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# Immunohistochemical Evaluation of Androgen Receptor Expression in Prostatic Adenocarcinoma in a Sample of Iraqi Patients: A Clinicopathological Study

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***Abstract—Background****: Prostatic adenocarcinoma, which is the second most common cancer in men worldwide, is influenced by age, genetics, and androgen levels. Higher androgen receptor expression predicts poor survival outcomes, highlighting the role of androgen receptors in prostate cancer progression. Aim of the study: To evaluate the expression of androgen receptors within prostatic adenocarcinoma in Iraqi patients and to assess its correlation to some clinicopathological features like (age and grade) of prostatic adenocarcinoma in this specific population.* ***Patients and methods****: This cross-sectional study was conducted at Al Yarmouk teaching hospital and a private lab, involving 60 participants diagnosed with prostate adenocarcinoma over ten months from January to October 2023. Patients without prior hormonal therapy or chemotherapy were included, while those with benign tumors, mesenchymal tumors, or undergoing neoadjuvant therapy were excluded.* ***Results****: In this study, the majority exhibited positive androgen receptor expression (91.7%). Age distribution showed a mean age of 67.33 years. Gleason scores indicated an escalating trend in histological grade, with high androgen receptor expression which had statistically significant association with Gleason scores and histological grades with p-value <0.05.* ***Conclusion****: The findings note the higher prevalence of AR expression in prostate cancer patients in contrast with lower expression levels in normal prostate tissue. Moreover, the study reveals significant associations between AR expression and Gleason score and disease aggressiveness, emphasizing the potential utility of AR expression as a prognostic biomarker.*

***Keywords—*** *Prostatic Adenocarcinoma, androgen receptor, Immunohistochemistry.*

## I. INTRODUCTION

Prostate adenocarcinoma ranks as the second most prevalent cancer among males globally (1), with its frequency especially escalating with advancing age, affecting over (75%) of individuals aged 65 years or older (2). Genetic and environmental factors play pivotal roles. Evidence present for familial associations, with a 5-10 times higher risk observed in men with multiple affected first-degree relatives (3). Genetic instability contributes significantly to the pathogenesis and prognosis of various cancers, including prostate cancer, while heightened androgen levels have been implicated in its development and progression (4). While most cases of prostatic adenocarcinoma are asymptomatic and detected during prostate-specific antigen (PSA) screening, approximately (15%) of patients present with normal PSA levels. The disease typically manifests as acini formations, often necessitating a combination of architectural and cytological assessments for diagnosis. While light microscopic features suffice for most diagnoses, rare cases may warrant additional immunohistochemical studies (5).

The rising prevalence of prostate cancer can be caused by several factors, including the expanding utilization of prostate-specific antigen (PSA) screening, the aging demographic, and advancements in diagnostic technologies (6, 7).

Androgen receptor (AR) plays a crucial role in both the normal function of the prostate gland and its development. The action of androgens, such as testosterone, operates through a pathway involving the synthesis of testosterone in the testes, which is then converted into 5α-dihydrotestosterone (DHT) (8).

Castration leading to a significant reduction in acid phosphatase levels, a marker for prostate disease, was highlighted by Charles Huggins et al. in 2023 which emphasize the dependence of these tumors on androgens. This discovery showed the way for androgen ablation therapy as a primary treatment for metastatic prostate cancer. However, the precise biological roles of androgens and androgen receptors (AR) in the development and progression of human prostate cancers, including metastatic and androgen-independent disease, remain poorly understood (9).

Elevated AR expression was found to correlate with increased proliferative activity and shorter progression-free survival. These findings indicate that higher levels of AR expression are associated with poorer recurrence-free and overall survival outcomes in patients with hormone-refractory prostate cancer (10).

### *Aim of the study*

1. To evaluate the expression of androgen receptors within prostatic adenocarcinoma in Iraqi patients.
2. To assess the correlation to some clinicopathological features like (age and grade) of prostatic adenocarcinoma in this specific population.



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## II. PATIENTS AND METHODS

*Study design and settings*

This is a cross-sectional study that was conducted at Al Yarmouk teaching hospital and private lab cases. A total of 60 patients were included in the study during the period of ten months from January 2023 to October 2023.

All cases were obtained via TURP.

Inclusion criteria: Patients diagnosed with prostate adenocarcinoma. None of the patients had received neoadjuvant hormonal therapy or chemotherapy before the sample was taken. Exclusion criteria: Benign tumors, mesenchymal tumors and prostate intraepithelial neoplasia. Patients with prostate adenocarcinoma on neoadjuvant hormonal therapy or chemotherapy before the sample was taken.

EP120 Rabbit monoclonal antibody, Detection kit ready-to-use antibodies

Quality control: As recommended, in the evaluation of Androgen Receptor (AR) expression, it is imperative to employ the prostate and prostate carcinoma as recommended positive tissue controls. The inclusion of both positive and negative tissue controls, serving to monitor the accurate execution of tissue processing and the functionality of test reagents. Negative tissue controls are particularly crucial for assessing and mitigating nonspecific background staining.

The Steps of the study are mentioned in figure 1 below.

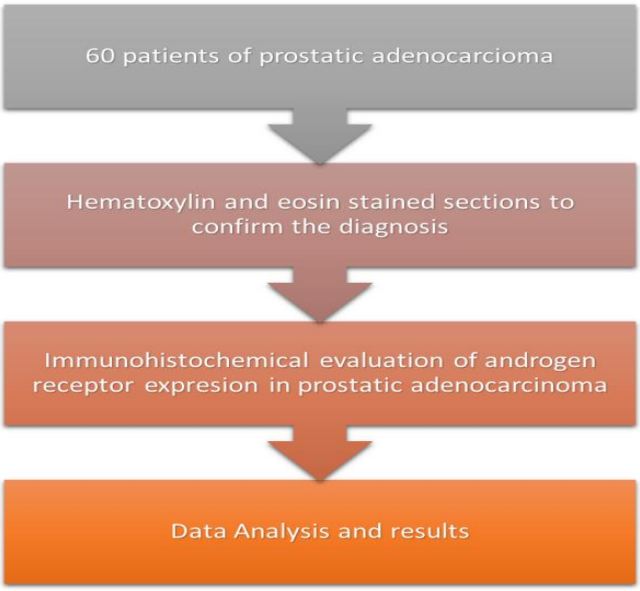


Figure 1: Steps of work for the study.

Scoring systems: Scoring was performed by a pathologist using prostatic assessment of androgen receptor (AR) protein staining score and Gleason score.

Gleason Score: Prostatic adenocarcinoma grading was done using the Gleason scoring system, which assumes the sum of the 2 most prevalent Gleason grades: primary and secondary, designated according to separate rules for biopsy and prostatectomy and according to 2019 consensus; Gleason score ranges from 6-10 according to the tumor grade present (11, 12).

Patients were further categorized according histological grading into (12):

- Well differentiated tumors = Gleason score (6)
- Moderately differentiated tumors = Gleason score (7)
- Poorly differentiated tumors = Gleason score (≥8)

Moreover, Gleason score was divided into two grade two assess the odds ratio of the event and as follows (12):

- High grade Gleason scored tumor = Gleason score (≥8)
- Low grade Gleason scored tumor = Gleason score (6-7)

Androgen receptor (AR) expression score: The assessment for androgen receptor (AR) nuclear staining was semi-quantitatively evaluated using quanitity and intensity scoring system. The scoring system was opted for after extensive literature review of previous studies and according to the following terms:

Androgen receptor (AR) quantity score (percentage of expression) on a scale of 1 to 3 (13, 14):

- Score 0 = No staining
- Score 1 = 1%-33% nuclei staining
- Score 2 = 34%-66% nuclei staining
- Score 3 = 67%-100% nuclei staining

Androgen receptor (AR) staining intensity score on a scale of 0 to 3 (13, 14):

- Score 0 = No staining
- Score 1 = Weak staining
- Score 2 = Intermediate staining
- Score 3 = Strong staining

An Immuno-Reactive Score (IRS) which is obtained by multiplying the quantity score and staining intensity score is used. A resulting score range from 0 to 9 is shown and is interpreted as follows:

- Negative staining = 0
- Mild staining = 1-2
- Intermediate staining = 3-4
- Strong staining = 5-9

Using the Immuno-Reactive Score (IRS), androgen receptor (AR) expression was categorized into:

- Low AR expression <6
- High AR expression ≥6

Statistical analysis: Analysis of data was carried out using the available statistical package of SPSS-26 (Statistical Packages for Social Sciences- version 26). Data were presented in simple measures of frequency, percentage, mean, standard deviation, and range (minimum-maximum values). The statistical significance difference for different percentages (qualitative data) was tested using Pearson Chi-square test with application of Yate's correction or Fisher Exact test whenever applicable. Odds ratio was calculated to measure the magnitude of the association between an exposure and an outcome. Statistical significance was considered whenever the P value was equal or less than 0.05.

## III. RESULTS

*Descriptive statistics*



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Sixty patients diagnosed with prostate cancer were involved in the study. Regarding androgen receptor status for cases, the majority of them had positive androgen receptor with 55 (91.7%) while only 5 (8.3%) had negative androgen receptor. The overall mean age of the patients was (67.33±8.31). Patients with positive androgen receptor had a mean age was (68.01±7.96) while those with negative androgen receptor had mean age of 59.8±9.2 as shown in table 1 below.

TABLE 1: The age distribution of patients with prostate cancer of the study.

| Androgen receptor status | | | | | Total |
|---|---|---|---|---|---|
| | | Negative | Positive | | |
| Age | Mean ± SD | 59.8±9.2 | | 68.01±7.96 | 67.33±8.31 |
| | 50-59 years old | Fr | 3 | 7 | 10 |
| | | % | 5.0% | 11.7% | 16.7% |
| | 60-69 years old | Fr | 1 | 23 | 24 |
| | | % | 1.7% | 38.3% | 40.0% |
| | 70-79 years old | Fr | 1 | 21 | 22 |
| | | % | 1.7% | 35.0% | 36.7% |
| | Older than 80 years old | Fr | 0 | 4 | 4 |
| | | % | 0.0% | 6.7% | 6.7% |
| Total | | Fr | 5 | 55 | 60 |
| | | % | 8.3% | 91.7% | 100.0% |

In terms of Gleason score, the patients who had Gleason score of (6) were 10 (16.67%) while those with Gleason score of (7) were 21 (35%), those with Gleason score of (8) were 15 (25%) and patients with Gleason score of (9) were 14 (23.33%) as shown in figure 2.

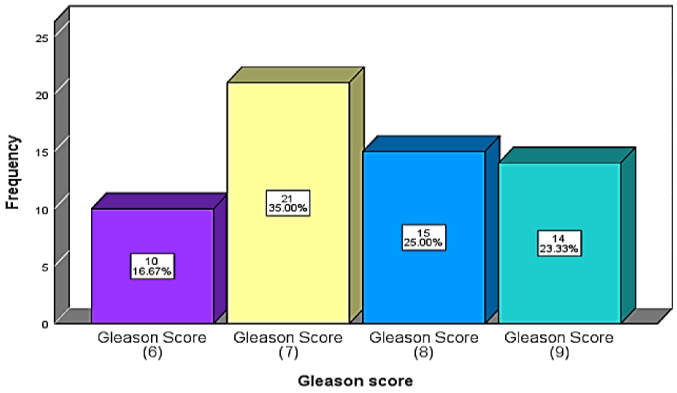


Figure 2: Gleason score for patients with prostate cancer of the study.

The histological grade based on the Gleason score showed an escalating trend with a large portion of the patients having poorly differentiated tumors with Gleason score ≥8 with 29 (48.33%) of the patients while those with moderately differentiated tumors who had Gleason score of 7 were 21 (35%). Lowest number of patients was for well differentiated tumors with Gleason score of 6 with 10 (16.67%) of patients as shown in figure 3.

Categorizing Gleason grade into high grade for patients with Gleason score ≥8 and low grade for patients with Gleason score ≤7 showed that 31 (51.67%) had low grade prostate cancer and 29 (48.33%) had high grade prostate cancer as shown in figure 4.

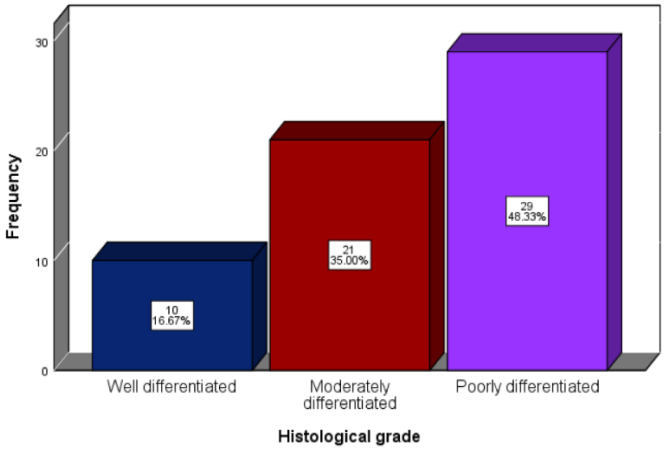


Figure 3: Histological grade for patients with prostate cancer of the study.

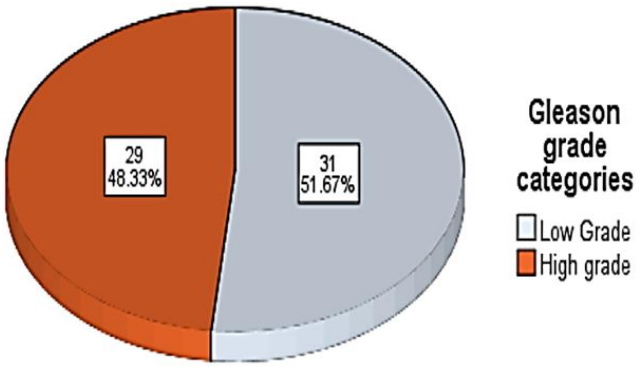


Figure 4: Gleason grade category for patients with prostate cancer of the study.

Figure 5 below shows the androgen receptor intensity (ARI) staining. Large number of patients had strong ARI staining with 25 (41.67%), patients with intermediate ARI staining were 23 (38.33%) while 7 (11.67%) had weak ARI and only 5 (8.33%) had negative ARI.

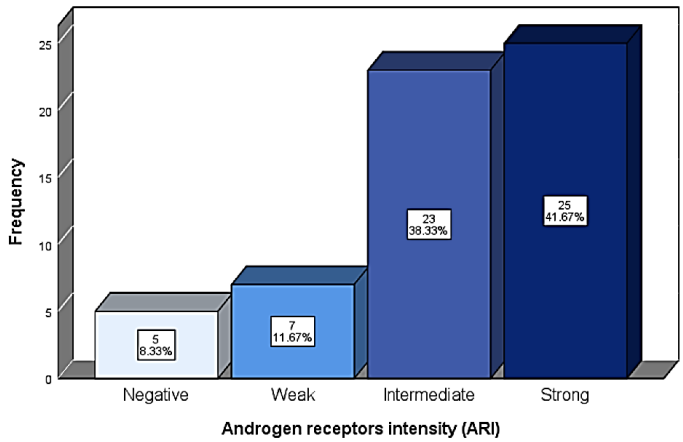


Figure 5: Androgen receptor intensity (ARI) for patients with prostate cancer of the study.

Androgen receptors staining quantity showed a trend of increasing frequencies with majority of the patients had (≥67%) androgen receptor staining with 31 (51.67%) of the patients, 16 (26.67%) had androgen receptor staining (34-



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66%), those who had (1-33%) androgen receptor staining were seen in 8 (13.33%) of the patients, 5 (8.33%) had negative staining for androgen receptor as shown in figure 6 below.

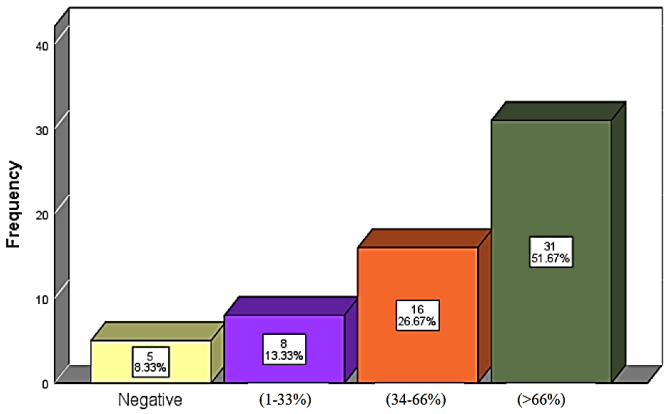


Figure 6: Androgen receptor staining quantity for patients with prostate cancer of the study, (1-33%) (34-66%) (>66%)

The immunoreactive score (IRS) calculating using androgen receptor staining quantity and androgen receptor staining intensity showed that 33 (55%) of the patients had strong immunoreactive score, 12 (20%) of the patients had intermediate immunoreactive score and 10 (16.67%) had mild immunoreactive score. Patients with negative androgen receptor staining were 5 (8,33%) as shown in figure 7 below.

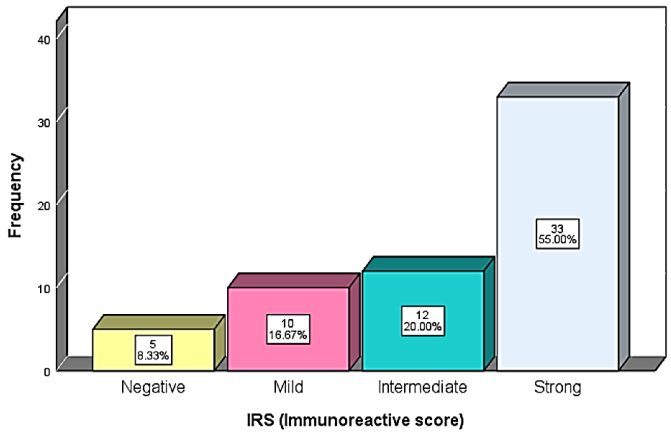


Figure 7: The immunoreactive score (IRS) for patients with prostate cancer of the study.

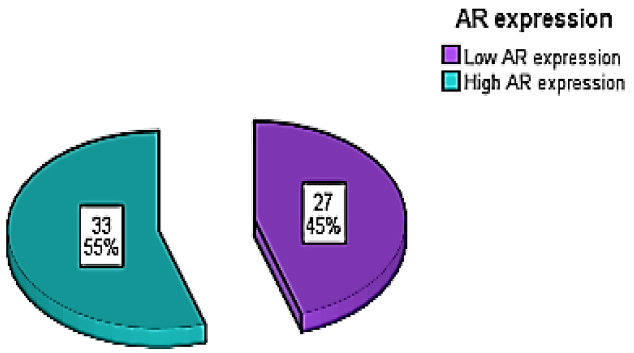


Figure 8: Androgen receptor (AR) expression for patients with prostate cancer of the study.

Androgen receptor (AR) expression based on the immunoreactive score (IRS) showing 33 (55%) of the patients had high androgen receptor (AR) expression while 27 (45%) had low androgen receptor (AR) expression as shown in figure 8.

Analytical statistics: For the association of age groups with Gleason score, there was no statistically significant difference with p-value 0.65 as shown in table 2.

Similarly, the association for age group with histological grade showed no statistically significant difference with p-value of 0.249 as shown in table 3 below.

TABLE 2: The association of Age groups with Gleason score for patients with prostate adenocarcinoma of the study.

| Gleason score | | | Gleason Score (6) | Gleason Score (7) | Gleason Score (8) | Gleason Score (9) | Total | x2 | P-value |
|---|---|---|---|---|---|---|---|---|---|
| Age groups | 50-59 YO | Fr | 4 | 2 | 2 | 2 | 10 | 6.93 | 0.652 |
| | | % | 6.7% | 3.3% | 3.3% | 3.3% | 16.7% | | |
| | 60-69 YO | Fr | 4 | 9 | 5 | 6 | 24 | | |
| | | % | 6.7% | 15.0% | 8.3% | 10.0% | 40.0% | | |
| | 70-79 YO | Fr | 2 | 9 | 7 | 4 | 22 | | |
| | | % | 3.3% | 15.0% | 11.7% | 6.7% | 36.7% | | |
| | >80 YO | Fr | 0 | 1 | 1 | 2 | 4 | | |
| | | % | 0.0% | 1.7% | 1.7% | 3.3% | 6.7% | | |
| Total | | Fr | 10 | 21 | 15 | 14 | 60 | | |
| | | % | 16.7% | 35.0% | 25.0% | 23.3% | 100.0% | | |

TABLE 3: The association of Age groups with histological grade for patients with prostate adenocarcinoma of the study.

| | | | Histological grade | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | Well Diff. | Moderately Diff. | Poorly Diff. | Total | $X^2$ | P-value |
| Age groups | 50-59 YO | Fr | 4 | 2 | 4 | 10 | 7.334 | 0.249 |
| | | % | 6.7% | 3.3% | 6.7% | 16.7% | | |
| | 60-69 YO | Fr | 2 | 9 | 13 | 24 | | |
| | | % | 3.3% | 15.0% | 21.7% | 40.0% | | |
| | 70-79 YO | Fr | 1 | 9 | 12 | 22 | | |
| | | % | 1.7% | 15.0% | 20.0% | 36.7% | | |
| | >80 YO | Fr | 0 | 1 | 3 | 4 | | |
| | | % | 0.0% | 1.7% | 5.0% | 6.7% | | |
| Total | | Fr | 7 | 21 | 32 | 60 | | |
| | | % | 11.7% | 35.0% | 53.3% | 100.0% | | |

The association for age group with Gleason grade also showed no statistically significant difference with p-value of 0.757 as shown in table 4 below.

For the association of androgen receptor (AR) expression with age group, there was no statistically significant association for both age group and androgen receptor expression with p-value of 0.082 as shown in table 5 below.

Meanwhile, the association for Gleason score with AR expression showed a statistically significant difference with p-value of 0.002 as shown in table 6 below.

Likewise, there was a high statistically significant association for histological grade with AR expression with p-value of 0.001 as shown in table 7 below.



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TABLE 4: The association of Age groups with Gleason grade for patients with prostate adenocarcinoma of the study.

| | | | Gleason grade categories | | | | |
|---|---|---|---|---|---|---|---|
| | | | Low grade | High grade | Total | X2 | P-value |
| Age groups | 50-59 YO | Fr | 6 | 4 | 10 | 1.48 | 0.757 |
| | | % | 10.0% | 6.7% | 16.7% | | |
| | 60-69 YO | Fr | 13 | 11 | 24 | | |
| | | % | 21.7% | 18.3% | 40.0% | | |
| | 70-79 YO | Fr | 11 | 11 | 22 | | |
| | | % | 18.3% | 18.3% | 36.7% | | |
| | >80 YO | Fr | 1 | 3 | 4 | | |
| | | % | 1.7% | 5.0% | 6.7% | | |
| Total | | Fr | 31 | 29 | 60 | | |
| | | % | 51.7% | 48.3% | 100.0% | | |

TABLE 5: The association of Age groups with androgen receptor (AR) expression for patients with prostate adenocarcinoma of the study.

| | | | Low AR expression | High AR expression | Total | X2 | P-value |
|---|---|---|---|---|---|---|---|
| Age groups | 50-59 YO | Fr | 8 | 2 | 10 | 6.39 | 0.082 |
| | | % | 13.3% | 3.3% | 16.7% | | |
| | 60-69 YO | Fr | 8 | 16 | 24 | | |
| | | % | 13.3% | 26.7% | 40.0% | | |
| | 70-79 YO | Fr | 9 | 13 | 22 | | |
| | | % | 15.0% | 21.7% | 36.7% | | |
| | >80 YO | Fr | 2 | 2 | 4 | | |
| | | % | 3.3% | 3.3% | 6.7% | | |
| Total | | Fr | 27 | 33 | 60 | | |
| | | % | 45.0% | 55.0% | 100.0% | | |

TABLE 6: The association of Gleason score with androgen receptor (AR) expression for patients with prostate adenocarcinoma of the study.

| | | | AR expression | | Total | $X^2$ | P-value |
|---|---|---|---|---|---|---|---|
| | | | Low AR expression | High AR expression | | | |
| Gleason score | Gleason Score (6) | Fr | 7 | 3 | 10 | 14.11 | 0.002 |
| | | % | 11.7% | 5.0% | 16.7% | | |
| | Gleason Score (7) | Fr | 14 | 7 | 21 | | |
| | | % | 23.3% | 11.7% | 35.0% | | |
| | Gleason Score (8) | Fr | 2 | 13 | 15 | | |
| | | % | 3.3% | 21.7% | 25.0% | | |
| | Gleason Score (9) | Fr | 4 | 10 | 14 | | |
| | | % | 6.7% | 16.7% | 23.3% | | |
| Total | | Fr | 27 | 33 | 60 | | |
| | | % | 45.0% | 55.0% | 100.0% | | |

Table 7: The association of histological grade with androgen receptor (AR) expression for patients with prostate adenocarcinoma of the study.

| | | | AR expression | | Total | $X^2$ | P-value |
|---|---|---|---|---|---|---|---|
| | | | Low AR expression | High AR expression | | | |
| Histological grade | Well Diff. | Fr | 7 | 3 | 10 | 13.43 | 0.001 |
| | | % | 11.7% | 5.0% | 16.7% | | |
| | Moderately Diff. | Fr | 14 | 7 | 21 | | |
| | | % | 23.3% | 11.7% | 35.0% | | |
| | Poorly Diff. | Fr | 6 | 23 | 29 | | |
| | | % | 10.0% | 38.3% | 48.3% | | |
| Total | | Fr | 27 | 33 | 60 | | |
| | | % | 45.0% | 55.0% | 100.0% | | |

The association for Gleason grade with AR expression showed a high statistically significant difference with p-value of 0.001, the odds ratio was 8 meaning that patients who had high AR expression were 8 times more likely to be of high-grade Gleason category that those with low AR expression as shown in table 8 below.

TABLE 8: The association of Gleason grade with androgen receptor (AR) expression for patients with prostate adenocarcinoma of the study.

| | | | AR expression | | Total | $X^2$ | P-value | Odds ratio |
|---|---|---|---|---|---|---|---|---|
| | | | Low AR expression | High AR expression | | | | |
| Gleason grade categories | Low Grade | Fr | 21 | 10 | 31 | 13.4 | 0.001 | 8.05 |
| | | % | 35.0% | 16.7% | 51.7% | | | |
| | High grade | Fr | 6 | 23 | 29 | | | |
| | | % | 10.0% | 38.3% | 48.3% | | | |
| Total | | Fr | 27 | 33 | 60 | | | |
| | | % | 45.0% | 55.0% | 100.0% | | | |

Histological analysis

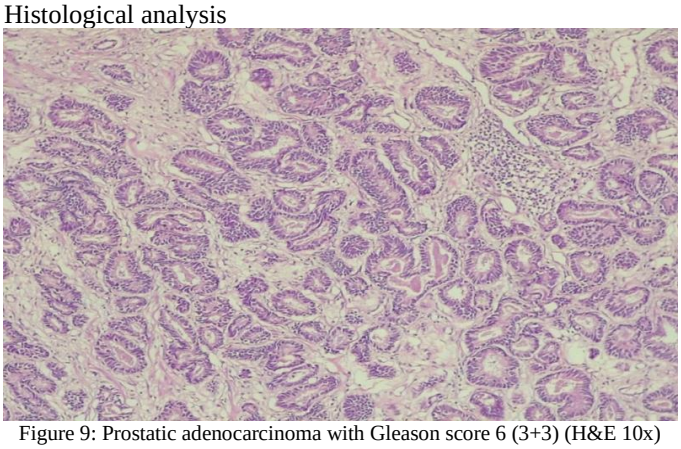

Figure 9: Prostatic adenocarcinoma with Gleason score 6 (3+3) (H&E 10x)

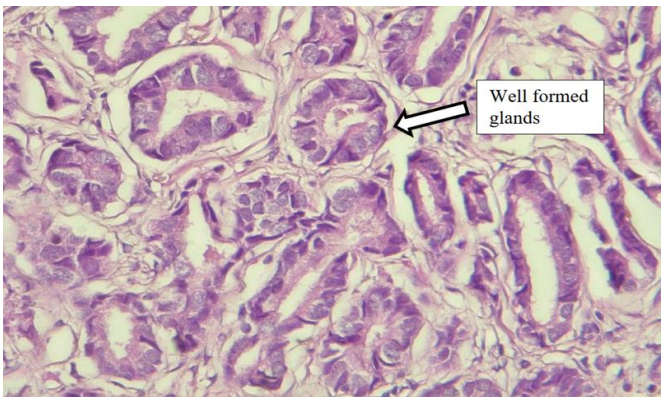


Figure 10: Prostatic adenocarcinoma with Gleason score 6 (3+3) (H&E 40x)

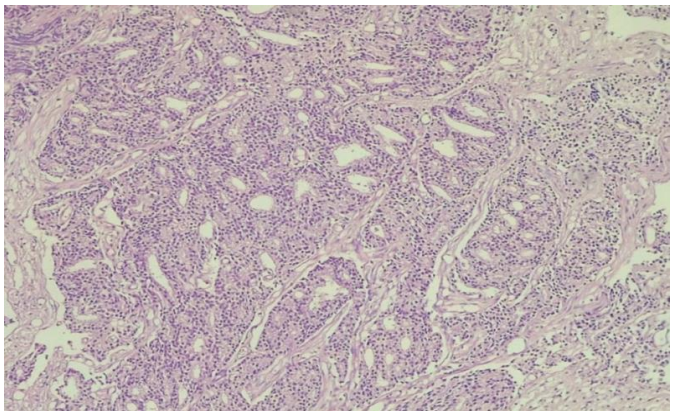

Figure 11: Prostatic adenocarcinoma with Gleason score 8 (4+4) (H&E 10x)



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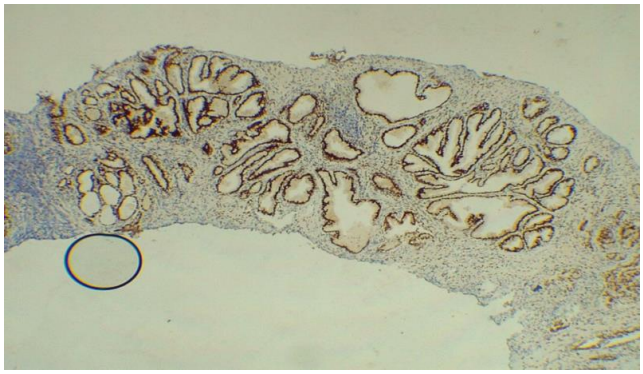

Figure 12: Positive internal control showing strong positive nuclear androgen receptor (AR) staining in prostatic stromal and epithelial cells (4x).

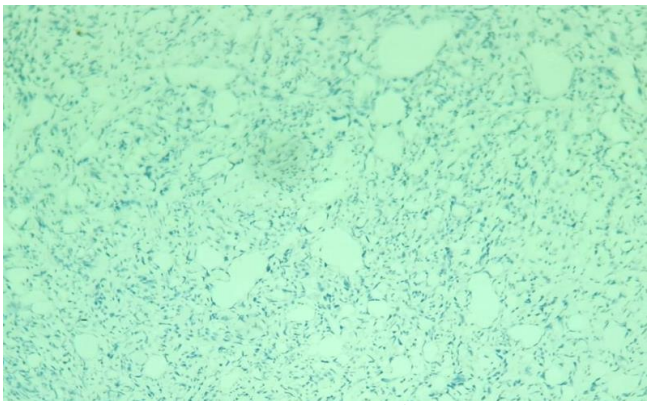

Figure 13: Negative nuclear staining control for androgen receptor (AR) protein (10x)

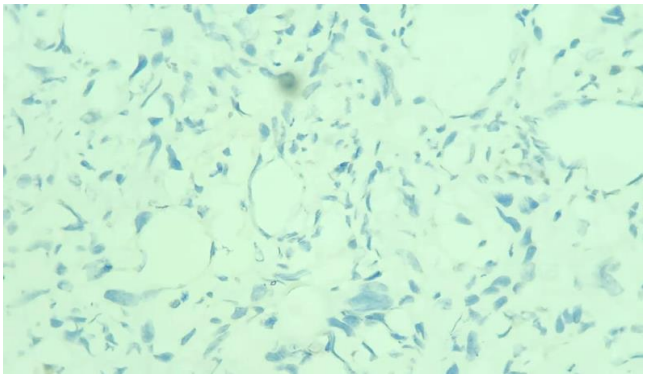

Figure 14: Negative nuclear staining control for androgen receptor (AR) protein (40x)

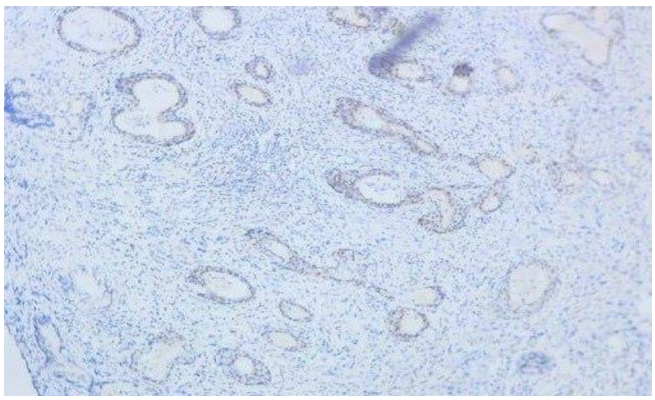

Figure 15: Prostatic adenocarcinoma with weak nuclear staining for 40% of the cells and Gleason score 6 (3+3) (10x)

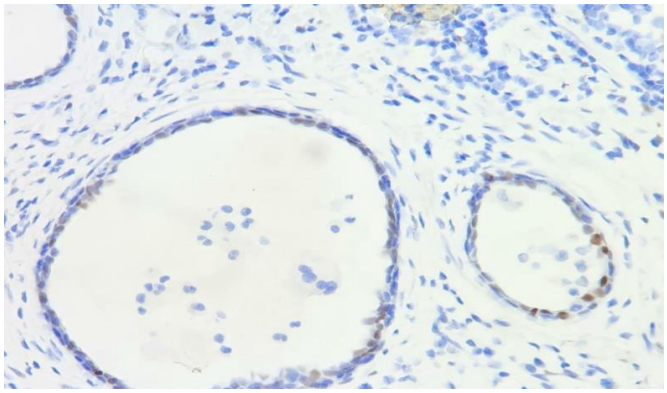

Figure 16: Prostatic adenocarcinoma with weak nuclear staining for 40% of the cells and Gleason score 6 (3+3) (40x)

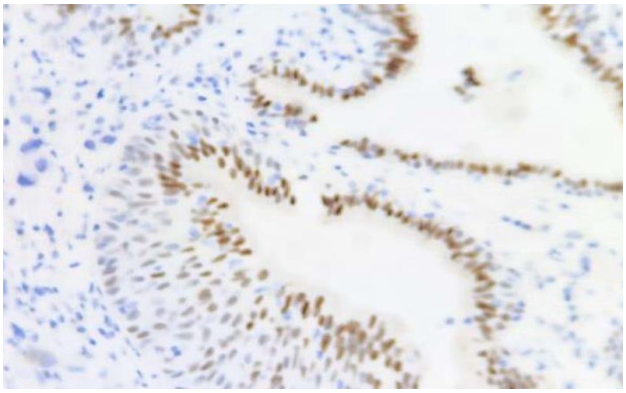

Figure 17: Prostatic adenocarcinoma with Intermediate nuclear staining for 60% of the cells (40x)

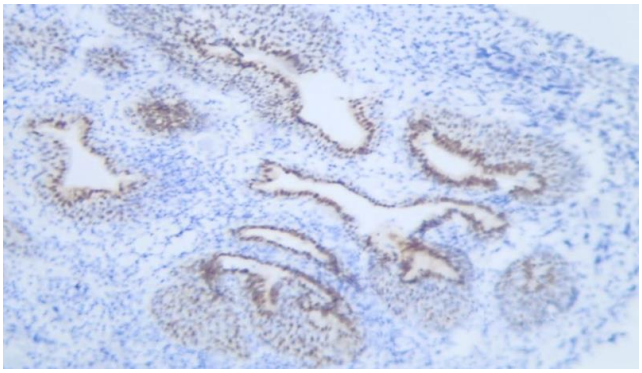

Figure 18: Prostatic adenocarcinoma with Intermediate nuclear staining for 60% of the cells (10x)

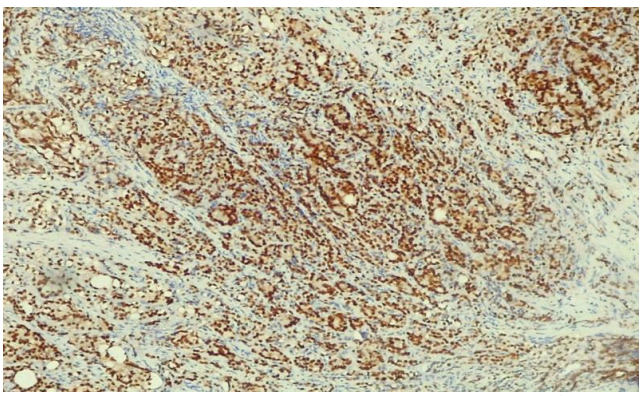

Figure 19: Prostatic adenocarcinoma with strong nuclear staining for 85% of the cells and Gleason score 9 (5+4) (10x)



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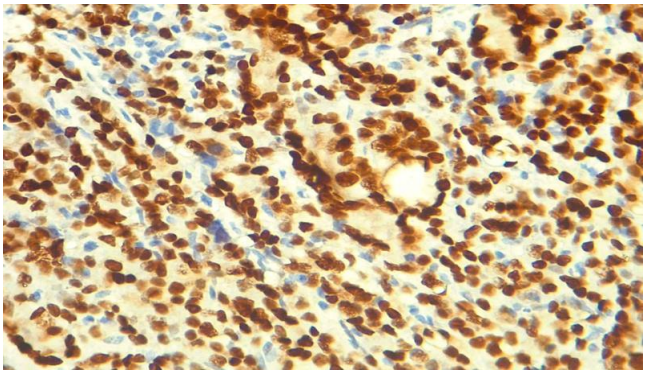

Figure 20: Prostatic adenocarcinoma with strong nuclear staining for 85% of the cells and Gleason score 9 (5+4) (40x)

## IV. DISCUSSION

Despite the significance of AR expression in prostate cancer, there is limited data on its use as a prognostic biomarker in different populations. Given the importance of AR signaling in prostate cancer and the potential utility of AR expression as a prognostic biomarker and its association with histological grade of the tumors, this study investigated its role and its association with histological grading among patients in Iraq, in which no previously reported studies could be

found that assessed such relationship after extensive literature review. The majority of patients included in the study exhibited androgen receptor (AR) expression, with approximately (92%) of them showing positivity. This aligns with the findings of a previous study conducted in 2015 by Williams et al., which reported a similar rate of AR expression (95%) in patients with prostate adenocarcinoma (15).

Additionally, Lekshmy et al. study in 2019 showed that AR expression in almost all prostate cancer cases, another study found that (82%) of cancer cells expressed AR, which is lower than that reported in this study but still significantly high (16).

Comparatively, the expression of androgen receptor (AR) in normal prostate gland tissue was lower, with approximately (69%) reported in a previous cohort study and 64% in another study (17, 18). These findings indicate that androgen receptors are overexpressed in prostate cancer compared to normal prostate tissue.

Patients in the study who demonstrated high androgen receptor (AR) expression reached (55%), a finding consistent with a study of Hashmi et al. reported a similar result with (56.2%) of cases showing high AR expression (19). The distribution of Gleason scores among patients varied across different studies. In this study, the highest percentage was observed in Gleason score 7, comprising (35%), and the lowest observed Gleason score was 6 in (16.67%).

Another study done in Iraq also showed highest percentage of patients with prostatic adenocarcinoma had Gleason score (7) which was seen in (47.8%) of cases (20). Similarly, a study conducted in Karachi reported (41.5%) with Gleason score 7 (19). In contrast, a study at RMDC, Lahore, found that (41.66%) of patients had Gleason score 9, (33%) had Gleason score 8, (8.33%) had Gleason score 7, and (8.33%) had Gleason score 6 (11). In a study of Imran et al. in Al-Hilla, the distribution also differed, with Gleason score 8 being the most common at (46%), followed by Gleason score 7 at (30%) (21). These variations highlight the importance of considering regional and population-specific factors in assessing Gleason scores and their implications for prostate cancer diagnosis and management.

Sample size difference could also play a significant role in this difference between the studies.

In this study, a statistically significant association between Gleason score and androgen receptor (AR) expression was identified, a finding consistent with previous research by Hashmi et al., Fatima et al., and Wheeler et al (11, 13, 19). These studies similarly reported a significant association between androgen receptor (AR) expression and Gleason score. Further analysis of the data of this study revealed that patients with higher AR expression tended to have higher Gleason scores, while those with lower AR expression exhibited lower Gleason scores.

Moreover, data analysis also demonstrated a significant association between AR expression and histological grading and Gleason grade of the tumor, aligning with the findings of Fatima et al. and Hermien et al (11, 22). These consistent findings strengthen the evidence supporting the relationship between AR expression levels and tumor aggressiveness as indicated by Gleason score and histological grading.

The odds ratio calculation for the association of Gleason grade with androgen receptor (AR) expression showed that patients who had high AR expression were 8 times more likely to be of high-grade Gleason category that those with low AR expression. A study of Putriyuni et al showed an odds ratio of 5, meaning that those with high androgen receptor (AR) expression were 5 times more likely to have high Gleason grade than those with low androgen receptor (AR) expression (12). This proved a strong association of androgen receptors (AR) expression with Gleason score and ultimately, the prognosis of the disease, the difference in the odds of occurrence of the event could be due to difference in sample size and population risk factors.

The androgen receptor (AR) molecule plays a crucial role in the regulatory [androgen/androgen receptor (AR)] complex, making it a critical component of the androgen/AR signaling pathway in prostate cancer (PCa). Historically, assessing androgen receptor (AR) status was a primary focus of research aimed at predicting prostate cancer (PCa) outcomes following hormonal therapy (23). The premise behind such investigations rested on the assumption that higher androgen receptor (AR) levels would indicate androgen dependence and predict response to androgen withdrawal, thus influencing the time to tumor progression. Endocrine therapy also aims to inhibit the androgen receptor (AR). However, despite androgen ablation therapy, prostate cancer (PCa) often progresses to a hormone-refractory state. Androgen receptor (AR) expression persists throughout prostate cancer (PCa) progression, including in the majority of patients with hormone-refractory disease. Moreover, many androgen receptor (AR) mutations identified in hormone-refractory prostate cancer (PCa) retain transcriptional activity. These



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findings suggest that loss of androgen receptor (AR) function is not a primary cause of androgen ablation

therapy failure, and androgen receptor (AR)-negative prostate cancer (PCa) cells do not possess a significant growth or survival advantage (23-25). Clinical and experimental evidence suggests that the progression of prostate cancer (PCa) is primarily driven by dysregulation of androgen receptor (AR) activity. This dysregulation occurs through various mechanisms, including alterations in signal transduction cascades, changes in the expression of AR coregulators, and mutations that enable AR to become transcriptionally active in response to ligands other than testosterone and dihydrotestosterone (DHT). These dysregulations contribute to the development of castrate-resistant prostate cancer (CRPC), where tumor cells continue to grow and proliferate despite androgen deprivation therapy. Therefore, understanding the intricate molecular mechanisms underlying AR dysregulation is crucial for developing effective therapeutic strategies to combat PCa progression (24).

In that context, immunohistochemical measurement of androgen receptor (AR) proved to be a valuable prognostic indicator for prostate cancer (PCa). the biological role of androgen receptor (AR) can become complex due to altered androgen receptor (AR) functions (26).

The overall mean age of the patients in this study was 67.33 years, this was similar to that reported in previous study with mean age of 69 years. According to research by Dr. Khalidah M. Khudur, majority of patients of the study with prostate cancer were aged 60 and above (27). Al-Badran et al. noted that prostate cancer incidence in Basra increased with age, with majority of patients' age being older than 66 years (28). Similarly, research by Walsks in the United States revealed that over 65% of all prostate cancer cases are diagnosed in individuals aged 65 years and older, with an average age of diagnosis being 69 years, similar to that of this study (29). Beyond this age, the likelihood of developing prostate cancer becomes more prevalent. This could be because, with increasing age, hormonal changes occur with disturbance in estrogen and testosterone levels, this could influence the growth and development of prostate cells, potentially leading to the development of cancer.

Cumulative genetic changes and reduced immune functions could be other reasons for increasing incidence with age. With all the previously mentioned findings in mind, there was no statistically

significant association for age with Gleason score, grade and histological grade, this was consistent with the findings of a previous study in Iraq which also showed no statistically significant association for age with Gleason score. Antunes et al. found that age was not a key factor in relation to pathological findings regarding the Gleason score (30).

There was also no statistically significant association for age with androgen receptor (AR) expression. This was consistent with the findings of Hashmi et al. (19).

## V. CONCLUSIONS

1. The findings note the higher prevalence of AR expression in prostate cancer patients in contrast with lower expression levels in normal prostate tissue.
2. Moreover, the study reveals significant associations between AR expression and Gleason score and disease aggressiveness, emphasizing the potential utility of AR expression as a prognostic biomarker.

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