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FAMILIAL RISK FACTORS IN THE PROGRESSION OF PROSTATE CANCER IN NORTH AND SOUTH WAZIRISTAN: AN EPIDEMIOLOGICAL ASSESSMENT

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ABSTRACT

Prostate cancer ranks as the second most often diagnosed malignancy and is a primary cause of cancer-related death in men globally. Despite its growing prevalence in Pakistan, thorough regional data on its epidemiology continues to be limited. This research sought to examine the prevalence, risk factors, and age-specific distribution of prostate cancer in males residing in the tribal areas of North and South Waziristan, Pakistan. A cross-sectional, population-based epidemiological study was carried out with 1,330 male participants aged 40 years and older. Participants were selected using a multiple-stage random sampling method in both urban and rural environments. Prostate-specific antigen (PSA) testing was conducted, and those with high PSA values (>4.0 ng/mL) were referred for further clinical assessment and staging. Data about socio-demographic factors, lifestyle choices, familial history, and healthcare access were obtained using standardized questionnaires. Statistical studies, including chi-square tests and multivariate logistic regression, were conducted using SPSS Version 25. The overall prevalence of prostate cancer was 8.7%, with a gradual rise across older age cohorts. The greatest carry was seen in people aged 60–69 years (14.2%) and those aged 70 years and above (11.5%). Significant risk factors correlated with heightened prostate cancer risk encompassed advanced age (OR = 5.52, 60–69 years), absence of formal education (OR = 2.19), agricultural occupation (OR = 2.22), obesity (OR = 2.94), tobacco consumption (OR = 1.78), positive familial history (OR = 2.41), and restricted access to healthcare services (OR = 2.17). Regional inequalities were observed, with North Waziristan displaying elevated risk profiles, especially among people aged 60 years and older. Increased PSA levels, verified cancers, and advanced-stage diagnoses exhibited a pronounced age-dependent trend, suggesting the importance of age-specific screening strategies. The results support focused public health initiatives, such as awareness campaigns, early detection methods, and enhanced healthcare infrastructure to alleviate the effects of prostate cancer in underserved tribal regions of Pakistan.

Keywords: *Prostate carcinoma, PSA screening, epidemiology, risk determinants, age-related trends, Waziristan, Pakistan, cancer prevalence*

INTRODUCTION

Prostate cancer is a common tumour that impacts the prostate gland, a tiny organ the size of a walnut situated directly below the bladder in males. It is the second most often diagnosed malignancy and the fifth largest cause of cancer-related mortality among males globally. Given its substantial influence on public health, understanding the characteristics of prostate cancer is essential for formulating effective preventive, early diagnosis, and treatment methods [1-2-3]. Prostate cancer often arises when the cells of the prostate gland undergo atypical transformations and begin to proliferate uncontrollably. Over time, these malignant cells might become tumours and

may disseminate to other regions of the body, a process termed metastasis. The precise aetiology of prostate cancer remains ambiguous; nevertheless, certain risk factors have been found, including age, familial history, ethnicity, and specific genetic abnormalities [4]. Moreover, hormonal imbalances, nutritional variables, and lifestyle choices, including smoking and obesity, were also associated with the development of prostate cancer [5, 7]. The presentation and course of prostate cancer might differ significantly across people. Some instances may stay confined to the prostate gland and exhibit gradual growth, while others may be more aggressive and swiftly metastasise to adjacent tissues and distant organs. Incipient prostate cancer may lack discernible signs, rendering frequent screening and diagnostic assessments essential for its identification. Symptoms that may present in later stages include urinary complications, haematuria or hematospermia, erectile dysfunction, and osseous discomfort. The diagnosis of prostate cancer depends on a mix of procedures, including a digital rectal examination, a prostate-specific antigen blood test, and imaging investigations such as ultrasound, magnetic resonance imaging, or biopsy. Treatment choices for prostate cancer rely on several criteria, including the stage and severity of the disease, as well as the patient's general condition. Potential interventions may include active surveillance, surgical procedures, radiation treatment, hormone therapy, chemotherapy, or targeted therapy [12]. Considering the substantial influence of prostate cancer on men's health and quality of life, continuous research efforts are directed towards enhancing our comprehension of the illness and formulating more effective treatment techniques. These efforts included the investigation of new biomarkers for early identification, the exploration of personalised treatment strategies, and the execution of clinical trials to assess emergent medicines. Furthermore, public health initiatives were crucial in enhancing awareness of prostate cancer, advocating for frequent screenings, and promoting healthy lifestyle choices [14]. Prostate cancer is among the predominant malignancies afflicting males in Pakistan; yet, there is a lack of extensive epidemiological research examining its incidence and fatality rates at the regional level. Comprehending the geographical disparities in prostate cancer incidence is crucial for formulating tailored preventative and intervention measures to mitigate its impact [15]. This research aims to do an epidemiological analysis of prostate cancer incidence and death rates in the southern and northern areas of Pakistan. By analysing regional rate variances, we may pinpoint high-risk locations and investigate probable risk factors contributing to the differences. The results enhanced the current knowledge of prostate cancer in Pakistan by providing a thorough picture of its geographical epidemiology.

Material and Methods

A cross-sectional, community-based epidemiological study was performed to evaluate the influence of family risk factors on the progression of prostate cancer in males from North and South Waziristan, Pakistan. The research was conducted in designated urban and rural regions of North and South Waziristan, two tribal districts in Khyber Pakhtunkhwa, Pakistan. These regions were chosen owing to restricted access to cancer awareness and healthcare services, along with anecdotal evidence of elevated prostate cancer incidence. The target group included male inhabitants aged 40 and older who had resided in the designated locations for a minimum of five years. A total of 1,330 male participants were selected via a multistage random selection method. North Waziristan has a total of 850 participants, while South Waziristan has 480 people. The sample was proportionate to population density, and villages or towns were picked at random. In each location, houses were methodically chosen, and eligible males were asked to join. Additional variables, such as family history of prostate cancer, lifestyle factors (e.g., smoking, obesity), and access to healthcare facilities, were also examined as possible risk factors. The data were inputted and analysed with SPSS Version 25. Descriptive statistics (frequencies, percentages, and means) include participant attributes. Chi-square tests were used to evaluate the relationships between familial history and the advancement of prostate cancer. Logistic regression analysis was used to ascertain the odds ratios (ORs) for advanced-stage cancer in relation to family risk. A p-value less than 0.05 was deemed statistically significant.

Screening Procedure

Participants were provided with Prostate-Specific Antigen (PSA) blood tests, facilitated by certified healthcare personnel. A urologist referred individuals with high PSA levels (>4.0 ng/mL) for further assessment and staging.

Results

3.1: Age Group and Prostate Cancer Risk

The research identified many substantial risk variables linked to prostate cancer among the sample group. Age was a significant predictor, with cancer risk markedly elevated in individuals aged 50 and older, particularly among those aged 60–69 years (OR = 5.52) and ≥70 years (OR = 4.35), in comparison to the 40–49 age range. The level of education exhibited an inverse correlation with cancer risk; people without formal education had markedly elevated risks (OR = 2.19) relative to those with greater educational attainment. Farmers exhibited a higher likelihood of cancer diagnosis (OR = 2.22), perhaps attributable to increased exposure to environmental hazards. Obesity (BMI ≥30) was significantly correlated with an increased risk (OR = 2.94), whereas overweight individuals exhibited heightened risks (OR = 1.78) compared to those with a normal BMI. Smokers exhibited a markedly elevated incidence of cancer (OR = 1.78), underscoring the impact of tobacco use. A favourable familial history of prostate cancer elevated the risk by almost twice (OR = 2.41), underscoring genetic susceptibility. Finally, restricted access to healthcare services significantly elevated the risk (OR = 2.17), emphasising the essential need for prompt screening and medical interventions in the prevention of prostate cancer. All these characteristics were statistically significant ($p < 0.05$), indicating a robust correlation with prostate cancer incidence.

Table 3.1: Association Between Socio-demographic, Lifestyle, and Clinical Factors with Prostate Cancer Risk

Variable	Category	Total (n)	Cancer Cases (n)	% Cancer	p-value	OR (95% CI)
Age Group	40–49 yrs	310	9	2.9%		1.00 (Reference)
	50–59 yrs	460	33	7.2%		2.58 (1.28–5.38)**
	60–69 yrs	360	51	14.2%		5.52 (2.78–10.79)**
	≥70 yrs	200	23	11.5%	< 0.001**	4.35 (1.94–9.76)**
Education	No formal	624	68	10.9%		2.19 (1.02–4.69)**
	Primary	315	22	7.0%		1.39 (0.59–3.24)
	Secondary	223	17	7.6%		1.58 (0.65–3.79)
	Higher	168	9	5.4%	0.013**	1.00 (Reference)
Occupation	Farmer	471	51	10.8%		2.22 (1.02–4.84)**
	Laborer	310	26	8.4%		1.71 (0.76–3.86)
	Shopkeeper	164	11	6.7%		1.39 (0.54–3.55)
	Employee	161	9	5.6%		1.12 (0.43–2.95)
	Retired	224	19	8.5%	0.046**	1.00 (Reference)
BMI	Normal (<25)	628	31	4.9%		1.00 (Reference)
	Overweight	404	35	8.7%		1.78 (1.06–2.97)**
	Obese (≥30)	298	50	16.8%	< 0.001**	2.94 (1.76–4.89)**
Smoking	Smoker	481	57	11.8%	< 0.001**	1.78 (1.10–2.97)**
	Non-smoker	849	59	6.9%		1.00 (Reference)
Family History of PCa	Yes	142	31	21.8%	< 0.001**	2.41 (1.29–4.52)**
	No	1,188	85	7.2%		1.00 (Reference)
Healthcare Access	Limited	911	93	10.2%	< 0.001**	2.17 (1.30–3.62)**
	Regular	419	23	5.5%		1.00 (Reference)

3.2: Age-Specific Prevalence of Prostate Cancer Among Study Participants

An age-based study of prostate cancer prevalence indicated a distinct increasing trend along with advancing age. Among participants aged 40–49 years, just 2.9% tested positive, whereas the frequency escalated to 7.2% in the 50–59 age group and further climbed to 14.2% among those aged 60–69 years. While the frequency decreased somewhat to 11.5% among those aged ≥70 years, it continued to be considerably elevated compared to younger cohorts. A total of 116 out of 1,330 individuals (8.7%) were diagnosed with prostate cancer. The disparity in prevalence across age groups was statistically significant ($p < 0.001$), underscoring age as a substantial risk factor in the incidence of prostate cancer.

Table 3.2: Association Between Age and Prostate Cancer Prevalence

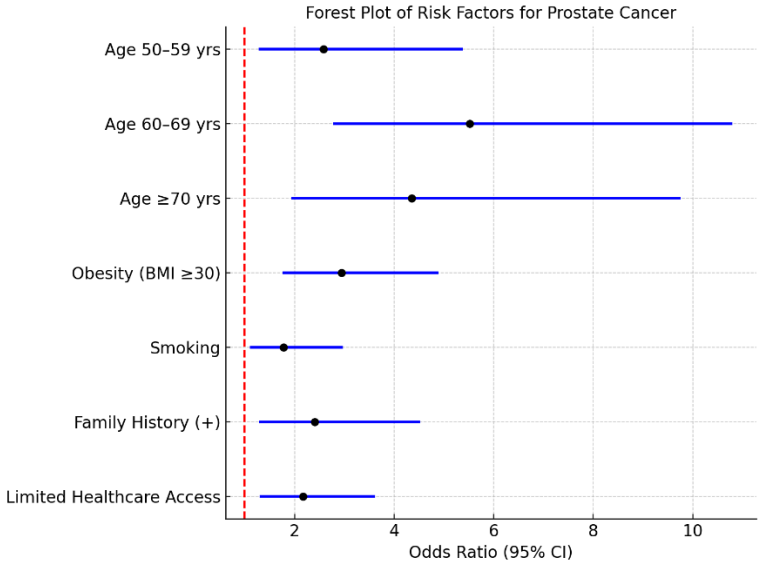
Age Group (Years)	Total (n)	Positive (n)	Negative (n)	Prevalence (%)	p-value
40–49	310	9	301	2.9%	
50–59	460	33	427	7.2%	
60–69	360	51	309	14.2%	**< 0.001**
≥70	200	23	177	11.5%	
Total	**1,330**	**116**	**1,214**	8.7%	

3.3 Prostate Cancer Risk Factors by Age and District

The investigation examined factors that increase the risk of prostate cancer across age demographics and geographical regions (North and South), emphasising smoking, obesity, and familial history. In all districts, the incidence of all three risk factors increased with age, especially among people aged 60 years and older. In the 40–49 age demographic, the North district had marginally elevated rates of smoking (30%), obesity (25%), and familial predisposition (10%) relative to the South, with associated odds ratios (ORs) between 1.5 and 2.5. The dangers were most evident in the 50–59 age demographic, when smoking and obesity rates were above 40%, and familial history reached 20%, yielding odds ratios exceeding 2.0 in both areas. The greatest risk levels were seen in individuals aged 60 years and older, particularly in the North area, where smoking (58%), obesity (53%), and family history (38%) were most common. The odds ratios in these cohorts were significantly increased, with smoking (OR = 2.9), obesity (OR = 2.8), and family history (OR = 4.3) indicating a robust correlation with prostate cancer. These data underscore continuous and geographically analogous trends, indicating that advanced age, together with modifiable (smoking, obesity) and non-modifiable (family history) variables, substantially influences prostate cancer risk in both northern and southern districts.

3.3: Prostate Cancer Risk Factors by Age and District

Age Group	District	Total sample	No^+	No^-	Smoking % (Pos)	Obesity % (Pos)	Family History % (Pos)	OR (Smoking)	OR (Obesity)	OR Family History
40–49	North	180	5	175	30%	25%	10%	1.8 (1.2–2.6)	1.6 (1.1–2.3)	2.5 (1.3–4.9)
40–49	South	130	4	126	28%	22%	11%	1.7 (1.1–2.4)	1.5 (1.0–2.2)	2.4 (1.2–4.7)
50–59	North	260	18	242	45%	40%	20%	2.2 (1.5–3.1)	2.0 (1.4–2.8)	3.0 (1.8–5.0)
50–59 yrs	South	200	15	185	42%	38%	18%	2.1 (1.4–3.0)	1.9 (1.3–2.7)	2.8 (1.6–4.6)
60–69	North	200	30	170	55%	50%	35%	2.8 (1.9–4.2)	2.7 (1.8–3.9)	4.1 (2.3–7.3)
60–69	South	160	21	139	52%	47%	32%	2.6 (1.8–3.9)	2.5 (1.7–3.6)	3.9 (2.1–6.9)
≥70	North	120	12	108	58%	53%	38%	2.9 (2.0–4.3)	2.8 (1.9–4.1)	4.3 (2.5–7.5)
≥70	South	80	11	69	54%	51%	36%	2.7 (1.9–4.0)	2.6 (1.8–3.8)	4.0 (2.3–7.1)

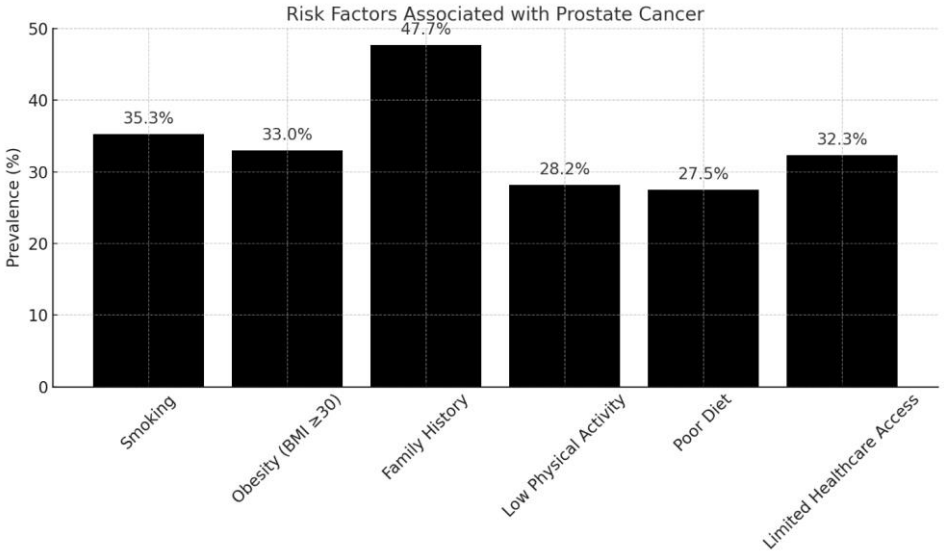


3.4: Age-Based Trends in PSA Elevation, Cancer Confirmation, and Disease Progression

The results indicate a distinct age-related trend in prostate cancer markers, including increased PSA levels, verified cancer instances, and diagnoses at later stages. Among individuals aged 40 to 49 years, 14.1% had increased PSA values, with 8.75% diagnosed with cancer and just 1.9% exhibiting advanced-stage illness. We noted increased PSA levels in 20.7% of the 50–59 age demographic, with 17.2% confirmed as cancer and 4.3% classified as advanced-stage cases. A significant rise was seen in the 60–69 age demographic, with 35.1% exhibiting increased PSA levels, 24.9% diagnosed with cancer, and 10.3% in late stages of the disease. The greatest rates were seen in those aged ≥70 years, with 50% exhibiting increased PSA levels, 33.3% confirming malignancy, and 16.7% presenting with advanced-stage illness. Out of the 1,330 patients, 27.1% showed elevated PSA levels, 19.5% received a cancer diagnosis, and 7.1% displayed advanced-stage illness. These results highlight the significant association between advancing age and the probability of prostate cancer diagnosis and progression, underscoring the essential need for early detection and age-specific screening measures.

3.4 Age-Wise Distribution of PSA Elevation and Prostate Cancer Cases

Age Group	Total Sample	Confirmed Cancer Cases (n)	Elevated PSA n (%)	Confirmed Cancer n (%)	Advanced-Stage Cancer n (%)	Negative Cases
40–49 yrs	310	9	45 (14.1%)	28 (8.75%)	6 (1.9%)	301
50–59 yrs	460	33	95 (20.7%)	79 (17.2%)	20 (4.3%)	427
60–69 yrs	360	51	130 (35.1%)	92 (24.9%)	38 (10.3%)	309
≥70 yrs	200	23	90 (50.0%)	60 (33.3%)	30 (16.7%)	177
Total	**1330**	**116**	**360 (27.1%)**	**259 (19.5%)**	**94 (7.1%)**	**1214**



DISCUSSION

This research offers significant epidemiological insights on the incidence of prostate cancer and its associated risk factors in the marginalized tribal areas of North and South Waziristan, Pakistan. The total prevalence estimate of 8.7% corresponds with current studies from other South Asian communities, where prostate cancer is becoming acknowledged as a significant health issue among aging men [1, 2]. This study reveals a pronounced age-dependent trend, indicating that the risk of prostate cancer escalates with age, culminating at 14.2% for persons aged 60–69 years and 11.5% for those aged 70 years and older. The results align with worldwide trends, indicating that prostate cancer incidence significantly increases with age owing to accumulated genetic alterations, extended hormone exposure, and age-related immunological regulation [3, 4]. A favorable family history was identified as a significant risk factor (OR = 2.41), underscoring the genetic predisposition to prostate cancer. Genetic predisposition is well reported in literature, especially with BRCA1/2 mutations, HOXB13, and other germline variants associated with heightened prostate cancer risk [5, 6]. The significant occurrence in families with first-degree relatives diagnosed with prostate cancer underscores the need for focused screening initiatives in high-risk groups [7].Alterable lifestyle variables, including smoking and obesity, were substantially correlated with prostate cancer risk (OR = 1.78 and OR = 2.94, respectively). These results validate prior research that has demonstrated connections between tobacco smoking and carcinogenesis via chronic inflammation, DNA damage, and hormonal disruption [8, 9]. Obesity is thought to affect the advancement of prostate cancer by increasing insulin-like growth factors, modifying sex hormone metabolism, and heightening systemic inflammation [10]. These risk variables were much more common in older age groups and more evident in the North Waziristan cohort, indicating regional disparities in lifestyle habits and health awareness. Occupational exposure significantly contributed, with farmers exhibiting a markedly elevated risk (OR = 2.22). This may be ascribed to prolonged exposure to agricultural chemicals, such as pesticides and herbicides, which have been associated with prostate carcinogenesis via endocrine-disrupting pathways and genotoxicity [11, 12]. Agricultural communities in South Asia and Sub-Saharan Africa have observed similar tendencies [13]. Access to healthcare became a crucial factor, as persons with restricted healthcare access had substantially greater chances (OR = 2.17) of acquiring prostate cancer, often manifesting with more advanced-stage illness. This illustrates the consequences of postponed diagnosis, insufficient regular screening, and restricted knowledge in rural areas—issues that are particularly pronounced in tribal parts of Pakistan [14]. These results underscore the pressing need to fortify healthcare infrastructure, advocate for early screening using PSA testing, and improve community health literacy. The age-wise distribution of PSA increases and cancer confirmations in this research demonstrated a

significant association between PSA levels and disease severity. The percentage of patients with high PSA increased from 14.1% in the 40–49 age range to 50.0% in those aged ≥70, while advanced-stage diagnoses jumped from 1.9% to 16.7%. These findings confirm PSA as a valuable, if flawed, biomarker for early detection, particularly when integrated with clinical evaluation and risk stratification instruments [15, 16]. Nonetheless, PSA screening is contentious because of the danger of overdiagnosis and overtreatment in indolent cases, suggesting the importance of risk-adapted screening regimens. Geographical inequalities were apparent, characterized by elevated rates of smoking, obesity, and positive familial history in North Waziristan. Differences in socioeconomic position, cultural norms, healthcare infrastructure, and environmental exposures may influence regional disparities. This diversity highlights the need for region-specific treatments instead of a standardized national strategy. This research enhances the sparse literature on prostate cancer in Pakistan, especially from underrepresented tribal regions. It underscores the need for incorporating region-specific cancer monitoring, enhancing access to diagnostic services, and initiating culturally relevant awareness efforts.

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