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Incidental Prostate Cancer Despite Normal PSA and DRE: Evidence from a Libyan TURP Cohort

Hamed M. A. Mahmood

Department of Urology, Tobruk Medical Center, Faculty of Medicine, Tobruk University, Tobruk, Libya.

*Corresponding author: E-mail addresses hamedmapas1987@gmail.com,

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ABSTRACT

Background: Incidental prostate cancer (IPC) is occasionally diagnosed following transurethral resection of the prostate (TURP) performed for benign prostatic hyperplasia (BPH). Although men with normal preoperative prostate-specific antigen (PSA ≤ 4 ng/mL) levels and unremarkable digital rectal examination (DRE) findings are typically considered low-risk, the true incidence of IPC in this subgroup remains inadequately characterised. This raises concerns about the reliability of PSA and DRE as sole screening tools. Objectives: The primary objective of this study was to determine the incidence of IPC among patients undergoing TURP at a single centre in Tobruk, Libya, with normal preoperative PSA and DRE results. A secondary objective was to explore potential associations between IPC detection and patient characteristics, including age and PSA levels. **Methods:** A retrospective analysis was conducted on 81 patients who underwent TURP for symptomatic BPH at Tobruk Medical Center between January 2022 and January 2024. All patients had normal preoperative PSA levels (≤ 4 ng/mL), normal DRE findings, and no prior clinical suspicion or diagnosis of prostate cancer. TURP specimens were routinely subjected to histopathological examination to identify IPC. Statistical analyses were performed to assess differences between IPC-positive and IPC-negative groups. **Results:** IPC was identified in 7 of 81 patients, corresponding to an incidence of 8.6% (95% confidence interval: 3.6%–17.2%). Patients with IPC tended to be older and exhibited slightly higher PSA levels compared to those without IPC; however, these differences did not reach statistical significance. The limited number of IPC cases constrained the statistical power of the analysis, warranting cautious interpretation. **Conclusion:** An IPC incidence of 8.6% was observed among patients with normal preoperative PSA and DRE findings undergoing TURP. These findings underscore the potential limitations of relying solely on standard screening methods and highlight the value of routine histopathological evaluation of TURP specimens, even in presumed low-risk populations.

Keywords:

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Incidental prostate cancer, Transurethral resection of the prostate, Benign prostatic hyperplasia, Prostate-specific antigen, Digital rectal examination, Histopathological analysis.

INTRODUCTION

Prostate cancer is the second most frequently diagnosed cancer and the fifth leading cause of cancer-related death among men worldwide, with over 1.4 million new cases and 375,000 deaths estimated in 2020 [1]. While early detection through prostate-specific antigen (PSA) testing and digital rectal examination (DRE) has improved outcomes, a subset of cancers remains clinically undetected. These are sometimes discovered incidentally in tissue resected during transurethral resection of the prostate (TURP) performed for presumed benign prostatic hyperplasia (BPH) [2]. Incidental prostate cancer (IPC) refers to prostate adenocarcinoma diagnosed unexpectedly in patients undergoing TURP, without prior clinical or biochemical suspicion. These tumours are pathologically staged as pT1a when they involve ≤5% of the resected tissue and pT1b when they involve >5% [3]. Before PSA testing became widespread, IPC was reported in up to 27% of TURP cases [4]. Although this incidence has declined in the PSA era, recent studies still report IPC rates ranging between 4% and 17%, even among men with normal PSA and DRE findings [5–7]. These findings challenge the assumption that low PSA values eliminate the need for cancer vigilance. This diagnostic gap is partly explained by prostate anatomy: while TURP primarily removes tissue from the transitional zone (TZ), approximately 70–80% of prostate cancers arise in the peripheral zone (PZ), which is not resected during the procedure [8]. Nevertheless, clinically significant tumours do occasionally originate in the TZ and may be missed by

PSA and DRE alone, making routine histopathological assessment of TURP specimens essential for accurate diagnosis [9]. The clinical relevance of IPC varies. Low-grade, low-volume (T1a) cancers may be suitable for active surveillance, while T1b tumours—particularly those with higher Gleason scores—may require further diagnostic workup and curative treatment [10,11]. Consequently, incidental detection during TURP not only informs diagnosis but can directly influence patient management. Moreover, with the increasing adoption of BPH treatments such as laser vaporisation and enucleation—which do not yield tissue—TURP remains an important method for identifying clinically unsuspected prostate cancer [12,13]. While the incidence and management of IPC have been widely reported in Western and Asian countries, there is a lack of data from North Africa. In Libya, prostate cancer ranks among the top five male cancers, but epidemiological data remain limited and fragmented. Hospital-based cancer registries suggest prostate cancer accounts for 5.6% to 13.5% of male cancers in southern Libya between 2016 and 2018 [14], and 16% in eastern regions [15]. The GLOBOCAN 2020 estimate for Libya reports

an age-standardised prostate cancer incidence of approximately 30.6 per 100,000 men [1], higher than local registry figures, suggesting potential underreporting or diagnostic gaps. Libya presents a unique public health context. PSA screening is not part of routine practice, and many patients present with advanced disease. Additionally, risk factors such as high smoking prevalence

among men (over 23%) may influence prostate cancer patterns, although the direct link between smoking and prostate cancer remains debated [16]. Environmental exposures, limited diagnostic infrastructure, and lower awareness of screening options further complicate early detection and may influence the likelihood of incidental diagnosis. Given the absence of published Libyan data specifically addressing IPC, this retrospective study aims to determine the incidence of incidental prostate cancer among men undergoing TURP at a single centre in Tobruk, Libya, who presented with normal preoperative PSA (≤4 ng/mL) and DRE findings. A secondary objective is to evaluate the relationship between IPC and clinical variables such as age and PSA level. The findings contribute important population-specific insights to the global understanding of IPC and reinforce the ongoing diagnostic value of TURP, particularly in settings with limited screening access.

The objectives of this study were:

The primary objective of this study was to determine the incidence of incidental prostate cancer (IPC) in patients undergoing transurethral resection of the prostate (TURP) at a single centre in Tobruk, Libya, who had normal preoperative prostate-specific antigen (PSA) levels and digital rectal examination (DRE) findings. The secondary objective was to evaluate potential associations between IPC detection and patient characteristics, including age and PSA levels.

MATERIALS AND METHODS

Study Design and Patient Population

This retrospective study was conducted by reviewing the medical records of patients who underwent transurethral resection of the prostate (TURP) for symptomatic benign prostatic hyperplasia (BPH) at our institution between January 2022 and January 2024. A total of 81 patients were included in the final analysis. Inclusion criteria were as follows: patients who underwent TURP for BPH-related lower urinary tract symptoms, had a normal and non-suspicious digital rectal examination (DRE), and a preoperative serum prostate-specific antigen (PSA) level of ≤4.0 ng/mL. Exclusion criteria included any preoperative suspicion of prostate cancer (PC), such as abnormal DRE findings or elevated PSA levels (>4.0 ng/mL), a previous diagnosis of prostate cancer, and patients who underwent other forms of prostate surgery.

Data Collection and Histopathological Analysis

Data were collected from patient records and included demographics (age), preoperative serum PSA levels, and DRE findings. PSA testing was conducted across approximately three different laboratories. Although all

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laboratories used immunoassay-based methods, the specific technologies employed varied between facilities. All resected tissue from the TURP procedures was fixed in formalin, processed, and embedded in paraffin. Sections were stained with hematoxylin and eosin and subsequently analysed by a certified pathologist to determine the final diagnosis (benign prostatic hyperplasia or prostatic adenocarcinoma. All tissue specimens were examined by a single pathologist who strictly adhered to the World Health Organization (WHO) criteria for tumour grading and staging.

Statistical Analysis

All data were collected, tabulated, and statistically analysed using the Statistical Package for the Social Sciences (SPSS). Descriptive statistics were used to summarise the data. Continuous variables, such as age and PSA levels, are presented as mean, standard deviation (SD), median, and range. Categorical variables are reported as counts and percentages with 95% confidence intervals (CI). The Student's t-test or the Mann–Whitney U test was used to compare continuous variables between the BPH and IPC groups, depending on data distribution. A p-value of <0.05 was considered statistically significant.

RESULT

A total of 81 patients met the inclusion criteria. The mean age of the cohort was 71.46 ± 7.88 years (range: 55 to 90 years), and the mean preoperative PSA level was 2.42 ± 1.61 ng/mL (range: 0.27 to 4.0 ng/mL). Of the 81 patients, 74 (91.4%; 95% confidence interval [CI]: 82.8%–96.5%) were diagnosed with benign prostatic hyperplasia (BPH) on final histopathological analysis. Incidental prostatic adenocarcinoma was detected in 7 patients (8.6%; 95% CI: 3.6%–17.2%) (Table 1).

Table 1: Patient Characteristics and Histopathology Results

Variable	Category	Count	Percentage	95% CI
DRE	NAD	81	100%	—
Histopathology	Benign prostatic hyperplasia	74	91.36%	82.81%–96.45%
Histopathology	Prostatic adenocarcinoma	7	8.64%	3.55%–17.19%

Analysis of baseline demographics showed that patients in the IPC group tended to be older, with a mean age of 75.57 ± 6.85 years, compared to 71.05 ± 7.89 years in the BPH group; however, this difference was not statistically significant (p = 0.1437). Similarly, PSA values were higher in the IPC group, with a mean of 3.16 ng/mL and a median of 3.22 ng/mL, compared to 2.35 ng/mL (mean) and 1.90 ng/mL (median) in the BPH group. Despite this trend, the difference was not statistically significant (p = 0.2240). Stratification by age group revealed a progressive increase in the incidence of IPC with advancing age. The cancer detection rate rose from 8.3% in the 55–64-year age group to 20.0% among patients aged 85 and older (Table 2).

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Table 2 : Age Group Analysis of Incidental Cancer Rate:

Age Group	Total Count	Cancer Count	Cancer Rate (%)
55–64	12	1	8.33
65–74	39	2	5.13
75–84	25	3	12.00
85+	5	1	20.00

A similar trend was observed with PSA stratification. The detection rate of IPC increased from 4.55% in patients with PSA levels between 0–2 ng/mL to 13.51% in those with PSA levels between 2–4 ng/mL (Table 3).

Table 3 : PSA Range Analysis:

PSA Range (ng/mL)	Total Count	Cancer Count	Cancer Rate (%)
0–2	44	2	4.55
2–4	37	5	13.51

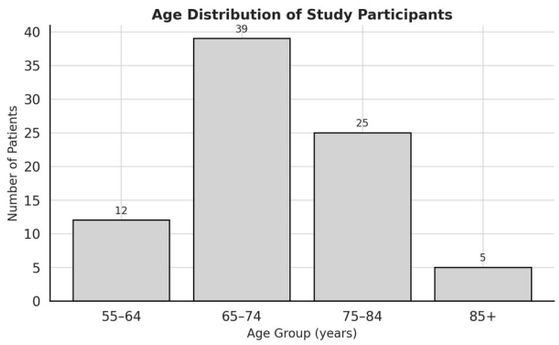

Figure 1: This figure provides a clear visual summary of the age distribution of patients included in the study

DISCUSSION

This study found an 8.6% incidence of incidental prostate cancer (IPC) among men undergoing transurethral resection of the prostate (TURP) with normal preoperative prostate-specific antigen (PSA) levels and digital rectal examination (DRE) findings. This rate is consistent with those reported in the contemporary international literature, where IPC incidence following TURP or endoscopic enucleation typically ranges from 4% to 18% in the PSA screening era. For instance, Cheng et al. reported an IPC rate of approximately 8% in a meta-analysis of enucleation procedures,

identifying age and PSA level as significant predictors of IPC (17). Similarly, Porcaro et al. observed an IPC incidence of 6.4% in a large Italian cohort, reinforcing the importance of routine histological analysis even when preoperative screening appears normal (18). Our results indicated that patients in the IPC group tended to be older and had higher PSA values compared to those in the benign prostatic hyperplasia (BPH) group, although these differences did not reach statistical significance. This trend aligns with findings by Afju et al., who reported significantly higher mean age and PSA levels in IPC patients, though significance was evident only in studies with larger sample sizes (19). In our case, the absence of statistical significance is most likely due to the small IPC subgroup (n = 7), which inherently limits the power to detect meaningful differences. These variations should be interpreted as descriptive rather than definitive, with the lack of statistical significance appropriately attributed to the limited sample size. Compared to other international cohorts, the IPC rate observed in our study falls within the mid-range. For example, Mohamed et al. reported a 17.6% IPC incidence in a Somali population, where delayed presentation is common due to limited

healthcare access (20). Meanwhile, studies from Germany and South Korea have reported IPC rates ranging from 4% to 10%, depending on PSA thresholds and the volume of tissue resected (21,22). Similarly, Elhadi et al. found that prostate cancer represented a substantial burden in the Libyan context, particularly when diagnosis occurred at later stages (23). The comparability of our findings with these

international studies suggests that TURP continues to serve as a valuable diagnostic tool, even in the modern era of PSA screening. This study addresses a notable gap in the urological literature concerning prostate cancer in North Africa. There is a pronounced scarcity of published data from Libya, and to our knowledge, no prior studies have specifically investigated the incidence of incidental prostate cancer in this population. Although national cancer registry data from 2016–2018 identified prostate cancer as the second most common malignancy among men in southern Libya, its detection via TURP had not previously been documented (12). Our findings thus provide the first estimate of IPC incidence in a Libyan cohort of men with normal PSA and DRE findings, offering foundational insights into regional cancer patterns and highlighting a potentially significant burden of undiagnosed disease. Despite the novelty of this study, several limitations must be acknowledged. The retrospective design, single-centre setting, and small number of IPC cases restrict the generalisability of our results. Additionally, key clinical and pathological variables such as tumour grade (e.g., Gleason score), tumour volume, prostate size, PSA density, and smoking status were not included in the analysis. The absence of tumour grading, in particular, limits our ability to assess cancer aggressiveness or guide post-operative clinical decisions. In contrast, other large-scale studies routinely classify IPC by Gleason grade to stratify patients into low-risk (T1a, Gleason 6) or high-risk (T1b, Gleason ≥7) categories, which significantly influences treatment

planning (18,21). Moreover, the high prevalence of smoking among Libyan men represents an important confounding factor that warrants future investigation. Although the role of smoking as a direct aetiological factor in prostate cancer remains debated, a growing body of evidence links tobacco use with higher-grade tumours and increased disease-specific mortality (24). Incorporating smoking status into future analyses would enable more comprehensive risk profiling and the identification of potential population-specific modifiers of disease risk. Clinically, our findings reinforce the importance of routine histopathological evaluation of all TURP specimens, regardless of PSA or DRE findings. In lower-resource settings, TURP tissue may provide the only opportunity to detect clinically silent malignancy. Our results also support international recommendations for post-TURP evaluation in IPC cases, including follow-up with multiparametric MRI, PSA surveillance, or systematic biopsy of the residual prostate tissue. Such measures are already endorsed in European and American guidelines, particularly for patients with T1b lesions or a longer life expectancy (22,25). In conclusion, this study highlights a notable 8.6% incidence of incidental prostate cancer, demonstrating that a substantial proportion of malignancies may go

undetected by standard screening alone and are only identified through pathological examination of tissue removed during BPH surgery. This finding powerfully illustrates that no PSA threshold can be considered entirely "safe," as cancer risk increases even within the traditionally normal range. Notably, we found that the cancer detection rate was nearly three times higher in patients with PSA levels between 2.0 and 4.0 ng/mL compared to those with levels below 2.0 ng/mL (13.5% vs. 4.5%). These findings underscore the continued diagnostic value of TURP in identifying occult prostate cancer. Unlike newer BPH treatments such as laser vaporisation, which do not yield tissue for analysis, TURP provides a critical opportunity to uncover otherwise unsuspected malignancy. It is therefore essential that all tissue specimens obtained during TURP undergo thorough histopathological evaluation to ensure early detection and timely intervention. This study has several limitations. First, its retrospective, single-centre design and small sample size limit the generalisability of the findings and reduce statistical power. Second, PSA measurements were obtained from multiple laboratories using different immunoassay platforms, which may introduce variability. Third, DRE is a subjective examination, and very small or non-palpable lesions could have been missed. Lastly, follow-up data regarding patient outcomes were not available. Despite these limitations, this study contributes valuable local data on the incidence of IPC in Tobruk, Libya. It confirms that even in the PSA era, TURP remains a clinically meaningful diagnostic tool for detecting prostate cancer, particularly in resource-constrained healthcare systems..

ETHIC APPROVAL

This retrospective study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. The study protocol received full ethical approval from the Research Ethics Committee of Tobruk University (Reference No. NBC:009.H.25.17). Due to the retrospective nature of the research, the committee granted a waiver of the requirement for individual informed consent. To protect patient privacy, all data were fully anonymised and de-identified prior to analysis. The confidentiality of patient information was strictly maintained, and the data were used exclusively for research purposes.

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