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Prevalence of Indolent Prostate Cancer in Iraq, an Autopsy Study: Prevalensi kanker prostat indolent di Irak, sebuah studi otopsi

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Abstract

General Background Prostate cancer shows wide global variation in incidence and mortality, partly due to differences in detection strategies. **Specific Background** Autopsy studies provide an unbiased estimation of indolent prostate cancer prevalence by avoiding screening and reporting bias. **Knowledge Gap** Data on incidental prostate cancer detected through autopsy remain limited in Iraq. **Aims** This study aimed to estimate the prevalence of incidental or indolent prostate cancer in Iraqi men using autopsy specimens. **Results** One hundred male autopsies aged 40 years and above were examined, revealing prostate cancer in six cases, yielding a prevalence of 6%. All detected cancers were adenocarcinoma with Gleason score 6, confined to the prostate, and showed no capsular or seminal vesicle involvement. Cancer detection increased significantly with age. **Novelty** This study provides rare autopsy-based evidence on indolent prostate cancer prevalence in Iraq. **Implications** The findings support the need for improved prostate cancer detection, reporting systems, and public awareness programs tailored to the local context.

Keywords:

Indolent Prostate Cancer, Autopsy Study, Prevalence, Iraq, Gleason Score

Key Findings Highlights:

1. Occult prostate cancer was detected in a small proportion of autopsy cases
2. Cancer detection increased consistently with advancing age
3. All identified tumors were low grade and organ confined

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Introduction

Prostate cancer (PCa) is a highly important health care issue worldwide; putting aside skin cancer (which is considered rare in Iraq) prostate cancer represent the most commonly diagnosed cancer worldwide however it is not the leading cause of cancer death but the fifth in rank; [Figure 1], that's is due to the fact that Pca is one of the most curable malignancies in comparison to other cancers

One of the most evident reasons of Pca curability is its slow growth, especially for the low grade, low risk; thus less aggressive Pca; which represent most of the diagnosed cases , especially the ones which are diagnosed through screening before showing any symptoms.

Early cases which are small tumors with no breach to the prostatic capsule can only be diagnosed by screening with PCA before showing symptoms, however more advanced cases where capsular breach is inevitable, symptoms of Pca would develop including localized prostate symptoms like LUTS and hematuria, systemic and metastatic symptoms like pallor (anemia), back pain and pathological fractures (due to bone metastasis), and paralysis from spinal metastases, and renal failure from bilateral ureteral obstruction by the tumor .

Diagnosis of Pca is usually done by DRE, high PSA, and prostate biopsy with TRUS is these represent the primary diagnostic tool, although PSA testing for screening remains controversial , .

During the last two decades, a lot of new modalities has been adopted in the initial diagnosis, in the field of lab tests for instance and to differentiate potential Pca from indolent once, in which all may have elevated PSA (in the range of gray zone PSA 4-10 ng/ml) like PSA health index (PHI), post DRE urine examination for mRNA/ PCA3, 4 kallikrein test, genomic testis, and in the realm of imaging the introduction of PRIADS, multi-parametric MRI, bi-parametric MRI with DWI and DAC measurement, and finally MRI-US fusion for directed biopsy to suspicious masses .

Early diagnosis represent the pivot point in cure, with highest survival rates in localized diseases even in high grade cancers .

Treatment options differ when Pca extends beyond the prostatic capsule, with the addition of more aggressive combinations like radical surgery proceeded by radiotherapy, or salvage surgery after radical radiotherapy, or commencing with systemic therapy in metastatic Pca on diagnosis, along with pain medications, hormonal blocks, bisphosphonate, Radium ligand therapy, survival depends on risk grouping which is stratified according to tumor histology, staging and extend .

Number of PCa annual cases diagnosed globally is increasing; accompanying westernization of many non-western countries .

In Asia, PCa prevalence is lower than in the US and Europe, however it is increasing in the last two decades and more cases are being detected especially with adoption of screening protocols and early detection techniques .

Death rates from PCa shows higher rates in developing countries in comparison to developed countries, moreover, men from developed countries have the highest age-standardized death rates among all urologic cancers (kidney, bladder and prostate) , .

In Iraq; the incidence is exceedingly low in comparison to other countries; and to other urological and non-urological cancers, PCa comes in the tenth rank of cancers in Iraq due to the high numbers of other malignancies detected like leukemia and lymphoma; however, PCa annual cases are increasing according to the Iraqi cancer registry .

Studies of indolent prostate cancer (IPCa) prevalence in autopsies are one of the oldest going back to 1898, with more than 29,000 autopsies included all around the world, and it represent an important value in understanding the behavior of PCa since IPCa incidences calculated by detected tumors in autopsies are not affected by the statistical bias factors that may interfere with incidences of clinical PCa (PSA screening protocols, efficient cancer registration) and PCa related deaths (availability, access and quality of advanced surgical and medical treatment options) .

An Iraqi study was performed in 2017 on autopsies for detection of prostatic intra-epithelial neoplasm was considered in our data for comparison purposes .

The aim of this study was to estimate the prevalence of incidental/ indolent prostate cancer (IPCa) detected through autopsy specimens of men who deceased from causes other than prostate cancer, and determine its correlation to the incidence of clinically detected symptomatic PCa reported in Iraq.

Material and Methods

One hundred Iraqi deceased men were selected randomly for this stud, medical history, family history of prostate diseases including PCa, and social habits were reported by family and included as risk factors, formal consents for dissection and pathological examination were obtained routinely as well .

All subject s' causes of death were non PCa, being mostly natural causes (myocardial infarction), as well as accidents, chronic illnesses, and postoperative fatal complications (non-urological).

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Dissection was performed at Baghdad Forensic Institute (Medico-Legal Directorate) by forensic Pathologist; pathological examinations were performed at a proper pathology laboratory in Baghdad by pathologist.

Surgical and anatomical aspects of the dissection were respected whenever time was appropriate, and no delay in the forensic work was caused by our study.

Dissection was done with an assistant, using surgical instruments and head lights, following Wallace retropubic radical prostatectomy steps in order to obtain complete prostate specimen with its apex, base, seminal vesicle and intact capsule.

Prostates were inspected, weighed and its dimensions measured, then fixed immediately by formalin buffer saline and sent for pathological examination.

Gross examination was done by histopathologist under dissecting microscope, suspicious plus randomized pieces were taken from each prostate, mainly from peripheral zone, measuring 1 cm in diameter each, 10 pieces per prostate, and fixed in a single cassette per sample and mounted in a single slide per single prostate.

Hematoxylin and Eosin was used as a dye for further microscopic examination.

Study Design:

We used a descriptive study design to estimate the prevalence of the IPCa's; data collected included name, age, cause of death, clinical history, gross description of the prostate gland, weight, size and zone of cancer (for the cases that has been positively detected with cancer), and status of prostate capsule and seminal vesicles.

Data input was done in an individual Data Proforma designed by us included the family's consent.

Statistical analysis was done using IBM SPSS Statistics software version 20.

Results:

Deceased men with an age range of 40 to 80 years were studied, the mean age was 52.91 years (SD. 8.19).

Six PCa's were detected in 49, 54, 57, 58, 63 & 68 years old deceased men autopsies (one in the 40-50 years of age category, 3 in the 50-60 years category, and 2 in the above 60 years of age category), non-had history of PCa, all were evaluated by histopathologist and all were adenocarcinoma and of Gleason Score 6, No breach was detected in prostatic capsule, nor seminal vesicle involvement, every cancer was of a single focus, no multiple cancers were detected.

Prostate volume was measured using the formula:

(H x W x L x 0.5)17.

Average prostate volume was 56.6 cm3 (SD. 17.8), the volume increased with increased age group, measuring 44.3, 60.5, and 79.6 cm3 for age groups 40-49, 50-59, and above 60 years old groups respectively [Figure 1].

Most of the specimens showed increased prostate volume, which are enlarged prostate gland above 30 ml volume, and two specimens were below 30 ml volume18 [Figure 2].

Figure 1. Figure 1: distribution of prostate volume in different age groups

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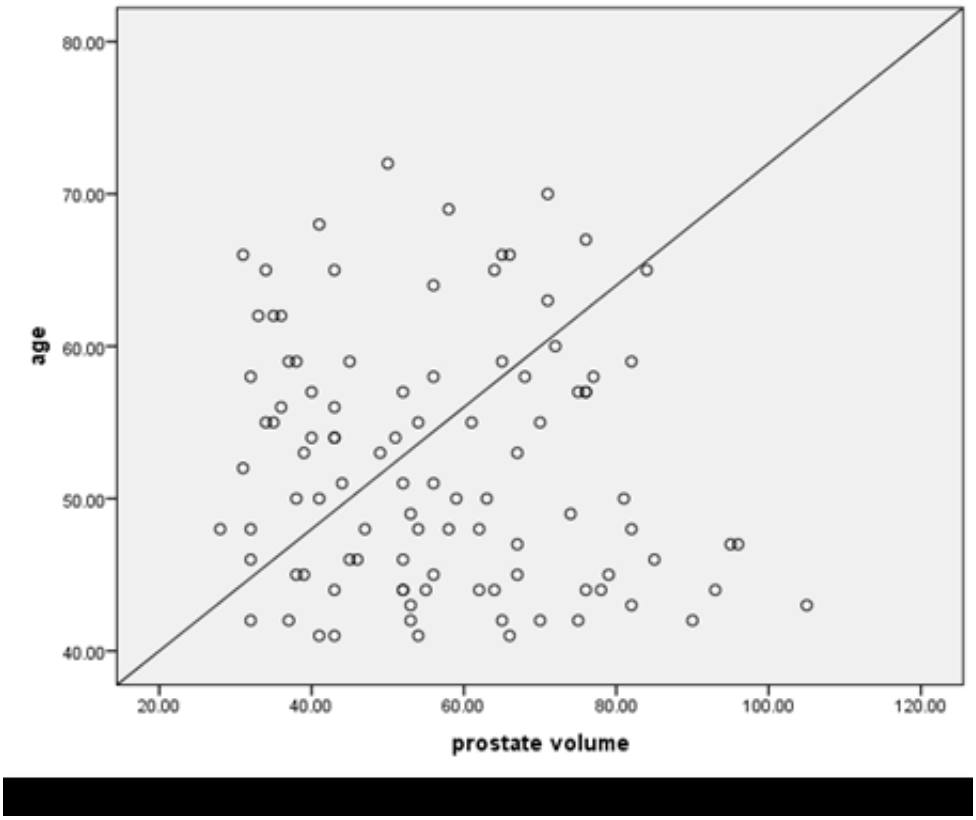

Figure 2. Figure 2: relation between prostate volume and age

The frequency of detecting PCa in our autopsy sample increased with increased age [Figure 3].

One cancer was detected in Group I (sample of 46 men below 50 years of age (2.17%)), three cancers in Group II (37 men of 50 to 60 years of age (8.1%)), and two cancer in Group III (17 cases above 60 years (11.7%)).

Age was the only risk factor for detecting PCa in our study, which was statistically significant ($p<0.05$).

Figure 3. Figure 3: percentage of cancer detection in different age groups.

Discussion:

It is undeniable that the fluctuating incidence of prostate cancer and its diagnosis is highly impacted by different factors related to diagnosis modalities and treatment options availability, thus we have chosen to study the prevalence of PCa in autopsies because it represent the least biased result, which was shown in some of the earliest studies in the last century, like the study performed by Mintz & Smith in 1934 in which the prevalence was 13 indolent PCa in 100 autopsies.

Oelke et al reported in a meta analyses of 29 studies conducted from 1948 up to 2013 of IPCa in autopsies that IPCa increased with age in a statistically significant manner 17, in addition the however with an obvious difference between counties and an increasing prevalence in autopsy detection of IPCa of the same country in different time line , that may be

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reflected in the difference of clinically diagnosed PCa in the these counties.

Kimura et al in 2016 compared different autopsy studies in Japan to detect IPCa in which the time line difference was significantly increasing . Zlotta et al even discovered in a prospective study that the gap in incidence is narrowing between Asian and Caucasian men diagnosed with PCa.

This also confirms the effect of westernization of life style that is affecting the increasing incidence of PCa in Asian countries, and not only the effect of the introduction of PSA screening to these countries.

In our study, IPCa discovered was of small size (5-10 mm) and of low grade (75%), with no breach to prostate capsule, and no metastasis, similar to the trend in most autopsy studies .

It is both possible that our discovered IPCa would not progress to clinically significant PCa, or in other instances would develop into clinically symptomatic disease if the deceased persons examined where to live longer .

In comparing clinically detectable PCa studies with IPCa autopsy studies, detection rates in both categories increased with age, and this may reflect in different level among different countries, emphasizing on race and availability of diagnostic and therapeutic services as well .

Estimating the prevalence of IPCa may be a valuable tool in managing PCa since it is devoted of the statistical bias that may interfere with PCa detection (PSA screening, cancer registry program, case diagnosis and reporting) 4.

From a diagnostic point of view, prostate cancer comes in the first rank of diagnosed cancers if screening protocols are being implemented like the in united states where Prostate cancer is the most commonly diagnosed organ cancer in men and the second leading cause of male cancer death in the United States 23; Lung cancer is first , .

Despite the low prevalence of prostate cancer in Iraq, and death rates are high 8, however improving detection capabilities will lead to improvement of survival .

This increase in PCa detected was obvious in the Asian countries which developed a more advanced detection and screening protocols .

Similarity, abandoning screening protocols will lead to increased diagnosis of PCa in advanced stages and increased mortality rates , .

In our study, we detected 6 cases of PCa in 100 autopsies, leading to a value of 6% occult cancers prevalence which can be relate it with the annual incidence of clinically significant PCa’s and annual death from this disease in Iraq, the prevalence increased with age similar to other studies of autopsy-detected prostate cancers, also similar results of the values can be compared with the worldwide percentages of these entities (i.e. IPCa, clinically significant PCa, and PCa deaths) and according to other similar studies , , , , , , , .

Despite this finding, We found that the clinically significant PCa was lower than expected in comparison to the IPCa, along with higher incidence of death in comparison to other studies .

The low prevalence might be due to the sampling methodology, which was done similar to Robert R. Moore., (1935) , who’s study was one of the first to be discussed at AUA meetings, who used random sampling per prostate rather than systemic sampling, this study was followed by multiple studies using more extensive systemic sampling that led to the highest autopsy prevalence for the same geographical area, thus we speculate that even higher prevalence’s might be detected in future studies in Iraq, especially if older males are included.

Conclusion

Iraqi men had low prevalence of Indolent Prostate Cancer as detected in autopsies, and age was the only risk factor that was significant in this study.

It is crucial to consider a more effective reporting system for PCa in Iraq, with improvement of the screening and detection protocols along with introducing TRUS biopsy equipment for as much centers as possible.

Also, there is a need for more educational campaigns about Prostate cancer in Iraq for patients, male population, and medical communities as well.

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