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EARLY DETECTION AND SCREENING FOR PROSTATE CANCER

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ABSTRACT

Purpose: The purpose of this review was to understand etiology, epidemiology, risks and predisposing factors of prostate cancer, recognize tests for early detection and prevention of prostate cancer to use it in a clinical setting and primary health care centers. **Materials and Methods:** Review of literature on prostate cancer screening for early detection from various dimensions, including etiology, epidemiology; risks and predisposing factors, screening strategies and lifestyle were examined to identify target populations. The discussion addresses PSA screening and offers guidelines to improve men's health. **Results:** Although prostate cancer mortality rates in developed countries have declined, in the developing world, men are diagnosed with prostate cancer at an advanced stage. **Conclusion:** The review article declared that there is a need to use consistent, continual and powerful educational activities for men, giving top priority to screenings.

Keywords: Digital Rectal Examination, Early Detection, Screening, Symptoms, Prostate Cancer, Prostate Specific Antigen.

INTRODUCTION

Prostate cancer is considered the third most common cancer worldwide with approximately 1.128 million cases [1]. Compared to other types of cancer, the death rate from prostate cancer has been estimated at 8% of the global population, accounting for 656,000 men in 2012 alone [1]. Statistical indications are alarming and demand more focus on prostate cancer screening for early detection and despite available screening tools with sensitivity and specificity to detect prostate cancer, preventive men's health has been neglected [2].

Most types of prostate cancer are slow growing, but some grow relatively fast [3; 4] and cause cancer cells to spread from the prostate to other parts of the body, particularly to the bones and lymph nodes [5]. It may initially cause no symptoms, but in later stages, it can cause difficulty urinating, blood in the urine, or pelvic pain and backache or dysuria [4].

If detected early, while the tumor is still confined to the prostate, there is a five-year survival rate at 90% compared to 35% for a more advanced state [6]. Early detection is a key factor for reducing morbidity and mortality associated with prostate cancer. In fact, the American Cancer Society recommends an annual digital rectal exam (DRE) and prostate-specific antigen (PSA) test starting at the age 40 for the high-risk group or those with a first-degree relative of any race diagnosed with prostate cancer before the age of 50. All others should be screened annually starting at 50 years of age [7].

Etiology of Prostate Cancer

Due to multiple factors, the prostate gland can form into adenocarcinoma as a slow growing and aggressively evolving cancer and metastasize in the bones and lymph nodes. Prostate cancer symptoms include pain, dysuria, sexual and erectile dysfunction [8]. Cellular changes in the prostate have been linked to genetic and environmental factors in various ethnic groups and in the global community other risk factors play an important role in developing prostate cancer, especially androgen hormone, the aging process, sexual lifestyle, environmental exposures, meat and animal-fat intake [8].

Epidemiology of Prostate Cancer

Prostate cancer incidence rates vary in regions and continents, largely because of the prostate cancer screening disparity and availability of services for biopsy compared to their widespread use in Europe and North America [9; 10]. Yet, developed countries have shown higher incidence rates, especially in certain developing regions such as the Caribbean, South America, and Sub-Saharan Africa [9;10].

In 2008 alone, there were an estimated 258,000 prostate cancer deaths worldwide and representing 6.1% of all cancers [9;10]. Mortality rates are predominantly high in black populations (Caribbean: 26.3/100,000; and Sub-Saharan Africa: 18.5/100,000), and very low in Asia, intermediate in Europe and Oceania [9;10]. In 2008, the European Union recorded 323,000 cancer cases leading to 71,000 deaths; South America had 334,000 cases with 76,000 deaths; the United States recorded 186,000 cases with 28,000 deaths; as cited in Ahmad et al., [11]. India reported 14,000 cases and 10,000 deaths; while China recorded 33,000 cases and 14,000 deaths [9;10].

Interestingly, Arab men have the lowest incidence of prostate cancer worldwide [12]. Although the exact incidence of prostate cancer in the Middle East and North African region is unknown, the reported incidence is approximately 5.8 cases per 100,000, with a mortality rate of 4.9 cases per 100,000 [13]. Similarly, Young [14] revealed the regional cancer databases from eight countries in the Middle East and North Africa—Jordan, Egypt, Bahrain, the Kingdom of Saudi Arabia, Kuwait, Qatar, Oman, and the United Arab Emirates—and found that prostate cancer was among the top four most frequently reported malignancies in five of those countries including Jordan. According to the published data by WHO (2011), when adjusted for age, prostate cancer death rates by world ranking in Lebanon was 35th; in Qatar, 93rd (6.58); and in Jordan 108th (5.77) [15].

Risk and Predisposing Factors

The specific causes of prostate cancer remain unknown [16] and the primary risk factors included age, family history, hormonal imbalance, environment, lifestyle, diet, men's health-seeking behaviors and sexually transmitted infections [8].

Age

Prostate cancer is uncommon in men younger than age 40 and gradually increases with advancing age at a risk of1 in 6 men developing prostate [17]. In the United States, 96% of prostate cancers occur in men ages 55 and older [18]. In a clinical study using prostate autopsy, Hsing et al., [19], found that 30% of cancers occurred in men age 50, and 90% in men age 90 and older. Moreover, autopsy studies of Chinese, German, Jamaican,

Swedish, and Ugandan men who died from other causes indicated that prostate cancer was present in 30% of men between the ages of 50–59 years, and in 80% of men ages 70–79 years [18].

A histological study on prostate cancer using prostatectomy and ultrasound-guided needle biopsy [20], found that among 108 Kenyan men ages 48–83 years, 76% had prostate hyperplasia and 26% had prostate cancer. These findings suggest that prostate cancer is common in men above 40 years in Kenya.

In Jordan, according to the Cancer Incidence Report of 2010, prostate cancer is more common (86.2%) in individuals 60 years and older with the highest age-specific incidence rate (230.7/100,000) among the 75–79 years, and the lowest (2.3/100,000) in men between 45–49 years. The incidence of prostate cancer steadily increases with age from (7.7) for men between 50–54 years; (31.3) for 55–59 years; (57.5) for men between 60–64 years; (103.2) for those between 65–69 years;(187.9) for 70–74 years; (230.7) for those 75–79 years; (217.4) for men between 80–84 years; to (56.1) for those above 85 years of age. All age-specific incidence rates are per 100,000 individuals with the Median age of 69 at diagnosis and the major morphology of 89% adenocarcinoma [21].

Genetics and Heredity

Previous studies have indicated that men with cancer diagnosis among their first-degree relatives are at a higher risk for prostate cancer, and that prostate cancer morbidity and mortality are more common in African-American and Caribbean males with routine diagnosis in later stages of the disease and lower survival rates [22;23].

In recent global studies evaluating the characteristics of prostate cancer across four populations in the United States (European and African Americans), Senegal, and India, researchers found that men from the developing countries (Senegal & India) were diagnosed at more advanced stages of the disease compared to men from the United States [24], which may have an unconfirmed familial relationship and genetic determinants for prostate cancer, if not early screening practices.

Hormonal Imbalances

Thirteen symptomatic men diagnosed with testosterone deficiency and untreated prostate cancer received low dose testosterone therapy and showed an increased rate of prostate cancer growth [25]. Researchers concluded that androgen was an important hormonal determinant for developing prostate cancer.

Environmental Factors

Exposure to heavy metals such as industrial cadmium and cigarette smoking appeared to increase the risk of prostate cancer as identified by elevated PSA levels and high cadmium levels in blood and urine among 295 men ages 50 and above. Researchers confirming that exposure to cadmium increased the risk of developing prostate cancer [26]. Similarly, exposure to Dioxin, an agricultural chemical known as 2-, 3-, 7-, and 8-tetrachlorodibenzo-p-dioxin) is an herbicide compound extensively used during the Vietnam War, and found in patients with an aggressive form of prostate cancer [27].

Lifestyle and Diet

Control of cancer includes several preventive approaches, such as lifestyle changes [28], a number of studies have identified nutrition as an important factor for the prevention of prostate cancer and treatment outcome. For instance, tomatoes, carotenoids, vegetables, vitamin E, selenium, marine fish, and soya beans have health benefits and prevent prostate cancer, while dairy products, calcium, zinc, saturated fats, and grilled meat appear to increase the risk of prostate cancer [8]. Another study has indicated that plant-and fish-based diets are associated with a reduced risk of developing prostate cancer [29], and no research evidence was found to relate diet and lifestyle with prostate cancer development in Jordan.

Health Seeking Behaviors

Health-seeking behaviors determine personal health practices, readiness to seek treatment for illness, and the extent of health care provided for family members. Assessing the health-seeking behaviors about screening and early detection of cancer is essential to design culturally appropriate and age-appropriate health promotion campaigns and services [30;31], the use of constant, persistent health promotion, educational activities can help to minimize anxiety, and enhance care for patients of such diseases [32].

Often, men, as the head of household, make health care decisions for themselves and their family [33], but frequently, their involvement in health-related issues are lacking. This can be improved through men's clinics, and by merging health services such as HIV counseling and testing with prostate or testicular cancer screening and treatment [34].

Studies in Jordan found that the improper practices toward cancer were existed among the participants and, if corrected, could improve the care, prevention, and early detection of cancer [28; 35].

Khalil and Maysoon [36], concluded that improvement in health seeking behavior among the population is needed to increase their awareness and practices to make appropriate and effective decisions towards health promotion and better quality of life.

In a study of African-American men, researchers found that worsening of urinary symptoms and local discomforts were associated with health-seeking behavior [37].

Collectively, these studies suggest that accessible and clear health information, health-related decision making, and disease manifestations promote men's health-seeking behavior. Health-seeking behavior about cancer found to be significant predictors of screening practice [38; 39].

Sexually Transmitted Infections

A number of sexually transmitted infections (STI) have been associated with an increased risk of prostate cancer. For instance, a study by Olusoga et al., [40], found associations between syphilis and high prostate-specific antigen (PSA) levels among Nigerian patients. Another study [41], indicated associations between Trichomonas Vaginitis infection and increased the risk of prostate cancer, advanced disease (stage 4), and death due to prostate cancer.

Studies have also shown that men with multiple sexual partners have an increased risk of developing prostate cancer [42]. Although no causal relationship has been established between STI and prostate cancer, it is possible that STI and multiple sexual partners—both of which are frequently observed in sexually active men —may contribute to the increasing prostate cancer rates.

Early Detection of Prostate Cancer

The purpose of screening is to detect prostate cancer at its earliest stages, before any symptoms have developed [43], because some of the symptoms experienced by men might indicate the presence of prostate cancer and these symptoms can be related to other prostate disorders, such as Benign Prostate Hyperplasia (BPH) or prostatitis requiring a more thorough work-up [7].

Typically, prostate cancer detected by screening in its very early-stages can be effectively treated. According to ACS [44], physicians can easily and quickly screen men for prostate cancer in their office by using prostate-specific antigen (PSA) blood test and digital rectal exam (DRE).In Jordan, a recent study conducted by Ahmad et al., [28], to enhance cancer prevention and care showed that the majority of the participants agreed that getting regular cancer checkup helps diagnose the disease early with a good prognosis.

Prostate-Specific Antigen (PSA)

With DRE and PSA men can be screened for prostate cancer [5;45], and PSA, which was discovered in 1971, has proven to be the most reliable biomarker for detecting, staging, and monitoring prostate cancer in its early stage [46]. In fact, PSA is more effective than other monitoring and diagnostic methods to detect prostate cancer and identifying new cases due to antigen specific affinity for prostatic tissues [47].

Prostate specific antigen is a 34kD glycoprotein enzyme produced by the prostate epithelium to liquefy the ejaculate and enable fertilization. Blood test for PSA finds both benign and malignant cells, because this specific antigen is found in the serum by benign and malignant prostate tissue as an organ specific product, but not cancer specific. A variety of non-cancer conditions may elevate serum PSA including urinary retention, prostatitis, vigorous prostate massage, and ejaculation. The normal range for the serum PSA assay in men is <4.0ng/mL, though this varies with age (table 1), Also, instrumentation such as cystoscopy, Foley catheter placement, and prostate biopsy can falsely elevate PSA. Therefore, a serum PSA should not be obtained immediately following such events and delayed for approximately 6 weeks [48].

Table 1: The age-adjusted normal range for PSA.

Age range	Normal PSA range (ng/mL)
All ages	<4.0
40–49	<2.5
50–59	<3.5
60–69	<4.5
>70	<6.5

Digital Rectal Examination (DRE)

The prostate gland is located immediately anterior to the rectum in men and DRE is the mainstay of prostate examination by digital palpation of in the left lateral position when the patient is lying on his left side, and hips and knees are flexed to 90degrees.Most men find DRE very uncomfortable or even painful and assessment should be avoided in the profoundly neutropenia patient to reduce the risk for septicemia, and in patients with anal fissure where DRE could cause severe pain [48].

Prostate Specific Antigen and Digital Rectal Examination

In the past, the digital rectal examination was the most accurate diagnostic modality to detect early stage of prostate cancer, but limited accuracy has reduced its use [47], and according to the American Cancer Society, men should be tested by PSA blood test. Digital rectal exam (DRE) may be done as a part of screening [44], and it is important to remember that no test is perfect. Combining PSA blood test with DRE provides more information for early and accurate detection of prostate cancer [49].

Time to Screen

According to the National Comprehensive Cancer Network, baseline DRE, and PSA testing is recommended for men at the age 40 for early screening and repeated annually for men with a PSA value ≥1.0 ng/mL. Men with PSA <1.0 ng/mL should be screened again at the age 45 and regular screening should be offered to all participants starting at the age 50 [50]. Furthermore, American Urology Association recommended early detection and risk assessment of prostate cancer should be offered to asymptomatic men age 40 and older, who wish to be screened and have an estimated life expectancy of more than 10 years [51].

In Canada, men age 40 and older are advised to establish a baseline PSA value and those at high risk for prostate cancer should discuss screening with their primary care provider before the age 40, whereas, men at or over the age of 70, can decide to end prostate cancer screening based on an informed discussion with their primary care provider [52].

The American Cancer Society recommends that men should make an informed decision with their health care provider about whether to be screened for prostate cancer and what are the limitations and potential benefits of early screening. Men should not be screened unless they have been informed and discussed screening with their primary care provider regarding base line data at the age 40 for those at higher risk (more than one first-degree relative diagnosed with prostate cancer at an early age), for men age 45 and at high risk for all other reasons related to developing prostate cancer. This includes African Americans men who have a first-degree relative (father, brother, or son) diagnosed with prostate cancer at an early age (younger than age 65), and age 50 for men who are at average risk for prostate cancer and are expected to live at least 10 more years [44].

Benefits and Limits of Prostate Cancer Screening

Prostate cancer screening detects cancer in men who do not have symptoms by DRE and PSA blood test [53], where DRE determines the approximate size and any unusual growths on the prostate gland. The DRE is beneficial because it can detect large masses at a low cost and it can be incorporated as part of a routine physical assessment in less than 15 seconds. However, DRE can miss small prostate tumors, has relatively poor specificity for prostate cancer screening, and can only evaluate the posterior-most aspect of the gland. Furthermore, DRE's effectiveness depends on the physician's assessment skills and experience [4].

The main benefit of the PSA is that with DRE could screen and detect prostate cancer. The limits are venipuncture for a blood test and misidentification of slow growing tumors with adverse consequences on a lifespan if left untreated. False diagnosis of cancer can cause unnecessary worry and treatments that lead to erectile dysfunction. In addition, the emotional toll and financial costs can burden many families [53]. Despite the exams 'limitations, they can provide important information to determine whether more testing is necessary and save lives [54].

Symptoms of Prostate Cancer

The vast majority of patients diagnosed with prostate cancer do not have any symptoms and it is important to note that most men with symptoms have benign (non-cancer) related causes such as urinary frequency, urgency, nocturnal urination, inability to start stream, a weak or interrupted stream, dysuria, incomplete emptying and feeling full, hematuria, back, hip and pelvic pain, weakness, weight loss, loss of appetite (the last three symptoms are common to all cancers when advanced) [55]. Furthermore, men experience difficulty with having or keeping an erection (erectile dysfunction), loss of bladder or bowel control [7].

Prevention of Prostate Cancer

As many as 32% of men in their 50's have histologically prostate cancer and knowing that clinical detection of the disease rarely occurs before the age of 50, is an indication that following preventative strategies for men are necessary [48]:

Choosing a healthy diet full of fruits and vegetables

High-fat foods should be avoided and a variety of fruits, vegetables, and whole grains added. Fruits and vegetables contain many vitamins and nutrients that can contribute to health. Whether diet can prevent prostate cancer, is yet to be conclusively proven, eating a healthy diet with a variety of fruits and vegetables can improve overall health [44;56].

Choosing healthy foods over supplements

No studies have shown that supplements play a role in reducing the risk of prostate cancer, but foods rich in vitamins and minerals can maintain healthy levels of vitamins in the body [44; 48;56].

Exercising most days of the week

Exercise improves the overall health, helps maintain weight and improves mood. There is some evidence that men who don't exercise have higher PSA levels, while men who exercise may have a lower risk of developing prostate cancer. Exercise most days of the week with a slow start and working up to every day of the week is the goal [45; 56].

Maintaining a healthy weight

If current weight is healthy, it should be maintained by exercising most days of the week. If weight loss is needed, more exercise should be added to increase metabolism, in addition to reduced number of calories through a plan for healthy weight loss [44;56].

CONCLUSIONS

Extensive reviews from global perspectives have identified a gap in providing sufficient information to men in their 40's and 50's at any clinical encounter to emphasize the importance of prostate cancer screening for early detection [57]. Testing to screen for prostate cancer with PSA is economical and accessible in most countries. The ongoing randomized studies to show the effectiveness of PSA screening could provide the best evidence and show risk: benefits of prostate cancer screening for early detection. Especially, that the paradigm for qualitative research is not well defined [58].

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