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Original article

The study of Mucin Stains and Cyclin D1 Expression in Benign Prostatic Hyperplasia and Prostatic Adenocarcinoma (Immunohistochemical Study)

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Abstract:

Background: Benign prostatic hyperplasia (BPH) is a frequent disease affecting up to 50% of men over the age of 50 years. Prostate cancer (PC) is the fourth most common cancer worldwide and the seventh in Egypt. Cyclin D1 belongs to D-type cyclin family involved in regulation of cell cycles in driving G1 to S phase. Alcian blue is a mucin stain, playing important roles in adenocarcinomas. Aim: To evaluate the significance of mucin stains and Cyclin D1 expression in BPH and PC and assess the diagnostic and prognostic roles of both in examined prostate lesions regarding the available clinico-pathological data. **Material and methods:** This is a selected retrospective study performed on 70 different cases included (24) BPH, (36) PC and (10) normal prostate. Clinico-pathological characteristics of examined cases were correlated with IHC of cyclin D1 and alcian blue special histochemical stain. **Results:** There was a significant statistical correlation between Cyclin D1 score in studied cases regarding serum PSA, Gleason group and score, and perineural invasion and a significant statistical correlation between alcian blue expression in studied cases regarding serum PSA and Gleason group and score, with significant statistical correlation between Cyclin D1 score and alcian blue. **Conclusion:** Cyclin D1 and alcian blue have a diagnostic role through differentiation between BPH and PC. Also, alcian blue has a prognostic role being correlated with high Gleason scores and with high PSA level.

Keywords: Benign prostate hyperplasia; Prostate cancer; Cyclin D1; alcian blue.

Introduction

Benign prostatic hyperplasia (BPH) is one of the most frequent diseases affecting Up to 50% of men over the age of 50. The prevalence is on the rise, owing to an increase in the modifiable metabolic risk factors [1].

Many factors contribute to the pathogenesis of BPH including hereditary factors, role of androgens and dihydrotestosterone and inflammation, initiated by variable stimuli including bacterial, viral and dietary factors [2].

Worldwide, Prostate cancer (PC) is the fourth most frequent malignancy (after Breast, lung and colorectal cancers), accounting for 7.3% of all cancers [3].

In Egypt PC is the seventh most common cancer type. Despite having a low mortality rate, PC greatly impacts the patients' quality of life [4].

Risk factors associated with increasing the risk of PC include increased age over 50 years, genetic factors, dietary factors as saturated animal fats and alcohol consumption in addition to sexually transmitted diseases with precancerous lesions including: Prostatic intraepithelial neoplasia (PIN) and Atypical small acinar cell proliferation [5].

Pathogenesis of PC involve multiple signaling pathways including Androgen receptor, PI3K/Akt, Wnt/B-catenin and Transforming Growth Factor-Beta (TGF-β) pathways along with several oncogenes; as: MYC, ERG and tumor suppressor genes as P53 and P53 [6].

Cyclin D1 is a protein that belong to D-type Cyclin family; involved in the regulation of cell cycles in driving G1 to S phase [7].

Cyclin D1 is an important oncogene, overexpressed in many human cancers including breast cancers, mantle cell lymphoma, hepatocellular carcinoma (HCC), non-small cell lung carcinoma and others [8].

Cyclin D1 overexpression is achieved by different mechanisms including: gene amplification, increased gene transcription, decreased micro RNA levels , and inefficiency or loss of ubiquitylation-mediated protein degradation [9].

Mucins are complex carbohydrates of high molecular weight, synthesized, stored and secreted by a variety of epithelial cells and glandular tissues of several organs, in which the structure and biochemical composition of mucins provides protection for the cell surface against different pathogens and toxins [10].

The characteristic patterns of mucin expression in different organs are maintained during the neoplastic transformation, some alterations may occur in cancers in comparison with normal tissue, and this may be helpful in the diagnostic techniques of different carcinomas using various mucin satins as Alcian blue stain for example [11].

However, the significance of Cyclin D1 and Alcian blue expression in BPH and PC remains unclear, and the study aims to evaluate the significance of their expression in Egyptian cases.

Material and methods:

Study group:

This is a retrospective study performed upon 70 cases designated as: 24 cases of BPH, 36 cases of PC of different Gleason scores and 10 cases of normal prostatic tissue as control.

The material included archival formalin fixed paraffin embedded blocks processed during the years 2019-2022 as well as stained Hematoxylin and Eosin (H&E) slides for review. The blocks were retrieved from Pathology Department and Early Cancer Detection Unit archives; faculty of medicine, Benha University, Egypt. Clinicopathological data were collected from the files of patients.

Inclusion criteria: Cases with available clinicopathological data regarding age, preoperative serum PSA level, Gleason score, Gleason group lymphovascular invasion and perineural invasion.

Exclusion criteria: Cases with no available paraffin blocks or clinicopathological data were excluded from the current study.

The Ethics Committee of Faculty of Medicine, Benha University, Egypt approved this study code (MS 27-1-2022).

Histopathological studies:

Formalin fixed /Paraffin embedded blocks were cut at 5 µm thickness and stained using (H&E). Two observers reviewed the microscopic sections from all cases. The cases were re-evaluated for their diagnosis and graded into different Gleason scores from 6 to 9 [(12)] and TNM staging system was applied to the cases according to AJCC, 8th edition [(13).]

Cyclin D1 immunohistochemical study:

For immunohistochemical staining, two positive slides were prepared:

Slides were immunostained according to manufacturer's instructions with Cyclin D1 rabbit polyclonal antibody (Bio SB, Netherland) at a dilution of 1:100, at room temperature overnight. Immunodetection was carried out using standard labeled streptavidin-biotin system (Genemed, CA94080, USA, and South San Francisco) Antigen retrieval was done by using 3% hydrogen peroxide in 30% methanol for 15 minutes in the microwave. The chromogen diaminobenzene (DAB, Envision TM Flex /HRP-Dako, REF K 8000) used was freshly prepared. The counter satin was Mayer's hematoxylin. Normal breast tissue used as an external positive control **(14).** For negative control, primary antibody was omitted (Phosphate-buffered Saline).

Immunohistochemical interpretation of Cyclin D1:

Positivity was considered as brownish homogenous nuclear staining of tumor cells, with cyclin D1 intensity divided into four categories: absent, weak, moderate and strong **(7).** The immunohistochemical scores were obtained by light microscopy (Olympus, Tokyo, Japan) as the percentage of positive cells within 5 high power fields in hot areas scored from (0–4). The percentage area of positive immunostaining was scored as: 0 (0%); 1(10%); 2(>10-25%); 3(>25-75%); 4(>75%) (7). 1, 2 considered low score, while 3, 4 is high.

Alcian blue special stain study:

Slides were stained according to manufacturer's instructions with alcian blue stain for 30 minutes and washed with tap water. Then 3 % acetic acid followed by running tap water for 10 minutes and nuclear fast red solution for 5 minutes. Freshly prepared chromogen diaminobenzine (DAB, Envision TM Flex /HRP-Dako, REF K 8000) was used. Normal colon tissue was used as an external positive control **(15).**

Interpretation of Alcian Blue expression:

Positivity was considered as deep blue coloration of tumor cell borders **(15).**

Statistical analysis:

Categorical data were presented as number and percentages while quantitative data were expressed as mean ± standard deviation (SD). Chi square test (χ 2), or Fisher's exact test were used to analyze categorical variables. Quantitative data were tested for normality using Shapiro-Wilks test, assuming normality at $P > 0.05$, using Student "t" test if normally distributed, or Man-Whitney U test and Kruskal-Wallis test if not normally distributed for analyzing the difference. Differences were considered significant at a calculated P value of >0.05. Statistical analysis was performed using SPSS version 25 (SPSS Inc, Chicago, IL, USA).

Results:

Clinicopathological results:

Age distribution of the studied cases ranged from 48 to 86 years. Age distribution of the studied 24 cases of BPH ranged from 48 to 72 years with mean age (60.29 ± 6.80) and age of the studied 36 cases of PC ranged from 48 to 86 years with mean age (65.08 ± 8.69).

Preoperative serum PSA level of the studied cases ranged from <4 ng/ml to ≥ 10ng/ml. Preoperative serum PSA level of

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BPH cases was 45.8% <4 ng/ml, 33.3% 4-10 ng/ml and 20.8% ≥ 10ng/ml, while for PC cases was 41.7% < 10 ng/ml and 58.3% ≥ 10ng/ml.

Gleason score of the studied PC ranged from 6-9 with mean 7.28 ± 1.0. For lymphovascular invasion 11.2% cases of PC were positive, and for perineural invasion 83.3% were positive. (Table 1- 2) (figure 1).

Table 1: Age distribution and preoperative serum psa level among cases of prostate cancer.

	Benign n = 24	**Malignant n = 36**
Age (years)		
<65	18 (75.0%)	17 (47.2%)
≥65	6 (25.0%)	19 (52.8%)
Mean ± SD.	60.29 ± 6.80	65.08 ± 8.69
Median	60.0	65.0
Min. – Max.	48.0 – 75.0	48.0 – 86.0
Preoperative serum PSA level		
<4 ng/ml	11(45.8%)	0 (0%)
4-10 ng/ml	8 (33.3%)	15 (41.7%)
≥10 ng/ml	5 (20.8%)	21 (58.3%)
Mean ± SD.	8.0 ± 0.55	9.40 ± 0.55
Median	9.50	10.50
Min. – Max.	4.0 – 13.0	4.0 – 14.50

Table 2. Gleason group, score, lymphovascular and perineural invasion among cases of prostate cancer.

	Prostate cancer n = 36
Gleason score	
Score 6	9 (25%)
Score 7	13 (36.2%)
Score 8	9 (25%)
Score 9	5(13.8%)
Mean ± SD.	7.28 ± 1.0
Median	7.0
Min. – Max.	6.0 – 9.0
Gleason group	
I	9 (25.0%)
II	5 (13.9%)
III	8 (22.2%)
IV	9 (25.0%)
V	5 (13.9%)
Lymphovascular invasion	
Positive	4 (11.2%)
Negative	32(88.8%)
Perineural invasion	
Positive	30 (83.3%)
Negative	6 (16.7%)

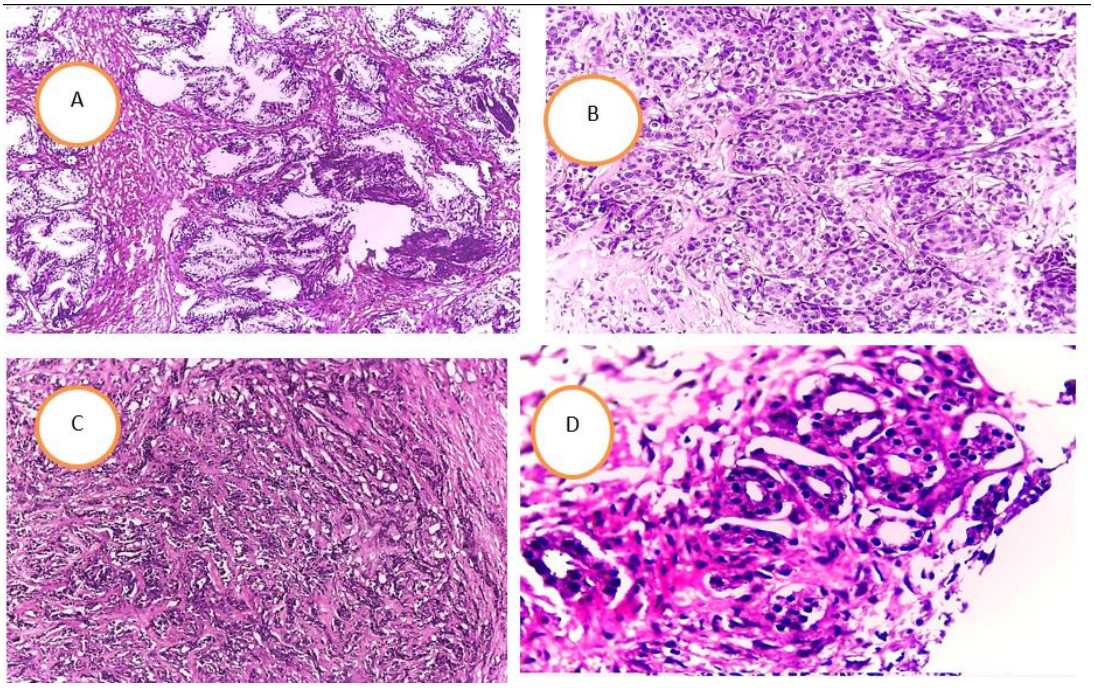

Figure 1: A: Benign prostatic hyperplasia (BPH) showing proliferated acini and fibromuscular stroma (H&E x100). B: Prostatic carcinoma (PC) Gleason score 4+4 showing mixed cribriform pattern (black arrow) and fused glands pattern (H&E x200) C: Prostatic carcinoma (PC) Gleason score 5+5 showing sheets of malignant cells (H&E x100). D: Prostatic carcinoma (PC) Gleason score 3+3 showing proliferating predominantly well-formed glands lined by malignant cells (H&E x200).

Cyclin D1 immunohistochemical stain results:

Positivity was considered as brownish homogenous nuclear staining of tumor cells.

3 cases of BPH (12.5%) were positive for cyclin D1 staining, while 21 cases (87.5%) were negative (figure 2).

33 cases of PC (91.7%) were positive, while 3 cases (8.3%) were negative (figure 2).

A statistically significant correlation was found between cyclin D1 expression and histopathological type of studied cases (P =<0.001) (table 3).

A statistically significant correlation was found between cyclin D1 score and preoperative serum PSA level, Gleason score, Gleason group and perineural invasion among cases of PC (P =<0.001, <0.00,1 <0.001 and <0.012 respectively).

Special histochemical stain results:

Positivity was considered as deep blue coloration of tumor cell borders.

Two cases of BPH (8.3%) were positive for alcian blue staining, while 22 cases (91.7%) were negative **(**figure 3).

23 cases of PC (63.9%) were positive, while 13 cases (36.1%) were negative (figure 3).

A statistically significant correlation was found between alcian blue staining and histopathological type of studied cases (P =<0.001) (table 4).

A statistically significant correlation was found between alcian blue staining and preoperative serum PSA level among cases of PC (P =<0.001) (table 4).

A statistically significant correlation was found between alcian blue staining and Gleason score and group among cases of PC (P =<0.001for both) (table 4).

A statistically significant correlation was found between alcian blue staining and Cyclin D1 score among cases of PC (P =<0.001) (table 4).

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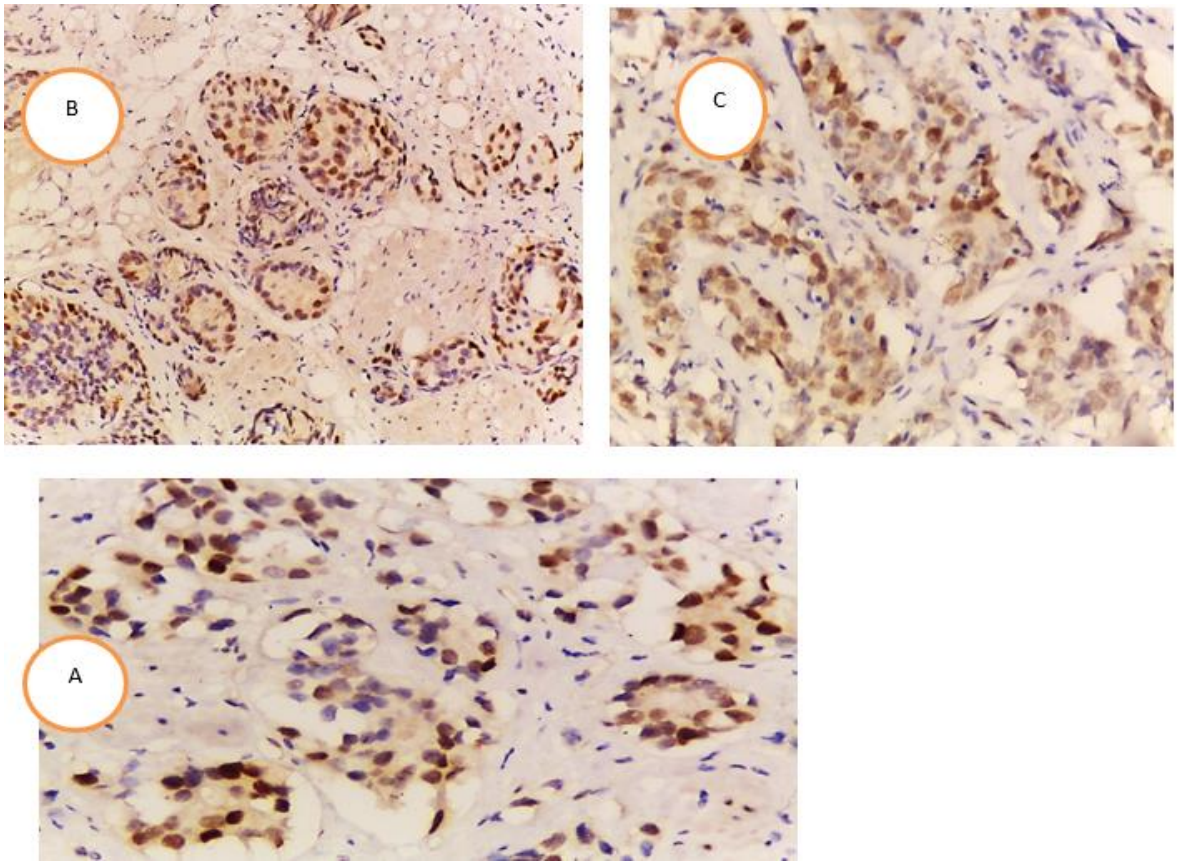

Figure 2: A: Prostatic carcinoma (4+3) showing positive nuclear expression of Cyclin D1 score 2 (10-25%) (IHC, ABC X400) B: Prostatic carcinoma (3+4) showing positive nuclear expression of Cyclin D1, score 2 (10-25%) (IHC, ABC x400) C: Prostatic carcinoma (4+4) showing positive nuclear expression of Cyclin D1 score 4 (IHC, ABC X400).

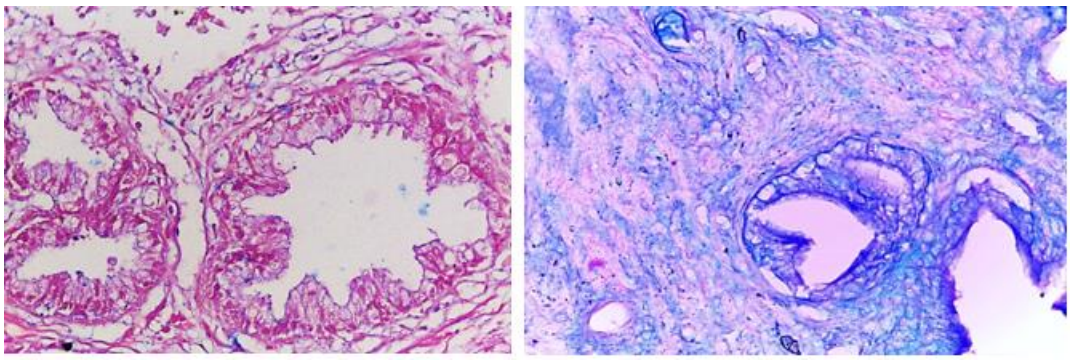

Figure 3: A: Benign prostatic hyperplasia negative for alcian blue expression (x400). B: Prostatic carcinoma (5+4) showing positive expression of alcian blue in the form of deep blue coloration of tumor cell borders (X400)

Table 3: Comparison between cases of benign prostatic hyperplasia and prostatic adenocarcinoma regarding Cyclin D1.

Cyclin D1	Benign n = 24 № (%)	Malignant n = 36 № (%)	Test	P
Expression				
Negative	21 (87.5%)	3 (8.3%)	χ^2=	<0.001*
Positive	3 (12.5%)	33 (91.7%)	37.604	
Intensity				
Absent	21 (87.5%)	3 (8.3%)	χ^2=	MC
Weak	2 (8.3%)	6 (16.7%)	43.080	<0.001*
Moderate	1 (4.2%)	6 (16.7%)		
Strong	0 (0.0%)	21 (58.3%)		
Percentage				
0%	21(87.4%)	3(8.3%)		
10%	1 (4.2%)	3 (8.3%)	U=	<0.001*
>10-25%	1 (4.2%)	8 (22.2%)	810.5	
>25-75%	1 (4.2%)	9 (25%)		
>75%	0 (0%)	13 (36.2%)		
Mean ± SE.	1.88 ± 1.31	51.39 ± 5.48		
Median	0.0	60.0		
Min. – Max.	0.0 – 30.0	0.0 – 90.0		
Scoring				
Score 0	21(87.4%)	3(8.3%)		
Score 1	1 (4.2%)	3 (8.3%)	U=	
Score 2	1 (4.2%)	8 (22.2%)	805.0	<0.001*
Score 3	1 (4.2%)	9 (25%)		
Score 4	0 (0%)	13 (36.2%)		
Low (1 - 2)	2 (66.7%)	11 (33.3%)		
High (3 - 4)	1 (33.3%)	22 (66.7%)		
Mean ± SE.	0.21 ± 0.13	2.72 ± 0.21		
Median	0.0	3.0		
Min. – Max.	0.0 – 3.0	0.0 – 4.0		

SE. Standard error, Min.: Minimum, Max.: Maximum, U: Mann-Whitney

χ^2: Chi-Square, MC: Monte-Carlo, P: Comparing between benign and malignant.

*: Significant when p value <0.05.

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Table 4 : Alcian blue expression in the studied cases and alcian blue correlation with different parameters of prostate cancer cases

Alcian blue expression	**Benign n = 24 № (%)**	**Malignant n = 36 № (%)**	**Test**	**P**
Negative	22 (91.7%)	13 (36.1%)	χ^2=	<0.001*
Positive	2 (8.3%)	23 (63.9%)	18.286	

Alcian blue expression	**PSA level**		**Test**	**P**
	<10 ng/ml n = 15 № (%)	**≥10 ng/ml n = 21 № (%)**		
Negative	11 (73.3%)	2 (9.5%)	χ^2=	<0.001*
Positive	4 (26.7%)	19 (90.5%)	15.442	

Alcian blue expression	**Glasson group**					**Test**	**P**
	I n = 9	**II n = 5**	**III n = 8**	**IV n = 9**	**V n = 5**		
Negative	8 (88.9%)	3 (60.0%)	2 (25.0%)	0 (0.0%)	0 (0.0%)	χ^2=	MC
Positive	1 (11.1%)	2 (40.0%)	6 (75.0%)	9 (100.0%)	5 (100.0%)	19.863	<0.001*
P1		FE0.505	FE 0.015*	FE<0.001*	FE 0.003*		
P2			FE 0.293	FE 0.027*	FE 0.167		
Pairwise	FE P3=0.206, FE P4=0.487, P5-						

Alcian blue expression	**Gleason score**				**Test**	**P**
	6 n (%)	**7 n (%)**	**8 n (%)**	**9 n (%)**		
Negative	8 (88.9%)	5 (38.5%)	0 (0.0%)	0 (0.0%)	χ^2=18.8	<0.001*
Positive	1 (11.1%)	8 (61.5%)	9 (100.0%)	5 (100.0%)		
Pairwise comparison						
Versus 6	-	0.031	<0.001	0.003		
Versus 7	-	-	0.053	0.249		

Alcian blue expression	**Cyclin D1 scoring.**			**Test**	**P**
	Mean ± SE.	**Median**	**Min. – Max.**		
Negative n=13	1.69 ± 0.26	2.0	0.0 – 3.0	U= 264.5	<0.001*
Positive n=23	3.30 ± 0.22	4.0	0.0 – 4.0		

χ^2: Chi-Square, FE: Fisher-Exact, P: Comparing between PSA <10 and ≥10 ng/ml.
*: Significant when p value <0.05. SE. Standard error, Min.: Minimum, Max.: Maximum, U: Mann-Whitney
P: Comparing between different categories, *: Significant when p value <0.05.

Discussion:

Benign prostatic hyperplasia is a common disease among old men. The age-specific prevalence of BPH has been estimated from specimen studies to be 8% in the fourth decade, 50% in the sixth decade, and 80% in the ninth decade [(16).]

Various scientific evidences proved that both BPH and PC share common features including; risk factors, hormone-dependent

growth, signaling pathways and response to antiandrogen therapy [17].

Regarding pathogenesis of PC, the testosterone-vascular-inflammation-ageing triad are critical in tumorigenesis microenvironment, and BPH being aging problem, so it has a significant role in cancer development [18].

Regarding the age in relation to Gleason group, cases were classified into two groups, <65Y and ≥65y according to the statistical analysis in this study. (58.3%) were aged < 65 years and (41.7%) were aged ≥ 65y. There was insignificant statistical correlation between age of patients & Gleason group among cases of PC. These results were consistent with studies that reported no significant relation [19 ,20].

In contrast to those who found that elderly men (over 60 years) had a higher probability of high-grade PC. [21, 22].

In PC patients, the serum PSA level is increased due to an additional release of PSA in the blood after disruption of the basement membrane of the prostate [23].

Concerning pre-operative serum PSA level in relation to Gleason group, (41.7%) were <10 ng/ml while (58.3%) were ≥10 ng/ml. There was a statistically significant correlation between Gleason group of the tumor and PSA level (p value <0.001), as (66.7%) with Gleason group IV and V showed PSA level ≥10 ng/ml, while (93.3%) with Gleason group I and II showed PSA level <10 ng/ml. These results were consistent with studies that reported significant correlation [24]. This may be explained as PSA reflects the volume of cancer in the gland, and as cancer volume increases in high Gleason group and advanced PC this leads to higher PSA levels [25].

In contrary to these results, who found insignificant correlation between Gleason group of the tumor and PSA level [26]. This may be explained as patients with Gleason score 8– 10 diseases, a proportion of these tumors is so poorly differentiated that they produce relatively little PSA resulting in lower PSA levels [27].

Regarding lymphovascular invasion in relation to Gleason group, (11.2%) were positive, while (88.8%) were negative. (100%) of group I were negative and (60%) of group V cases were positive. There was a statistically significant correlation between Gleason group & lymphovascular invasion (P value=0.012).

In agreement with these results, those who found that permeation of vascular channels as found in radical prostatectomy specimens has been related with Gleason group and possibility of tumor progression with possible explanation for this correlation being tumor angiogenesis [28, 29].

Regarding perineural invasion in relation to Gleason group, (83.3%) were positive while (16.7%) were negative. (100%) of group I were positive for perineural invasion while (60%) of grade V cases were negative. There was a statistically significant correlation between Gleason group & perineural invasion (P value=0.008). This agrees with studies that reported significant concentration [30 ,31]. This can be explained as PC cells adjacent to nerves show increased proliferation compared to those located further away and the association between perineural invasion and high-grade cancers may indicate an independent mechanism by which cancer cells can leave the prostate [32]. Another explanation, that perineural space provides cancer cells with a path of lesser resistance to spread beyond the prostate [33].

Cyclin D1 is a protein encoded by CCND1 gene, involved in the physiological regulation of the cell cycle. It is upregulated in several human tumors, and is an oncogene that promotes uncontrolled cell proliferation [34].

Regarding immunohistochemical results in the current study, there was a significant statistical correlation between cyclin D1 expression and BPH and PC (p value <0.001) with 87.5% of BPH cases were

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negative for cyclin D1 expression, while 91.7% of PC cases were positive. These results were in agreement with [35]. This can be explained as the mutation of many cell cycle regulating proteins was involved in the initiation of PC to late stage of disease progression [36]. Also, Cyclin D 1 might act as an activated oncogene and thus playing a role in the pathogenesis of cancer development and progression [37].

In the present study, the patients` age had insignificant correlation with cyclin D1 expression in prostate. These results were in agreement with [37]. In contrast to these results, those who found significant correlation [38].

Regarding pre-operative serum PSA level in relation to cyclin D1 scoring, there was a significant statistical correlation between cyclin D1 scoring & preoperative serum PSA level (p value < 0.001), in which high score of cyclin D1 were detected in 95.2% in patients with ≥10 ng/ml PSA level. This simulates the results of studies that reported significant correlation [39]. This may be explained as cyclin D1 expression might be regulated by sex hormones, suggesting a relationship between PSA levels and cyclin D1, since PSA production is dependent on hormonal stimulation [40].

In contrast to these results, who reported negative statistical correlation [40] which may be explained by the established ability of cyclin D1 to modulate AR function in the control of prostate cancer cellular function [35].

In this study, a significant statistical correlation was found between the score of cyclin D1 and Gleason score and group (p value <0.001 for both), in which tumors with high Gleason group (IV and V) displaying high cyclin D1 score compared with tumors of low group (I and II). Similar results were reported by studies that reported significant correlation [14]. Explained as cyclin D1-positive PC cells have been reported to show greater motility, increased invasion capability and a hormone-independent phenotype in cell cultures, supporting that cyclin D1 plays an important role in aggressiveness of prostate cancer, therefore explaining its relation with high Gleason score PC [40].

In contrast to these results, who revealed insignificant statistical correlation, suggesting that this variation may be related to many factors as type of biopsy, sample size and method of immunohistochemical staining [41, 42].

Regarding perineural invasion in relation to cyclin D1 scoring, there was significant correlation with cyclin D1 scoring (p value=0.012). These results were consistent with studies that reported significant correlation [39]

In contrast to these results, who found insignificant statistical correlation, explained as cyclin D1 increases the mobility and invasion of tumor cells, the overexpression of Cyclin D1 is related to the aggressiveness of PC Therefore, cyclin D1 was expressed mostly among patients with perineural invasion [35]. This difference may be related to sample size and type of biopsy.

Regarding lymphovascular invasion in relation to cyclin D1 scoring, there was no significant statistical correlation with cyclin D1 scoring. These results were consistent with studies that reported no significant correlation [43]. In contrast to these results who revealed significant correlation [44], explained as cyclin D1 expression levels are elevated in malignant prostatic epithelial cell lines and its overexpression can increase cell proliferation rate, migration and invasive ability [37].

Mucins are complex carbohydrates of high molecular weight, synthesized and secreted by a variety of epithelial cells and glandular tissues of several organs. Classified into neutral and acidic mucins [45]. Alcian blue mucin stain is used to visualize mucopolysaccharides and acidic mucin on tissue sections and membranes and was used in different tumors [46].

Adenocarcinomas are distinguished from other cancers by the presence of glandular

structures. However, in poorly differentiated adenocarcinoma there is a lack or an absence of glandular formation, so other methods as special mucin stains are required to assess the diagnosis regarding their role in cell signaling, cellular functions and detection of acid mucin which is a feature of PC [47].

According to special stain results in the current study, 91.7% of BPH cases were negative for alcian blue staining, while 63.9% of prostate cancer cases were positive. There was a significant statistical correlation between alcian blue staining and studied groups (p value <0.001). These results were consistent with studies that reported significant correlation [48 ,49].

Regarding pre-operative serum PSA level, there was a significant statistical correlation between alcian blue staining & preoperative serum PSA level (p value < 0.001). These results were in agreement with studies that reported significant correlation [50]. This is explained as PC overexpress transmembrane mucins to exploit their role in signaling cell growth and survival resulting in increased alcian blue expression and since PSA level increases in PC, suggesting correlation between alcian blue staining & PSA level [51].

In this study, a significant statistical correlation was found between alcian blue staining and Gleason group and score (p value <0.001 for both), in which tumors with high Gleason group (IV and V) and score showed positive alcian blue staining This is explained by results reported by [52] Who found that mucin secretion increased with increased Gleason score. In contrast to these results who found no significant correlation [53, 54]. This difference may be attributed to different sample size and experimental methods.

In the current study, a significant statistical correlation was found between alcian blue staining and cyclin D1 scoring (p value <0.001). No other studies till the end of this study have found a relation between both. This may be explained as cyclin D1 scoring has significant correlation with pre-operative serum PSA level and Gleason group and score. Since alcian blue has also significant correlation with the same parameters. This suggests the presence of significant correlation between alcian blue staining and cyclin D1 scoring.

Conclusion:

Cyclin D1 is associated with higher serum PSA level and higher Gleason group of the tumor suggesting that it might be involved in prostate carcinogenesis and tumor progression.

Cyclin D1 and alcian blue have a diagnostic role, as they differentiate between BPH and PC. Also, alcian blue is associated with higher serum PSA level and higher Gleason grade suggesting that it may play role in the prognosis of PC.

There was a significant statistical correlation was found between alcian blue staining and cyclin D1 scoring.

Conflict of interest:

None of the contributors declared any conflict of interest.

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