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ORIGINAL ARTICLE

The Relationship Between Acne Vulgaris and Prostate Cancer: A Comprehensive Survey Study

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ABSTRACT

Background: Prostate cancer and acne vulgaris (AV) are distinct conditions that share common developmental mechanisms. A potential relationship between them has been frequently cited in the literature. In light of this, our study aims to investigate the presence of acne vulgaris during adolescence in patients diagnosed with prostate cancer, along with other potentially related parameters, and to explore its correlation with clinicopathological

Methods: A retrospective study was done on 432 cases presenting with symptoms of prostate cancer at Mersin University Hospital over the past five years. Mini-surveys were administered to assess the presence and severity of AV during adolescence, along with additional factors such as sleep disorder, physical activities, occupational exposures, and androgenetic alopesia. The collected data were analyzed by comparing them with various parameters including prostate cancer subtypes, perineural invasion, prostate-specific antigen levels, prognostic grades, and Gleason scores.

Results: The analysis revealed no significant relationship between AV and prostate carcinoma. However, several other factors exhibited statistically significant correlations with different histologic subtypes of prostate carcinoma. Although the relationship between AV and prostate carcinoma remains inconclusive, our results highlight the need for further in-depth prospective research.

Conclusions: Despite the absence of a strong link between AV and prostate cancer, our study identified significant correlations with other investigated parameters. This emphasizes the importance of conducting more comprehensive prospective studies to clarify the potential relationship between AV vulgaris and prostate cancer risk.

Keywords: Acne vulgaris; Prostate cancer; Mini-survey; Risk factors; Prognostic factors.

INTRODUCTION

Prostate cancer and acne vulgaris are two distinct medical conditions that have interested significant attention in the scientific community. Prostate carcinoma is a malignant tumor that develops in the prostate gland, while AV is a chronic inflammatory cutaneous disorder that mainly involves the sebaceous glands of the skin. At first glance, these two conditions may appear unrelated, recent research has suggested a possible link between these two conditions [1-3].

Prostate carcinoma is a World health concern, with an almost 1 400 000 new patients and 375,000 deaths all around the world in 2020 [4]. The incidence of prostate carcinoma changes mostly across geographic areas, with higher prevalances observed in developped countries compared to developping ones [4]. In Türkiye, prostate carcinoma is the second most common carcinoma among men, with an age-standardized prevalence ratio of 35 per 100,000 men [5].

Acne vulgaris, on the other hand, is a frequent cutaneous condition that affects up to 80% of adolescents and young adults [6].The global prevalence of AV is estimated to be around 9.38%, with significant variations across

different populations [7]. In Türkiye, the incidence of AV among adolescents is reported to be around 60%, which is higher than the global average [8, 9].

The relationship between AV and prostate carcinoma is a topic of interest due to the potential shared mechanisms involving dihydrotestosterone (DHT) and 5-alpha reductase (5AR). A published research has shown that the existence of Cutibacterium acnes (C. acnes) in prostate gland is more frequent in males with prostate carcinoma than in control patients, suggesting a potential role in prostate carcinogenesis [1]. The bacteria may start inflammatory reactions, partially by induction of toll-like receptors, and production of proinflammatory mediators including IL-6 and IL-8, which are involved in the etiopathogenesis of AV and prostate carcinoma [2].

In a previous study it is found that, the men with acne had higher sedimentation rates, a marker of systemic inflammation, but this was not an independent determinant of prostate carcinoma risk [2]. However, the study did not establish a direct causal link between AV and prostate carcinoma, and suggested that further analyses is needed to explain the role of C. acnes in prostate carcinoma development.

Subsequently, studies were conducted over time showing the relationship between these two pathological conditions and some claims were made. Such as intracellular C. acne infection in non-cancerous prostate tissues and inflammation caused by the C.acnes can involve to the development of prostate carcinoma [3]. The frequency of C. acnes-positive glands and nuclear NF-κB-positive glands and the number of C. acnes-positive stromal macrophages were significantly common in carcinoma tissues than control tissues, suggesting a possible relationship between C. acnes infection and prostate gland carcinogenesis [3].

Our main hypothesis in this report was to search the presence of AV during adolescence in cases with prostate carcinoma, given that they share similar pathogenetic pathways, and to examine whether there is a important relationship between AV and prognostic parameters. In addition to AV, the questionnaire administered to the patients included questions about physical activity, alopecia, sleep patterns, and occupation, and explored the relationship between these parameters and prognostic factors.

METHODS

This retrospective analyses was performed at the Pathology Department of Mersin University Hospital. The hospital serves as a tertiary care hospital and provides healthcare services to a diverse population from the Mersin region and surrounding areas. The study population comprised 819 cases who were diagnosed with prostate carcinoma within the past five years.

Patient data were obtained from the department's electronic medical data system, ensuring a comprehensive representation of individuals with prostate cancer during the specified timeframe. The inclusion criteria for the analyse were a confirmed diagnosis of prostate carcinoma based on histopathological analyses of prostate biopsy or surgical specimens. Patients with a history of other malignancies or incomplete medical records were excluded from the study to supply the accuracy and reliability of the data. Additionally, cases with missing information on key variables of interest, such as acne vulgaris severity, sleep patterns, physical activities, occupational exposures, and alopecia, were excluded from the final analysis to minimize bias.

A comprehensive survey was administered to 413 eligible patients to collect demographic and clinical information, with a primary focus on acne vulgaris history. Before the survey, patients were informed about the study and consent was received from the patients for the use of their information in the study. The survey included questions regarding the severity of acne during adolescence, categorized as no, moderate, or severe based on the presence of inflammatory lesions requiring medical treatment or resulting in permanent scarring. The presence of AV limited to the facial area, which does not require medical treatment and does not result in scarring, was categorized as moderate; the presence of acne affecting not only the face but also the neck, back, chest and requires medical treatment and leads to scarring was

categorized as severe. [10]. For the adolescent period, the age range of 10-19 years has been considered, as defined by the World Health Organization [11]. Additionally, the survey assessed secondary variables such as sleep patterns, physical activities, occupational exposures, and androgenetic alopecia. In addition to the survey, the hospital automation system was also used and the patients' cancer histological subtype, Gleason score (GS), prognostic grade, perineural invasion (PNI), age, survival status, and prostate-specific antigen (PSA) levels were obtained. Patient data were anonymized and stored securely to ensure confidentiality.

Statistical Analysis

Statistical analyses were obtained using STATISTICA 13.0 software. Continuous variables were assessed for normal distribution using the Shapiro-Wilk test. Determination of variance (ANOVA) and post hoc Bonferroni tests were employed to evaluate age distribution across diagnostic and prognostic grade groups. Differences in PSA levels among diagnostic groups and AV severity categories were evaluated using the Kruskal Wallis test. The relationships between categorical variables were assessed using the chi-square test and likelihood ratio test. The association between GS and survival, as well as PNI, was evaluated using independent t-tests. Pearson correlation analysis was utilized to evaluate the relationship between age and GS. Statistical significance was set at $p < 0.05$.

This study was performed in accordance with the principles outlined in the Declaration of Helsinki. Ethical approval was received from the Institutional Review Board of Mersin University Hospital (Approval No: 2024/1050). Informed consent was achieved from all patients included in the study.

RESULTS

1. Demographic characteristics

A total of 413 cases were involved in this research. The average age was found to be 67.6. It was informed that 35 patients had passed away.

2. Survey data

The survey assessed AV existence during the adolescence, sleep patterns, physical activities, occupational exposures, and androgenetic alopecia. Although 413 patients were involved in the study, data were obtained from 411 patients for AV, 385 patients for sleep patterns, 352 patients for physical activity, 406 patients for alopecia, and 412 patients for occupation. Acne vulgaris was reported in 171 cases during adolescence, 150 cases being mild and 21 cases being severe. Sleep disturbance was present in 276 patients. 89 cases had a sedentary lifestyle, while 263 cases had varying degrees of physical activity. Alopecia was not present in the majority of patients (67.48%). When the cases were questioned in terms of occupational exposure, it was determined that 141 cases worked in occupations that were risky in terms of various chemicals (farmer, construction worker, driver, painter, carpenter). The distribution of the data is shown in detail in Table 2.

No significant relationship was found between survey data and histologic subtypes. A significant relationship was found between prognostic grade and alopecia ($p=0.028$), but not with other survey data. Similarly, a significant relationship was found between Gleason score and alopecia ($p=0.028$). The detailed data are shown in Table 3 & 4.

3. Clinicopathologic data

PNI showed a significant relationship with histologic subtype, with higher PNI rates observed in certain cancer types ($p<0.0001$). PNI was observed in all of our 6 (100.00%) cases of neuroendocrine prostate cancer and in all of our 15 (100.00%) cases of mixed type prostate cancer. Furthermore patients with PNI-positive cancers exhibited higher GS ($p<0.001$). It was observed that increasing age correlating with higher prognostic grade ($p<0.0001$). Similarly, a weak but positive relationship was found between age and GS ($r=0.223$, $p<0.001$). Moreover, the relationship between age and GS varied depending on histologic subtype, with a strong correlation observed in ductal adenocarcinoma subtype cases ($r = 0.80$, $p = 0.009$). As expected, prognostic grade was positively correlated with both PSA levels and PNI rates ($p= 0.0106$, $p<0.0001$ respectively). The detailed data are shown in Table 3 & 4.

4. Comparison of acne vulgaris and other data

No statistically significant difference was observed in the AV between the histologic subtype, prognostic grade groups, PNI and GS (p=0.4872, P=0.7080, p=0.850, and p=0.647 respectively). Similarly no statistically significant difference was observed in the AV existence between the survival and PSA levels (p=0.290, and p=0.9973 respectively).

Table 1: Demographic and clinicopathologic data

Demographic and clinicopathologic data	
Age (Mean±SD)	67,65±8.49
Survival (n-%)	
Ex	35 (8,47%)
In life	378-(91,53%)
PSA (Mean±SD)	50,23±244,32
Histologic types (n-%)	
Aciner Adenocarcinoma	381 (92,25%)
Ductal Adenocarcinoma	9 (2,17%)
Mixed Adenocarcinoma	15 (3,63%)
Small Cell Neuroendocrine Carcinoma	2 (0,48%)
Others Neuroendocrine Neoplasms	6 (1,45%)
PNI (n-%)	
No	202 (49,02%)
Yes	210 (50,98%)
Gleason score (n-%)	
Score 6	138 (33,49%)
Score 7	102 (24,75%)
Score 8	46 (11,16%)
Score 9	83 (20,14%)
Score 10	43 (10,43%)
Prognostic grade (n-%)	
Grade 1	140 (34,06%)
Grade 2	48 (11,67%)
Grade 3	53 (12,89%)
Grade 4	45 (10,94%)
Grade 5	125 (30,41%)

PNI: Perineural invasion, PSA: Prostate-specific antigen

Table 2: The distrubition of survey data

Survey data		
Items	**Groups**	**N (%)**
Acne vulgaris	No	240 (58.39%)
	Moderate	150 (36.49%)
	Severe	21 (86.31%)
Sleep pattern	No history of sleep disorders	109 (28.32%)
	History of sleep disorders	276 (71.68%)
Physical activity	Sedentary lifestyle	89 (25.28%)
	Low activity	162 (46.02%)
	Moderate activity	65 (18.47%)
	Highly active atlete lifestyle	36 (10.23%)
Alopecia	No	274 (67.49%)
	Mild	92 (22.66%)
	Moderate	39 (9.61%)
	Severe	1 (0.25%)
Occupation	Unemployed	166 (40.29%)

Survey data		
Items	**Groups**	**N (%)**
	Farmer	76 (18.45%)
	Construction worker	44 (10.68%)
	Driver	12 (2.91%)
	Painter	5 (1.21%)
	Carpenter	4 (0.97%)
	Other	105 (25.49%)

Table 3: Distribution of clinical, histopathological and survey data according to histological types

		Aciner Adenocarcinoma	**Ductal Adenocarcinoma**	**Mixed Adenocarcinoma**	**Small Cell Neuroendocrine Carcinoma**	**Others Neuroendocrine Neoplasms**	**P value**
Age	Mean±SD	67.42±8.23	66.33±12.57	71.93±8.11	80.50±6.36	69.16±14.40	0.0586
PNI	No	197(51.71%)	4(44.44%)	0(0.00%)	2(100.00%)	0(0.00%)	<0.0001
	Yes	184(48.24%)	5(55.56%)	15(100.00%)	0(0.00%)	6(100.00%)	
PSA	Median (Min-Max)	3.61 (0.007-2563)	10.25 (0.007-1205)	0.58 (0.007-2050)	5.06 (2.280-7.850)	1.13 (0.01-105.5)	0.6799
Survival	Ex	32(8.40%)	2(22.22%)	0(0.00%)	0(0.00%)	1(16.67%)	0.2866
	in life	349(91.60%)	7(77.78%)	16(100.00%)	2(100.00%)	5(83.33%)	
Acne vulgaris	No	224(58.79)%	4(44.44%)	10(66.67%)	2(100.00%)	2(33.33%)	0.4872
	Moderate	137(35.96%)	4(44.44%)	5(33.33%)	0(0.00%)	4(66.67%)	
	Severe	20(5.25%)	1(11.11%)	0(0.00%)	0(0.00%)	0(0.00%)	
Sleep pattern	No history of sleep disorders	100(26.25%)	2(22.22%)	6(40.00%)	0(0.00%)	1(16.67%)	0.5669
	History of sleep disorders	281(73.75%)	7(77.78%)	9(60.00%)	2(100.00%)	5(83.33%)	
Physical activity	Sedentary lifestyle	81(21.54%)	4(44.44%)	2(13.33%)	1(50.00%)	2(33.33%)	0.338
	Low activity	197(52.39%)	3(33.33%)	12(80.00%)	1(50.00%)	3(50.00%)	
	Moderate activity	62(16.49%)	2(22.22%)	1(6.67%)	0(0.00%)	1(16.67%)	
	Highly active atlete lifestyle	36(9.57%)	0(0.00%)	0(0.00%)	0(0.00%)	0(0.00%)	
Alopecia	No	256(67.90%)	5(55.56%)	10(71.43%)	2(100.00%)	3(50.00%)	0.557
	Mild	83(22.02%)	4(44.44%)	4(28.57%)	0(0.00%)	1(16.67%)	
	Moderate	37(9.81%)	0(0.00%)	0(0.00%)	0(0.00%)	2(33.33%)	
	Severe	1(0.27%)	0(0.00%)	0(0.00%)	0(0.00%)	0(0.00%)	
Occupation	Unemployed	150(39.47%)	4(44.44%)	7(46.67%)	1(50.00%)	4(66.67%)	0.455
	Farmer	70(18.42%)	0(00.00%)	4(26.67%)	1(50.00%)	1(16.67%)	
	Construction worker	39(10.26%)	3(33.33%)	1(6.67%)	0(00.00%)	1(16.67%)	
	Driver	12(3.16%)	0(00.00%)	0(00.00%)	0(00.00%)	0(00.00%)	
	Painter	5(1.32%)	0(00.00%)	0(00.00%)	0(00.00%)	0(00.00%)	
	Carpenter	3(0.79%)	1(11.11%)	0(00.00%)	0(00.00%)	0(00.00%)	
	Other	101(26.58%)	1(11.11%)	3(20.00%)	0(00.00%)	0(00.00%)	

PNI: Perineural invasion, PSA: Prostate-specific antigen

Table 4: Distribution of clinical, histopathological and survey data according to prognostic grade

		Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	P value
Age	Mean± SD	65.52±7.28	65.85±8.24	66.15±8.36	68.53±6.68	70.82±9.36	<0.0001
PNI	No	120(86.33%)	31(64.58%)	14(28.89%)	13(28.89%)	22(17.60%)	<0.0001
	Yes	19(13.67%)	17(35.42%)	39(73.58%)	32(71.11%)	103(82.40%)	
PSA	Median (Min-Max)	4.70 (0.007-138.2)	0.84 (0.007-2563)	1.51 (0.007-657.0)	0.63 (0.007-134.3)	3.06 (0.007-2563)	0.0106
Survival	Ex	6(4.29%)	2(4.17%)	3(5.66%)	4(8.89%)	20(16.00%)	0.102
	in life	139(95.71%)	46(95.83%)	50(94.34%)	41(91.11%)	105(84.00%)	
Acne vulgaris	No	84(60.00%)	28(58.33%)	32(60.38%)	24(53.33%)	72(57.60%)	0.7080
	Moderate	50(44.71%)	19(39.58%)	18(33.96%)	20(44.44%)	43(34.40%)	
	Severe	6(44.29%)	1(2.08%)	3(5.66%)	1(2.22%)	10(8.00%)	
Sleep pattern	No history of sleep disorders	38(27.14%)	16(33.33%)	13(24.53%)	10(22.22%)	32(25.60%)	0.7862
	History of sleep disorders	102(72.86%)	32(66.67%)	40(75.47%)	19(77.78%)	93(74.40%)	
Physical activity	Sedentary	34(24.46%)	11(23.91%)	11(20.75%)	9(20.45%)	24(19.35%)	0.291
	Low activity	19(51.80%)	28(60.87%)	23(43.40%)	26(59.09%)	66(53.23%)	
	Modarate activity	22(16.55%)	6(13.04%)	9(16.98%)	4(9.09%)	24(19.35%)	
	Highly active atlete lifestyle	10(7.19%)	1(2.17%)	10(18.87%)	5(11.36%)	10(8.06%)	
Alopecia	No	94(67.63%)	25(53.19%)	30(58.60%)	30(68.18%)	95(77.24%)	0.028
	Mild	25(17.99%)	18(38.30%)	15(28.30%)	12(27.27%)	22(17.89%)	
	Moderate	19(13.67%)	4(8.51%)	8(15.09%)	2(4.55%)	6(4.88%)	
	Severe	1(0.72%)	0(0.00%)	0(0.00%)	0(0.00%)	0(0.00%)	
Occupation	Unemployed	56(40.29%)	19(39.58%)	19(35.85%)	17(37.78%)	54(43.20%)	0.275
	Farmer	20(14.39%)	5(10.42%)	9(16.98)	10(22.22)	31(24.80)	
	Construction worker	18(12.95%)	7(14.58%)	6(11.32%)	6(13.33%)	7(5.60%)	
	Driver	6(4.32%)	1(2.08%)	0(0.00%)	1(2.22%)	4(3.20%)	
	Painter	2(1.44%)	0(0.00%)	2(3.77%)	1(2.22%)	1(0.00%)	
	Carpenter	0(0.00%)	1(2.08%)	2(3.77%)	0(0.00%)	1(0.80%)	
	Other	37(26.62%)	15(31.25%)	15(28.30%)	10(22.22%)	28(22.40%)	

PNI: Perineural invasion, PSA: Prostate-specific antigen

DISCUSSION

The association between AV and prostate cancer has been a topic of interest in recent research due to the potential role of inflammation in prostate carcinogenesis. The exact mechanism by which acne may influence prostate carcinoma risk is not fully understood, but it has been suggested that the inflammatory response induced by C. acnes may play a role. C. acnes is a bacterium closely associated with acne and has been found to be associated with prostate gland inflammation and carcinogenesis [12]. The induction of proinflammatory cytokines, such as IL-6 and IL-8, partly through activation of toll-like receptors (TLRs), is thought to be involved in the etiopathogenesis of AV and prostate cancer.

In our study, AV was reported in 171 cases from 413 patients, 150 cases being mild and 21 cases being severe. Some studies have suggested that AV in late adolescence may increase the risk of prostate carcinoma, while others have reported an inverse association or no association [2, 3, 12, 13]. According to the study by Ugge et al., a diagnosis of AV was associated with a statistically significant increased risk for prostate carcinoma (adjusted HR: 1.43 95%; CI: 1.06–1.92). Some studies claimed that, men who used tetracycline for four or more years, as a marker for severe AV, had a significantly higher risk of prostate carcinoma than men who did not use tetracycline. A recent meta-analysis evaluating the relationship between AV in adolescence and prostate carcinoma risk included 5 case-control reports and 3 cohort reports. The results indicated that AV was not significantly associated with the risk of prostate carcinoma (OR = 1.08, 95% CI 0.93–1.25) [3]. However, the heterogeneity of the existing studies has been highlighted, emphasizing the need for large prospective studies.

Several studies have found that men who work night shifts, which can disrupt circadian rhythms, have a higher risk of developing prostate carcinoma compared to daytime workers [14-16]. Actigraphy studies, which objectively measure sleep characteristics, have found that higher levels of wakefulness after sleep onset, indicating poorer sleep quality, are associated with a greater risk of prostate carcinoma [17]. Disruption of the body's circadian clock, which regulates sleep-wake cycles, appears to impair DNA repair mechanisms and promote tumor growth in prostate cancer [18]. Alterations in "clock genes" that control circadian rhythms have also been observed in prostate cancer patients. In our case group, 71.68% of the cases were found to have sleep disturbance.

When the occupational distribution of the cases included in our study was examined, it was noted that individuals working in professions such as farming, construction work, carpentry and driving constituted the dominant group. Particularly striking was the disproportionate number of farmers and construction workers among the surveyed population, which surpassed other professional groups by a considerable margin. In our study, the high prevalence of farmers and construction workers raised questions about whether these work environments provide exposure to various chemicals or pollutants that may cause prostate cancer. When the literature is reviewed in this respect occupational exposure, particularly in farming, has been linked to an increased prevalance of prostate carcinoma. Studies have shown that farmers and agricultural workers face various compunds including organic and inorganic dust, pesticides, fungi, microbes, and more, which contribute to this risk [19-22].

A link between prostate cancer and alopecia has been hypothesized because they share common risk factors such as age and androgens, but the general consensus in the literature is that they are not related [23]. According to some sources, prostate cancer has been associated with various patterns of baldness. [24]. Similarly, whether alopecia seen at a young age can be an indicator for prostate carcinoma is another controversial area in the literature [25-27]. Moreover, in the literature, alopecia and aggressiveness-related

parameters such as prognostic grade and Gleason score were found to be unrelated [25, 28]. In our study, approximately one third of the cases (%32.52) had alopecia and alopecia was associated with prognostic grade and Gleason score (p=0.028, p=0.0287 respectively).

One of the survey parameters questioned in our study was physical activity. Although definitive evidence linking regular physical exercise to a reduced risk of prostate carcinoma is lacking, the majority of studies in the literature suggest that regular physical activity may influence the development and progression of prostate carcinoma. According to our results, physical activity levels were not associated with GS and prognostic grade (p=0.852, and p=0.291 respectively)[29].

Considering the limitations of our report, it should be noted that the survey was administered via telephone, and the exclusion of patients whose contact information was unavailable in the automation system resulted in a narrowing of the initially determined patient population. Additionally, asking about the presence of acne vulgaris during adolescence posed challenges for some patients in recalling distant past events. As a result, it was not possible to obtain responses from all 413 patients included in the study.

CONCLUSIONS

While some analyses have reported a positive association, others have identified an inverse relationship or no association at all. Similarly, the relationship between other survey data and prostate cancer remains controversial. Further research is required to confirm these associations and to elucidate the underlying mechanisms.

Availability of Data and Materials: The datasets used and/or analysed during the current study were available from the corresponding author on reasonable request.

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