01$) and Group C 16.4 ± 3.8 ($p<0.01$).

Progressively increasing serum prostate specific antigen (PSA) levels were also observed with increasing age, with mean levels of 1.2 ± 0.5 ng/mL, 2.8 ± 1.1 ng/mL, and 4.6 ± 1.5 ng/mL in Group A, Group B and Group C respectively ($p<0.01$); and maximum urinary flow rate decreased from 15.8 ± 2.4 mL/s in Group A to 9.7 ± 3.1 mL/s in Group C ($p<0.01$). These results show that prostate enlargement is an important contributor to worsening of LUTS and urinary flow in the older age groups (Table 2).

Table 2: Clinical and Laboratory Findings Across Age Groups

Parameter	Group A (40-50 years)	Group B (51-65 years)	Group C (66-80 years)	P-value
IPSS Score	8.5 ± 2.3	12.7 ± 3.1	16.4 ± 3.8	<0.01
Serum PSA (ng/mL)	1.2 ± 0.5	2.8 ± 1.1	4.6 ± 1.5	<0.01
Maximum Urinary Flow Rate (mL/s)	15.8 ± 2.4	12.3 ± 2.9	9.7 ± 3.1	<0.01

Imaging and Morphometric Analysis: Prostate volume was significantly increased with age by transabdominal ultrasound (TAUS). Group A was 25.6 ± 4.3 cm^3, Group B was 35.2 ± 5.7 cm^3 and Group C was 48.9 ± 6.8 cm^3 ($p<0.01$). We also observed that transition zone volume, an important marker of benign prostatic hyperplasia (BPH), was much larger in the older groups (12.4 ± 3.2 cm^3 in Group A vs. 26.7 ± 5.6 cm^3 in Group C, $p<0.01$) as shown in table 3.

Table 3: Imaging and Morphometric Analysis

Parameter	Group A (40-50 years)	Group B (51-65 years)	Group C (66-80 years)	P-value
Prostate Volume (cm^3)	25.6 ± 4.3	35.2 ± 5.7	48.9 ± 6.8	<0.01
Transition Zone Volume (cm^3)	12.4 ± 3.2	18.1 ± 4.1	26.7 ± 5.6	<0.01

It is shown in this study that aging is directly associated with prostate enlargement and worsening of LUTS. For example, older patients had greater PSA levels, less urinary flow rate, and higher IPSS scores. Histological and imaging findings confirmed significant prostatic hyperplasia, stromal proliferation and fibrosis. Statistical correlations indicate the need of early screening and intervention to effectively manage age related prostate health complications.

DISCUSSION

The results of this study are consistent with previous literature that describes benign prostatic hyperplasia (BPH) as a progressive disease and a function of aging[10]. The relevance of our results is supported by prior studies that have shown a similar trend of increase of prostate volume and LUTS severity with increasing age. This second observation is in accord with the previous epidemiological data, and also supports the role of cellular proliferation and inflammation in age related prostate enlargement[11].

Chronic inflammation is important in the progression of BPH as confirmed by histological findings of increased stromal proliferation and fibrosis consistent with previous studies. Research that suggests an immune mediated pathogenesis to prostate enlargement is supported by the alignment of macrophage infiltration with the hypothesis that BPH is not simply a result of hormonal shifts but also with inflammatory and fibrotic pathways [12].

Clinically, the strong correlation between the LUTS and prostate volume suggests that early detection and proactive intervention is of critical importance[13]. Prior trials have shown that pharmacological management strategies (5-alpha reductase inhibitors and alpha-blockers) can alleviate LUTS and slow prostate growth. Prior cohort studies also indicate that lifestyle modifications, such as weight management and dietary interventions, may also be beneficial[14].

However, there are some limitations of this study. The findings were based on a small sample size, and are not validated with larger population-based studies. Findings may not be generalizable to various populations[15].

In addition, absence of longitudinal follow up impedes the evaluation of the progression of prostate enlargement over time.

Future research should be long term studies with a larger and more diverse cohort[16].

Additional studies in molecular mechanisms of inflammation and fibrosis in BPH should be conducted using novel biomarkers that may facilitate early diagnosis and therapeutic targeting. Emerging treatment modalities for reducing prostate enlargement and LUTS severity such as minimally invasive surgical techniques and novel anti-inflammatory agents need to be assessed for effectiveness[17]. Also in future research, the role of metabolic disorders, including obesity and diabetes, in worsening prostate growth needs to be further uncovered, because recent evidence indicates that metabolic health and BPH progression are closely associated[18].

CONCLUSION

The strong association between aging and prostate enlargement found in this study supports the notion of the relationship between prostate enlargement and urinary function. The findings indicate that early diagnosis and treatment of BPH and related LUTS are important for effective management of BPH. The future research should be directed towards the role of inflammation and fibrosis in prostate enlargement and the effects of targeted therapies to slow down the progression of disease. The improvement of outcomes for aging male populations is going to rely on proactive healthcare strategies including routine screening and patient education.

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