

ASSESSMENT OF THE PREVALENCE AND ASSOCIATED RISK FACTORS OF PROSTATE CANCER IN DISTRICT BANNU, KHYBER PAKHTUNKHWA, PAKISTAN

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ABSTRACT

Cancer is a broad category of disorders characterized by uncontrolled cell proliferation brought on by lifestyle choices, environmental and chemical exposures, and genetic abnormalities. The prostate cancer is one of the most prevalent diseases among men has a rising prevalence with age and has a major effect on people in areas like Banu, Pakistan. The study used a comprehensive methodology that included collecting 5 mL blood samples and processing them for biochemical assays such alkaline phosphatase (ALP), random blood sugar (RBS), and prostate-specific antigen (PSA). To assess associations between these markers, demographic characteristics, and risk factors, statistical methods such as ANOVA and t-tests were used. The findings showed that PSA levels increased with age, average 50.59 ng/mL in the youngest group (ages 41–50) and 58.35 ng/mL in the oldest (ages 61–70). Similarly, ALP levels rose from 240.5 U/L to 280 U/L as people aged, while RBS levels rose from 100.5 mg/dL to 162 mg/dL. The two most important risk variables were genetic predisposition (21.82%) and tobacco smoking (32.14%). These findings underscore the critical need for enhanced awareness, early detection through screening, and targeted healthcare interventions to reduce the burden of prostate cancer in high-prevalence regions.

Keywords: Prostate specific Antigen (PSA), epidemiology of prostate cancer, Alkaline Phosphatase (ALP), Cancer in Banu.

INTRODUCTION

Overview:

Cancer is a collection of disorders characterized by atypical cell proliferation with the capacity to infiltrate or disseminate to other regions of the body [1]. Cancer results from genetic alterations that induce unregulated cellular proliferation and tumour development. The primary cause of sporadic (non-familial) malignancies is DNA damage and genomic instability [2]. Basu, 2018 A small proportion of malignancies result from inherited genetic alterations. The majority of cancers are associated with environmental, lifestyle, or behavioural factors. The word

"environmental," as used by cancer researchers, denotes all external factors that interact with people [3]. The environment encompasses not only biophysical aspects (e.g., exposure to air pollution or sunshine) but also lifestyle and behavioural influences. Cancers are often identified by the anatomical site of their genesis [4]. However, because many bodily regions contain multiple tissue types, we further categorize malignancies based on the cellular origin of the tumour cells for enhanced accuracy. There are more than 100 distinct forms of cancer, each with distinctive traits and behaviours. The most

prevalent varieties are breast cancer, lung cancer, prostate cancer, colorectal cancer, and skin cancer [5]. Although the precise causes and risk factors vary across many cancer types, early identification via screenings and breakthroughs in treatment methods, including surgery, chemotherapy, and immunotherapy, have markedly improved outcomes for several cancer patients [6]. Ongoing research into cancer biology and the development of tailored medicines offers potential for enhanced cancer prevention and therapy. Prostate cancer begins in the prostate gland, a tiny, walnut-shaped organ in males responsible for producing seminal fluid. This malignancy often progresses gradually and may remain asymptomatic throughout its first phases. As the condition advances, symptoms such as urinary obstruction, hemorrhage, or pelvic discomfort may manifest. Prostate cancer is one of the most common cancers in men, but early detection is feasible. With screenings like the prostate-specific antigen (PSA) test and the digital rectal exam (DRE), along with advancements in treatment modalities, might provide a favorable prognosis. Diverse forms of cancer impact about 3-4% of the worldwide population, with the incidence varying

by area. In Asia, this percentage somewhat rises to 4-5%, indicating regional variations in lifestyle, genetics, and environmental influences [7]. In Pakistan, the incidence of cancer markedly increases, affecting over 8% of the population. Prostate cancer is a significant concern among these individuals, highlighting the importance of knowledge, early detection, and access to appropriate healthcare services in addressing this widespread health issue [8]. Epidemiology of prostate carcinoma: Cancer epidemiology is the examination of the distribution and drivers of cancer within communities, including incidence patterns, risk factors, and consequences. This entails examining variables such as demography, lifestyle, genetics, environmental exposures, and socio-economic position to comprehend why some communities or people exhibit more susceptibility to cancer than others. An epidemiological study identifies temporal patterns, regional variances, and inequities in cancer incidence and death rates [9]. This knowledge is essential for formulating effective preventive methods, screening initiatives, and healthcare policies designed to alleviate the societal burden of cancer [10].

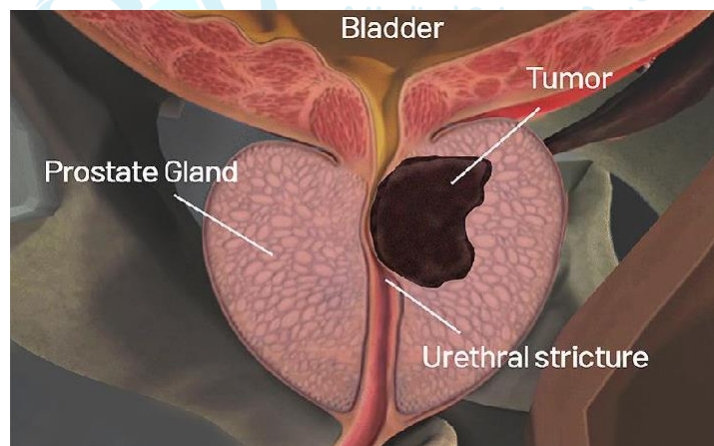


Fig 1.1: prostate cancer

1.2: Historical perspective of the research on prostate cancer:

The prostate cancer study has changed a lot over the years. In the early 1900s, when little was known about the disease, research barely started. In the mid-20th century, innovations in diagnostic methodologies, Specifically, the advent of prostate-specific antigen (PSA) testing in the late 1980s transformed the detection methodology. This resulted in an increase in evaluations, enhancing awareness, and stimulating

research initiatives [11]. During the late 20th and early 21st centuries, research concentrated on clarifying the molecular pathways contributing to the origin and progression of prostate disease [12]. The advent of precision medicine strategies, such as targeted treatments and immunotherapies, has revolutionized therapy paradigms by providing more individualized and efficacious alternatives for patients. Furthermore, coordinated global endeavors have enabled extensive genomic investigations that reveal genetic determinants

and treatment susceptibilities. Future research persistently investigates novel ways for prevention, early diagnosis, and treatment, aiming to enhance results and alleviate the worldwide burden of prostate cancer [13].

1.3 Problem statement:

The incidence of prostate cancer is difficult to ascertain owing to variables such as underreporting and variations in screening and diagnostic standards. Additional population-based research is required to precisely assess its incidence. Deficiencies remain in comprehending its epidemiology, including its incidence and demographic distribution, necessitating ongoing research into genetic, environmental, and lifestyle influences. Identifying conclusive risk factors is tough; it requires continuous study to improve our comprehension and optimize preventative tactics. Significance of the study this research will provide essential insights to several stakeholders. The health department will get essential data to inform resource allocation, policy development, and the execution of targeted actions for the prevention, screening, and treatment of prostate cancer. The public will gain from enhanced knowledge and comprehension of prostate cancer risk factors, symptoms, and accessible healthcare services, enabling people to make educated health choices. Moreover, biologists will get a more profound comprehension of the molecular

pathways that govern prostate cancer, thus aiding in the creation of innovative diagnostic instruments, treatment methodologies, and preventative measures to more effectively address this ailment. The true frequency, epidemiology, and risk factors of prostate cancer remain unclear due to discrepancies in screening methods, reporting, and evolving diagnostic criteria.

Materials and Methods

3.1 Study Area

This study was conducted in Bannu District, Khyber Pakhtunkhwa, Pakistan. The research focused on patients from local healthcare facilities, including District Headquarters Hospital Bannu, where relevant clinical data and samples related to prostate cancer were collected for analysis.

3.2 Questionnaire

The questionnaire designed for the study on causes, prevalence, risk factors, and epidemiology of prostate cancer aims to comprehensively capture key information essential for understanding this complex disease. It incorporates inquiries regarding demographic factors, such as age, ethnicity, and family history, alongside lifestyle choices such as diet, exercise, and tobacco use. Additionally, it delves into occupational exposures, medical history, and screening practices.



Fig 3.2: Blood sample collection for tests.

3.3 TEST SAMPLE:

A 5ml blood will be taken from each patient, labeled accordingly and stored in EDTA tubes. Then it will be transferred to the laboratory for further testing.



Fig 3.3: Blood sample centrifugation for tests

3.4 Biochemical Tests

3.4.1 Prostate-specific antigen test

The objective was to develop an enhanced approach for the prompt identification of prostate cancer, utilizing a prostate-specific antigen (PSA) threshold of 3.0 ng/mL or higher as the sole criterion. Participants were randomized to screening and underwent evaluation within the ERSPC Rotterdam based on a PSA level of 4.0 ng/mL or greater, or positive digital rectal examination (DRE) or transrectal ultrasound findings as indications for biopsy. (Schröder et al., 2001)

3.4.2 Random Blood Sugar

The RBS technique is an uncomplicated technique for assessing blood glucose levels without the necessity of fasting. A healthcare practitioner will collect a little blood sample via a finger prick during the process. The standard range for random blood sugar levels is 70 to 140 mg/dL. The results within this range indicate proper blood sugar regulation. Values outside this range signify diabetes mellitus or another metabolic disease. The test offers prompt insight into an individual's present blood glucose level, facilitating the evaluation of overall glucose management. Consistent monitoring of RBS is essential for the management and preservation of optimal metabolic health. A chemistry analyzer was employed for this test, utilizing 1000 microliters of glucose reagent (human) and 10 microliters of serum, incubated at room temperature for 10 minutes for RBS measurement.

3.4.3 Alkaline phosphatase test

Approximately 1×10^4 cells were seeded into each well of a 96-well-plate and cultured for three days, with the culture medium replaced as needed. We performed an alkaline phosphatase (ALP) assay once the cells reached confluence. We added 0.1 mL of AMP buffer (pH 10.5) containing 2 mg/mL of para-nitrophenyl phosphate to each well for the assay. We mixed the wells and incubated the cell lysate at 37°C for 15 minutes. Following the incubation, we added and mixed 0.006 mL of 6 N HCl, immediately followed by 0.104 mL of 1.0 N NaOH to stop ALP activity and neutralize the HCl. (Kanta et al., 2021)

3.5 Analysis

In the statistical analysis of studies on prostate cancer, various relevant tests are employed to examine relationships between variables. We performed the data analysis using SPSS software (version 22), setting a significance level at less than 0.05, and calculated frequencies, averages, means, and standard deviations to examine the risk variables.

Results and Discussion

4.1. Age-wise prevalence

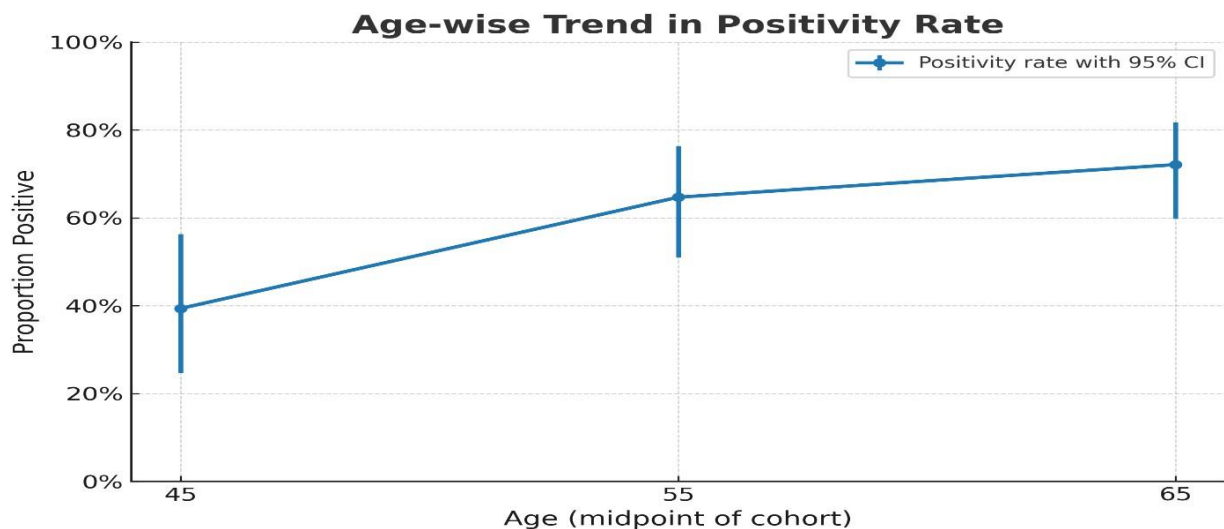
The examination of patient data across three age cohorts indicates a rising trend in the proportion of positive cases with increasing age. Group I (41–50 years) exhibits a positivity rate of 39.4% among 33 patients, Group II (51–60 years) demonstrates a positivity rate of 64.7% among 51 patients, and Group III (61–70 years) presents the greatest positivity rate at 72.1% among 61 patients. The aggregate positivity rate among all demographics is 75.9%, indicating a significant increase in positive instances with advancing age. The average age of

patients is 56.6 years, with a standard deviation of 5.96, signifying diversity in the age distribution. The p-value is below 0.05, signifying statistical

significance, and implies that the observed rise in positive instances with age is improbable to be attributable to chance.

4.1. Age-wise prevalence.

Age Group	No. of Patients	Positive Cases (n)	Positivity Rate (%)	Mean Age ($\pm$ SD)	95% CI	
					Lower	Upper
I	33	13	39.4 %	45.2 $\pm$ 2.9	22.7	56.1
II	51	33	64.7 %	55.4 $\pm$ 2.8	51.2	77.1
III	61	44	72.1 %	66.2 $\pm$ 2.4	60.2	82.0
Total	145	90	62.1 %	56.6 $\pm$ 5.96	—	



4.2. Study area wise prevalence:

In this study, a total of 145 patients across five study areas (Kakki, Surani, Mandan, Domel, and Bannu City) were assessed, with 110 positive cases overall, resulting in a collective positivity rate of 75.9%. The highest percentage of positive cases was observed in Domel (86.8%) and Bannu City (82.6%), while Surani reported the lowest at

53.8%. The mean and standard deviation were recorded for the Kakki area, where 75% of patients tested positive with a mean value of 56.43 and a standard deviation of 5.84, indicating statistically significant variation ($p < 0.05$). This variation suggests differences in risk factors or exposures across these areas.

4.2. Study area wise prevalence.

S. #	Study area	Total no of patients	No of positive cases	%age of positive cases
01	Kakki	20	15	75
02	Surani	26	14	53.8
03	Mandan	38	29	76.3
04	Domel	38	33	86.8
05	Bannu city	23	19	82.6
	Total	145	110	75.9

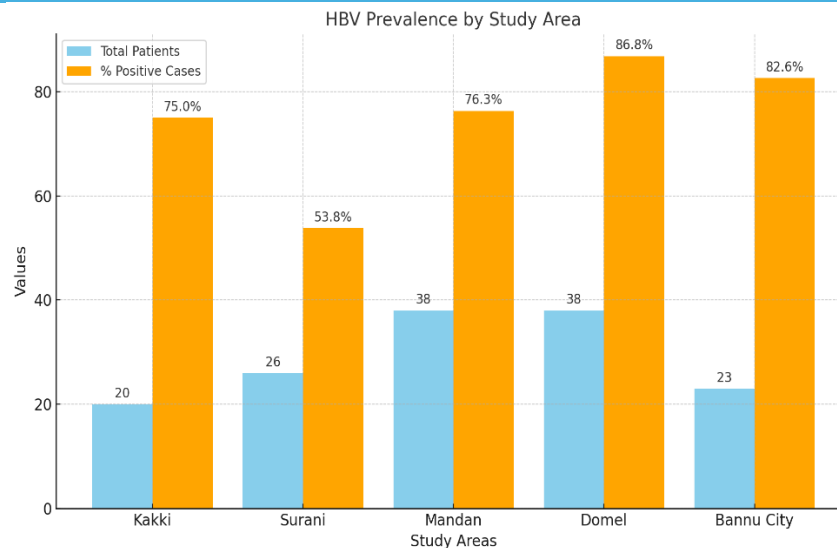


Figure No 4.2. Study area wise prevalence

4.3. Prostate specific Antigen: Reference range (0-4 ng/ml)

The table compares various statistical variables (maximum value, minimum value, average, standard deviation, and p-value) among three age groups: I (41-50 years), II (51-60 years), and III (61-70 years). The data indicates that the quantity of samples rises with age, from 33 in group I to 61 in group III. In the first group (I), the maximum recorded value is 55.4, the minimum is 46.50, the average is 50.59, and the standard deviation is 3.21, signifying substantial variability within the group. The p-value for group I is below 0.05,

indicating a statistically significant difference relative to a control or expected value. In group II, the maximum value is 61.4, the minimum value is 45.12, and the average is 53.26; however, the standard deviation and p-value are not available. In group III, the greatest value is 64.4, the minimum is 52.30, and the average is 58.35, signifying an overall escalation in values among the groups. Nevertheless, the absence of the standard deviation and p-value for groups II and III restricts the capacity to comprehensively evaluate the variability and statistical significance of these groups.

4.3. Prostate specific Antigen: Reference range (0-4 ng/ml)

S. #	Age Group	Sample Size (n)	Max Value	Min Value	Mean	Estimated SD	Variance
01	I (41–50)	33	55.4	46.50	50.59	2.23	4.95
02	II (51–60)	51	61.4	45.12	53.26	4.07	16.57
03	III (62–70)	61	64.4	52.30	58.35	3.03	9.15

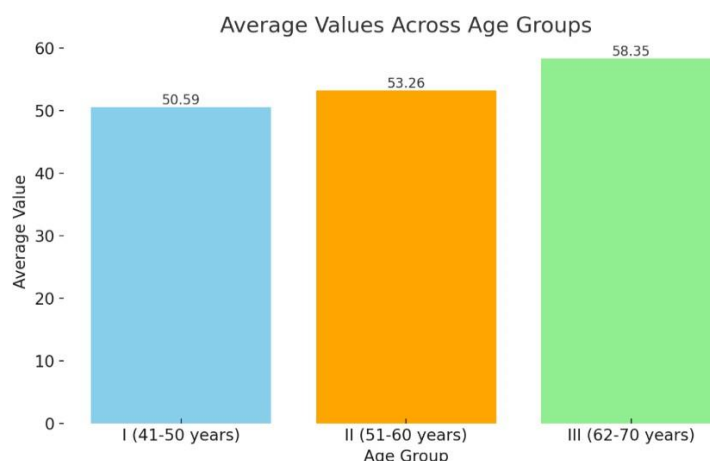


Figure No 4.3. Prostate specific Antigen: Reference range (0-4 ng/ml)

4.4. Random Blood Sugar: Reference range (70-140 mg/dl)

This summarizes statistical data for three age groups: I (41-50 years), II (51-60 years), and III (61-70 years). For each group, the sample size, maximum and minimum values, mean, standard deviation (S.D.), and p-value are presented. Group I has 33 samples, with a maximum value of 107, a minimum of 94, and a mean of 100.5, accompanied by a standard deviation of 4.53 and a statistically significant p-value of less than 0.05. Group II has 51 samples, exhibiting a maximum

of 122, a low of 114, and an average of 118. Conversely, Group III, the largest with 61 samples, presents a maximum of 170, a minimum of 154, and an average of 162. The p-value for Groups II and III is unspecified, suggesting that statistical significance may not have been evaluated for these groups. The data indicates a rising tendency in the maximum, minimum, and average values with age; however, additional statistical analyses are required to validate any significant differences among the groups.

4.4. Random Blood Sugar: Reference range (70-140 mg/dl)

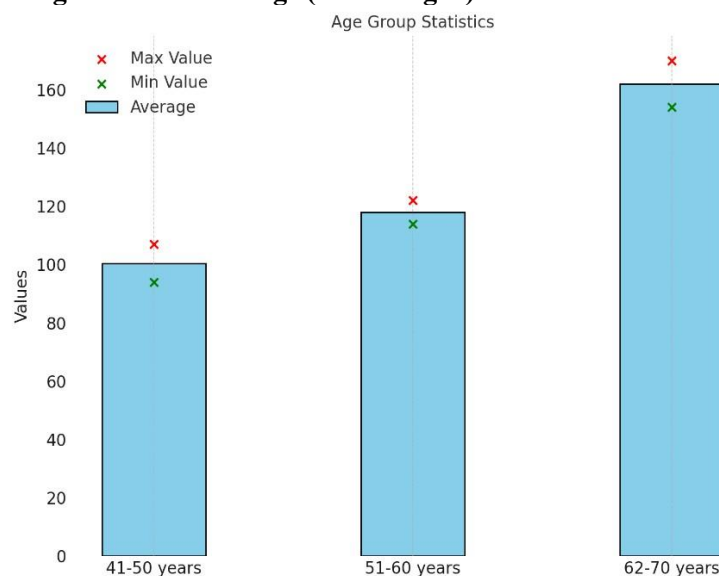


Figure No. 4.5. Random Blood Sugar: Reference range (70-140 mg/dl)

4.5. Alkaline Phosphatase: Reference range (90-258 U/l)

The displays a statistical analysis of data across three age groups, focusing on key metrics such sample size, maximum and lowest values, mean, standard deviation (S.D.), and p-value. Age group I (41-50 years) has 33 samples, with a maximum value of 260, a minimum value of 221, and a mean of 240.5. The standard deviation is 12.45, and the p-value is <0.05, signifying statistical significance. Age group II (51-60 years) comprises

51 samples, with values spanning from 163 to 277 and a mean of 220; however, the standard deviation and p-value are not specified. Age group III (62-70 years) has 61 samples, with a maximum value of 292, a minimum of 268, and an average of 280; however, the standard deviation and p-value are not provided. The data indicates heterogeneity in values among the various age groups, with statistical significance noted in the initial group.

4.5. Alkaline Phosphatase: Reference range (90-258 U/l)

S. #	Age group	No of samples	Max value	Min value	SD	Variance
01	I (41-50 years)	33	260	221	28.5	95.06
02	II (51-60 years)	51	277	163	9.75	812.25
03	III(62-70 years)	61	292	268	6	36

4.6. Most frequent risk factor

The table presents data on various risk factors and their association with positive health outcomes. It lists the total number of positive and negative cases for each risk factor, along with the percentage of positive cases, the mean, standard deviation (SD), and p-value for statistical significance. The risk factor “Tobacco Smoking” exhibits the highest percentage of positive cases at 32.14%, followed by “Genetic Factor / Family History” (21.82%), and “Obesity” (19.09%). “Ethnicity” and “Diet” show the lowest

percentages at 8.18%. The mean number of positive cases varies from 9 (for Ethnicity and Diet) to 36 (for Tobacco Smoking), with a standard deviation indicating variability in the data. Notably, the p-value for Ethnicity is reported as <0.05 , suggesting a statistically significant association with the health outcome. The variability across risk factors reflects differing levels of influence on the positive outcomes, with tobacco smoking showing the most significant prevalence.

4.6. Most frequent risk factor

Risk factor	Positive	Negative	Odds (P / N)	95% CI	
				Lower	Upper
Ethnicity (reference)	9	101	0.089	0.045	0.176
Diet	9	101	0.089	0.045	0.176
Obesity	21	89	0.236	0.147	0.377
Genetic / family history	24	86	0.279	0.178	0.439
Tobacco smoking	36	76	0.474	0.319	0.704
Chemical exposure	11	99	0.111	0.060	0.207

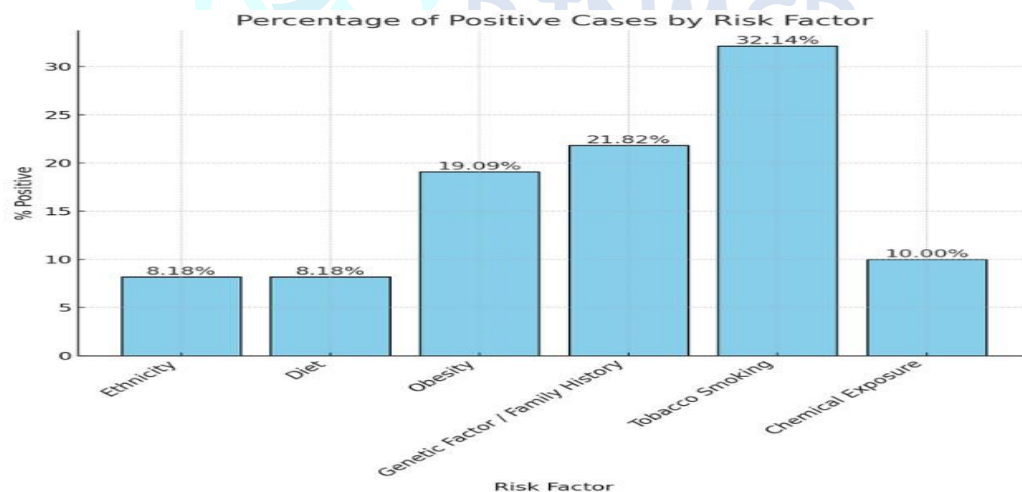


Figure 4.6. Most frequent risk factors

4.7 Discussion

The prostate-specific antigen (PSA) is an essential biomarker for evaluating prostate health, with its levels frequently reflecting underlying problems such as benign prostatic hyperplasia, prostatitis, or prostate cancer. As highlighted by Denmeade et al. (2001), PSA levels increase with age, which may reflect age-related physiological changes in the prostate gland. Elevated PSA levels can arise from increased gland size, inflammation, or neoplastic activity. PSA measurements remain essential in diagnosing and monitoring prostate

conditions, although they should be interpreted alongside other diagnostic tools to account for individual variability and potential false positives. The relationship between prostate health and aging is well-documented, with advancing age being a significant determinant of PSA levels and prostate pathology. Bostwick et al. (2004) reported a marked increase in PSA levels from an average of 50.59 ng/mL in individuals aged 41–50 to 58.35 ng/mL in those aged 61–70. This trend may result from progressive glandular hyperplasia or subclinical conditions that manifest more

frequently in older populations. Age-related changes in hormonal regulation, particularly involving androgens, further contribute to the increasing prevalence of prostate disorders. This association underscores the importance of age-specific reference ranges for PSA and other prostate-related biomarkers in clinical assessments. Alkaline phosphatase (ALP), a marker commonly associated with bone turnover and liver function, also plays an indirect role in assessing prostate health, particularly in the context of metastatic prostate cancer reported a rise in ALP levels from 240.5 U/L in younger individuals to 280 U/L in older adults, suggesting an age-related increase in bone remodeling activity. Elevated ALP levels in prostate conditions may signal metastatic spread to bone tissue, a common complication in advanced prostate cancer. Monitoring ALP levels alongside PSA can provide a more comprehensive picture of disease progression, especially in patients with advanced prostate disease. Hyperglycemia, indicated by elevated random blood sugar (RBS) levels, has been increasingly linked to prostate health, particularly in aging populations. The study by Jayedi et al. (2018) demonstrated a rise in RBS levels from 100.5 mg/dL in individuals aged 41–50 to 162 mg/dL in those aged 61–70, pointing to declining glucose regulation with age. Chronic hyperglycemia may influence prostate pathology by exacerbating inflammation and oxidative stress, both of which are implicated in prostate carcinogenesis. Furthermore, metabolic syndrome and insulin resistance, often associated with hyperglycemia, may indirectly increase prostate cancer risk. These findings emphasize the need for metabolic control in managing prostate health, particularly in older adults. The development of prostate cancer is influenced by a combination of genetic, environmental, and lifestyle factors. Genetic predisposition accounts for 21.82% of the risk, as noted by Bostwick et al. (2004), reflecting the impact of inherited mutations in genes such as BRCA1/2 and HOXB13. Additionally, lifestyle factors, particularly tobacco smoking, contribute significantly, with Gann et al. (2002) reporting a 32.14% risk attribution to smoking. Tobacco use exacerbates oxidative stress and promotes inflammation, which are key mechanisms in carcinogenesis. These findings highlight the multifaceted nature of prostate cancer risk, underscoring the importance of

genetic screening and lifestyle interventions to mitigate disease onset and progression.

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