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Integration of Glycolytic Metabolic Marker (GLUT1) and CD147 Expression in Progression of Prostatic Carcinoma; An Immuohistochemical Study

MARWA S. ABD ALLAH, M.D. and OMNEYA Y. BASSYONI, M.D.

The Department of Pathology, Faculty of Medicine, Benha University, Egypt

Abstract

Background: Increased glycolysis has been considered one of the characteristic features of cancer. Glucose Transporter 1 (GLUT1) plays a central role in the transport of glucose in tumor cells. CD147 is multifunctional glycoprotein overexpressed in many solids tumors.

Methods: This is a retrospective controlled study on 46 cases of prostatic carcinoma to recognize the expression of GLUT1 and CD147 by immunohistochemistry and to identify their correlation with different clinicopathological parameters.

Results: GLUT1 and CD147 positive expression was detected in 25/46 (54.3%) and 29/46 (63.0%) of prostatic carcinoma, respectively. GLUT1 and CD147 expression was significantly higher in prostatic carcinoma than BPH and HGPIN. Significant positive correlation between GLUT1 and CD147 immunoreactivity in prostatic carcinoma was seen. Positive GLUT1 expression was statistically correlated with high Gleason score (p<0.01), advanced tumor stage (p<0.01) and lymph nodes metastasis (p<0.01), distant metastasis (p< 0.05) and higher TNM stage (p=<0.01). Positive CD147 expression was statistically correlated with high Gleason score (p<0.05), advanced tumor stage (p<0.01), lymph nodes metastasis (p<0.01), distant metastasis (p<0.01), higher TNM stage (p<0.01) and perineural invasion (p<0.01).

Conclusions: Positive GLUT1 and CD147 expression was significantly associated with progression and aggressiveness of prostatic carcinoma. Consequently, they might be considered as prognostic markers in prostatic carcinoma.

Key Words: *GLUT1 – CD147 – Prostatic carcinoma.*

Introduction

PROSTATE Cancer (PC) is the second most diagnosed cancer accounting 15% of all newly diagnosed male cancers and the fifth cause of cancer death among men globally [1]. TNM clinical staging, Gleason score, tumor grade, and PSA serum levels are clinical-pathological landscapes of prostate cancer that can predict patients' prognosis [2]. It is essential to identify prognostic and predictive biomarkers for prostate cancer patients for new therapeutic approaches.

Malignant cells are approved to reprogram their metabolism to support rapid growth, proliferation, and long-term maintenance [3]. The common characteristics of this increased metabolism are elevated glucose uptake and lactic fermentation of glucose even under aerobic conditions, defined as "the Warburg effect "the increase in glucose uptake in malignant tumors depends largely on the specific transmembranous Glucose Transporter proteins (GLUTs) [4].

Glucose Transporter 1 (GLUT1) is human glucose transporter protein encoded by the SLC2A1 gene. The over-expression of GLUT1 during oncogenesis has been identified in several cancers. GLUT1 enhances increased glucose uptake into cytoplasm of tumor cells [5]. Many researches have shown that GLUT1 is involved in the progression and metastasis of cancer [6]. GLUT-1 level was proved to be linked with oncogenes, growth factors, interleukin-1, local hypoxia, and matrix metalloproteinases [7].

CD147 or Emmprin is a widely distributed cell surface glycoprotein belonging to the immunoglobulin superfamily. It has conformed that CD 147 is enriched on the surface of many tumor cells, promoting tumor growth, invasion and metastasis by its stimulating effect on adjacent fibroblasts to yield matrix metalloproteinases [8]. Other functions of CD147 have been rendered, including the regulation of cell proliferation, Wnt signaling stimulation and the epithelial to mesenchymal transition [9].

Correspondence to: Dr. Marwa Said Abd Allah,
The Department of Pathology, Faculty of Medicine,
Benha University, Egypt

Direct cross-linking evidence between CD147 and the Glut1 has been lacking. Therefore, we initiated the present study to appreciate the correlation between CD147 and the GLUT1 in prostatic carcinoma and evaluate the degree of their expression in prostate carcinomas compared to BPH and HGPIN plus their correlation with the various clinical-pathological parameters.

Material and Methods

This is a retrospective controlled study enrolled 46 cases diagnosed as prostatic adenocarcinoma and obtained by radical prostatectomy in the period from 2009 till 2014. Nineteen (19) cases of nodular prostatic hyperplasia (BPH) and 25 cases of HGPIN were used as control. Archived formalin-fixed, paraffin embedded blocks of tumor specimens, were collected from Pathology Department, Faculty of Medicine, Benha University and Urology. Clinico-pathological data concerning age, pre-operative serum PSA level, lymph node metastasis, distant metastasis and TNM stage were extracted from the pathology reports and medical records after approval by the ethical committee at Faculty of Medicine, Benha University.

Histopathological evaluation: Three serial sections were prepared from each block and cut to at 5 microns thickness. A section was stained by Hematoxylin and Eosin (H & E) for histopathological evaluation and others were mounted on slides for the immunohistochemistry.

Two blind expert pathologists independently confirmed histologic diagnosis of each lesion and Gleason grading. Cases were grouped according to the Gleason score into two groups: The high Gleason Score (GS) group (Gleason score of 4+3=7, ≥8) and a low GS group (Gleason score 3+4=7, ≤6) [10]. TNM staging was regarded according to AJCC TNM-UICC (2010) classification system.

Immunohistochemical study: The immunohistochemical assay was applied using the standard streptavidin-biotin technique following the manufacturer's instructions. Details of the primary antibodies used are shown in (Table 1). For secondary reagents, a labeled streptavidin-biotin kit (Neomarker, Lab vision, USA) has been used. The sections were stained with 0.02% Diaminobenzidine (DAB) solution as the chromogen used. The negative control antibody was established by replacing a normal nonimmune serum.

Interpretation of immunohistochemical staining: GLUT 1: The expression was detected as diffuse cytoplasmic staining with occasionally plasma membrane staining. Tumors with up to 10% of stained cells were considered negative and over 10% were positive [11]. CD147: The expression was detected as membranous and/or cytoplasmic staining. The stain extension was catogrized as: 0:0% of immunoreactive cells; 1<5% immunoreactive cells; 2:5-50% of immunoreactive cells and 3:>50% of immunoreactive cells. The staining intensity was catogrized as 0: Negative; 1: Weak; 2: Moderate and 3: Strong. The final result was defined as the sum of both parameters (extension and intensity) and grouped as negative (score 0-3) and positive (score 4-6) [12].

Statistical analysis: SPSS Version 16 soft ware (SpssInc, Chicago, ILL Company) was used. The collected data were analyzed using chi square (χ^2) test or Fisher's Exact Test (FET). An analysis of the Receiver's Operating Curve (ROC) was performed to evaluate the GLUT 1 and CD 147 diagnostic performances to discriminate high Gleason score group from low Gleason score group. The accepted level of significance in this work was stated at 0.05 (p<0.05 was considered significant).

Table (1): Study markers.

Marker	Vendor	Clone	Host/Isotope	State	Dilution	Incubation	Positive control
GLUT1	Thermo Fisher	Polyclonal	Rabbit	Concentrated	1:100	2 hours at RT*	Cardiac muscle
CD 147	Scientific		/IgG	Concentrated	1:50	Overnight at RT*	Cervical squamous carcinoma

*Rt: Room Temperature.

Results

Clinicopathological data of patients:

The present retrospective study enrolled 46 prostatic adenocarcinoma cases. The mean age of patients was 66.30±4.34 (55 to 74) years. Among the study cases of prostatic carcinoma, 25 showed adjacent HGPIN. All clinicopathological data were presented in (Table 2).

Immunohistochemical results:

Analysis of GLUT1 immunostaaining:

GLUT1 positive staining was localized in the cytoplasm of prostatic cancer cells with focal

membranous staining Fig. (1). GLUT1 expression was positively expressed in 25/46 (54.3%) of prostatic carcinoma, 5/19 (26.3%) of BPH cases and 7/25 (28.0%) of HGPIN, respectively. The positive expression rate of GLUT1 in prostatic carcinoma tissues was significantly higher than that in BPH (p<0.05) and HGPIN (p<0.05), respectively.

Positive GLUT1 expression showed statistically significant correlation with high Gleason score (p <0.01), advanced pathologic tumor stage (p<0.01), lymph nodes metastasis (p<0.01), distant metastasis (p<0.05) and TNM stage (p<0.01). However, no statistically significant correlation was detected between GLUT 1 expression and age of patient (p=.095), pre-operative PSA level (p=.069) and perineural invasion (p=.182). The correlation between GLUT1 and different clinicopathologic variables of study cases was detailed in (Table 3).

Analysis of CD147 immunostaaining:

CD147 positive staining was localized at the cell membranes of prostatic cancer cells Fig. (1). CD147 expression was positively expressed in 29/46 (63.0%) of prostatic carcinoma and 3/19 (15.8%) of BPH cases and 6/25 (24.0%) of HGPIN, respectively. The positive expression rate of CD 147 in prostatic carcinoma tissues was significantly higher than that in BPH (p<0.01) and HGPIN (p <0.01) respectively.

Positive CD147 expression showed statistically significant correlation with high Gleason score (p <0.05), advanced tumor stage (p<0.01), lymph nodes metastasis (p<0.01), distant metastasis (p <0.01), TNM stage (p<0.01) and perineural invasion (p<0.01). However, no statistically significant correlation was detected between positive CD 147 expression and age of patient (p=.410) and preoperative PSA level (p=.091). The correlation between CD 147 and different clinicopathologic variables of study cases was detailed in (Table 4).

Correlation between GLUT1 and CD147:

The present study demonstrated a high significant positive correlation between GLUT1 and CD147 immunoreactivity in prostatic carcinoma since among 29 cases positive for CD 147 immunostaining, 20 cases (69.0%) were positive for GLUT1 while 9 cases (31.0%) were negative (p <0.01) as shown in (Table 5).

ROC curves:

The receiver operating characteristics curve analysis showed that the diagnostic performance of both GLUT 1 and CD 147 in discriminating patients with high Gleason score group from low Gleason score group was accepted.

For GLUT1, cut off value of was 5, AUC was (0.8494) and [Confidence Interval (CI)=0.705-0.958, p<0.001]. For CD147, cut off value of was 40, AUC was (0.8314) and [Confidence Interval (CI)=0.738-0.961, p<0.001].

Regarding sensitivity, Glut1 is more sensitive than CD 147 in discrimination of high Gleason score group from low Gleason score group. However, the SPECIFICITY of both Glut1 and CD147 in discrimination of high Gleason score group is the same as shown in (Table 6) and Fig. (2).

Table (2): Clinicopathological variables of study prostatic carcinoma cases.

Clinic pathological data	No. (N=46)	% (100%)
Age (ys):		
Mean ± SD (range)	66.30±4.34 (55-74)	
≤65	18	39.1%
>65	28	60.9%
Pre-operative PSA:	35.0±1.95 (8.0-85.5)	
Median ± SD (range)		
≤20ng/dl	15	32.6%
>20-40ng/dl	14	30.4%
>40-60 ng/dl	12	26.1%
>60ng/dl.	5	10.9%
Gleason Score (GS) group:		
Low GS group (3+4=7, 6)	24	52.2%
High GS group (4+3=7, 8)	22	47.8%
Pathologic tumor stage:		
T1	5	10.9%
T2	19	41.3%
T3	12	26.1%
T4	10	21.7%
L N metastasis:		
Negative	29	63.0%
Positive	17	37.0%
Distant metastasis:		
Negative	37	80.4%
Positive	9	19.6%
TNM stage:		
I stage	5	10.9%
II stage	18	39.1%
III stage	6	13.0%
IV stage	17	37.0%
Perineural invasion:		
Negative	15	32.6%
Positive	31	67.4%
Total	46	100%

Table (3): Correlation between GLUT1 and clinicopathologic variables of PC.

Clinicopathologic variables	GLUT 1			
	Negative	Positive	Total	*p*-value
Age (ys):				
≤65	11 (61.1%)	7 (38.9%)	18	.095
>65	10 (35.7%	18 (64.3%)	28	
Pre-operative PSA:				
≤20ng/dl	10 (66.7%)	5 (33.3%)	15	.069
>20-40ng/dl	6 (42.9%)	8 (57.1%)	14	
>40-60ng/dl	3 (25.0%)	9 (75.0%)	12	
>60ng/dl	2 (40.0%)	3 (60.0%)	5	
Gleason score group:				
Low Gleason score	16 (66.7%)	8 (33.3%)	24	.002**
High Gleason score	5 (22.7%)	17 (77.3%)	22	
Pathologic tumor stage:				
T1	5 (100.0%)	0 (.0%)	5	.003**
T2	10 (52.6%)	9 (47.4%)	19	
T3	4 (33.3%)	8 (66.7%)	12	
T4	2 (20.0%)	8 (80.0%)	10	
L N metastasis:				
Negative	18 (62.1%)	11 (37.9%)	29	.003**
Positive	3 (17.6%)	14 (82.4%)	17	
Distant metastasis:				
Negative	20 (54.1%)	17 (45.9%)	37	.02*
Positive	1 (11.1%)	8 (88.9%)	9	
TNM stage:				
I	5 (100.0%)	0 (0.0%)	5	.001**
II	10 (55.6%)	8 (44.4%)	18	
III	3 (50.0%)	3 (50.0%)	6	
IV	3 (17.6%)	14 (82.4%)	17	
Perineural invasion:				
Negative	9 (60.0%)	6 (40.0%)	15	.182
Positive	12 (38.7%)	19 (61.3%)	31	
Total	21 (45.7%)	25 (54.3%)	46 (100.0%)	

**: Correlation is significant at the 0.01 level (2-tailed)
* : Correlation is significant at the 0.05 level (2-tailed).

Table (4): Correlation between CD147 and clinicopathologic variables of PC.

Clinicopathologic variables	CD 147			
	Negative	Positive	Total	*p*-value
Age (ys):				
≤65	8 (44.4%)	10 (55.6%)	18	.410
>65	9 (32.1%)	19 (67.9%)	28	
Pre-operative PSA:				
≤20ng/dl	9 (60.0%)	6 (40.0%)	15	.091
>20-40ng/dl	3 (21.4%)	11 (78.6%)	14	
>40-60ng/dl	4 (33.3%)	8 (66.7%)	12	
>60ng/dl	1 (20.0%)	4 (80.0%)	5	
Gleason score group:				
Low Gleason score	13 (54.2%)	11 (45.8%)	24	.011*
High Gleason score	4 (18.2%)	18 (81.8%)	22	
Pathologic tumor stage:				
T1	4 (80.0%)	1 (20.0%)	5	.009**
T2	9 (47.4%)	10 (52.6%)	19	
T3	2 (16.7%)	10 (83.3%)	12	
T4	2 (20.0%)	8 (80.0%)	10	
L N metastasis:				
Negative	15 (51.7%)	14 (48.3%)	29	.006**
Positive	2 (11.8%)	15 (88.2%)	17	
Distant metastasis:				
Negative	17 (45.9%)	20 (54.1%)	37	.01**
Positive	0 (0.0%)	9 (100.0%)	9	
TNM stage:				
Stage I	4 (80.0%)	1 (20.0%)	5	.001**
II	9 (50.0%)	9 (50.0%)	18	
III	2 (33.3%)	4 (66.7%)	6	
IV	2 (11.8%)	15 (88.2%)	17	
Perineural invasion:				
Negative	10 (66.7%)	5 (33.3%)	15	.003**
Positive	7 (22.6%)	24 (77.4%)	31	
Total	17 (37.0%)	29 (63.0%)	46 (100%)	

**: Correlation is significant at the 0.01 level (2-tailed)
* : Correlation is significant at the 0.05 level (2-tailed).

Table (5): Correlation between GLUT1 and CD147 in PC cases.

CD 147	N	GLUT 1	
		Negative N (%)	Positive N (%)
Negative	17	12 (70.6%)	5 (29.4%)
Positive	29	9 (31.0)	20 (69.0)
Total	46	21 (45.7)	25 (54.3%)
p-value=0.009**			

**: Correlation is significant at the 0.01 level (2-tailed).

Table (6): Diagnostic performance for GLUT1 and CD147.

Variable (no.=46)	Cutoff point	Sensitivity (%)	Specificity (%)	AUC	95% CI	Correctly diagnosed (%)	*p*
CD147 score	5	72.73	87.50	0.8494	0.738-0.961	80.43	0.000 (S)
Glut1 score	40	77.27	87.50	0.8314	0.705-0.958	82.61	0.000 (S)

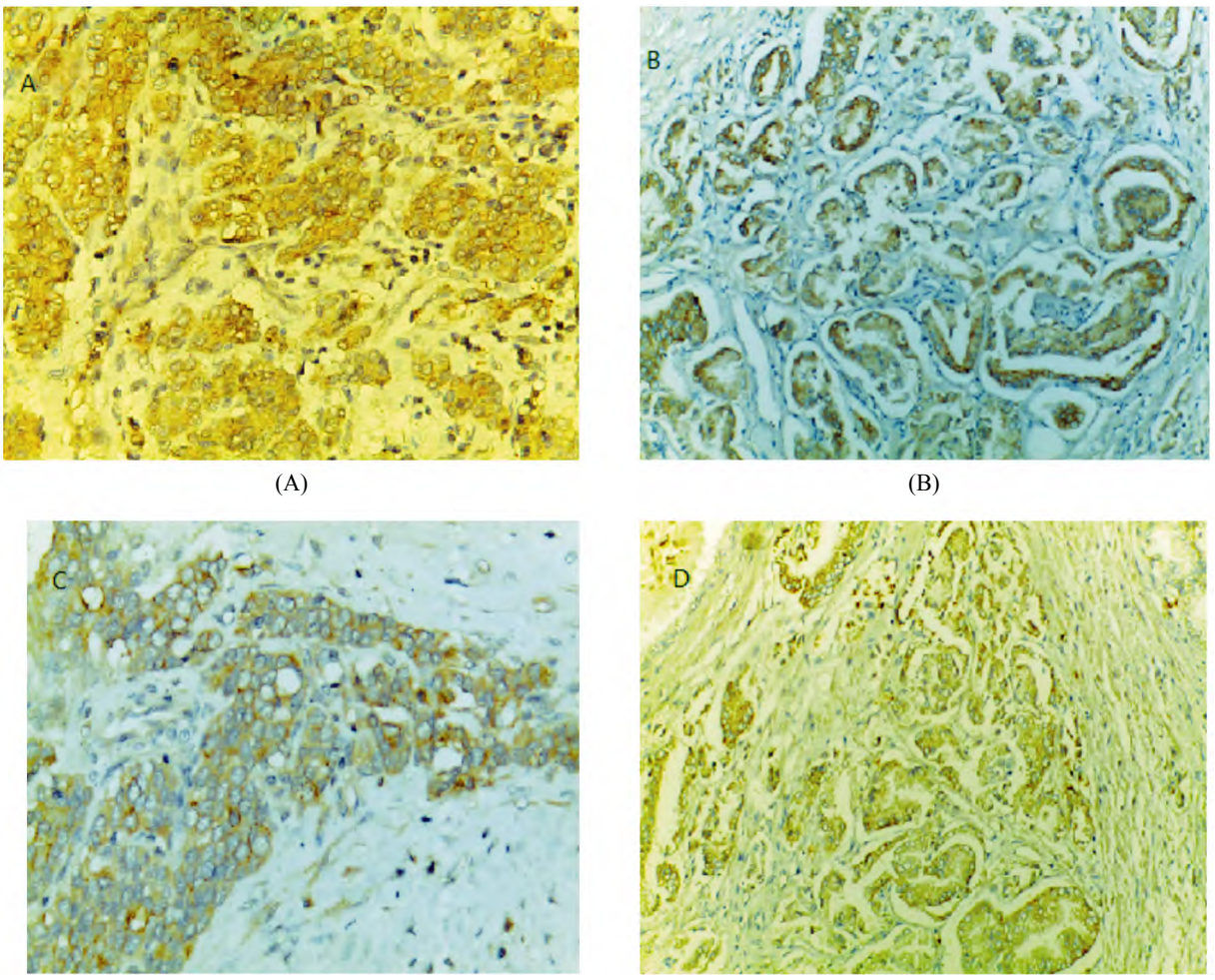

Fig. (1): GLUT1 and CD147 expression in high Gleason grade compred to low Gleason grade prostatic adenocarcinoma. (A) Strong diffuse cytoplasmic expression of GLUT 1 in high grade prostatic carcinoma (IHC, X200). (B) Low cytoplasmic GLUT1 expression in low grade prostatic carcinoma (IHC X200). (C) Higher membranous CD147 expression in high grade prostatic carcinoma (IHC X400). (D) Lower membranous CD147 expression in low grade prostatic carcinoma (IHC X200).

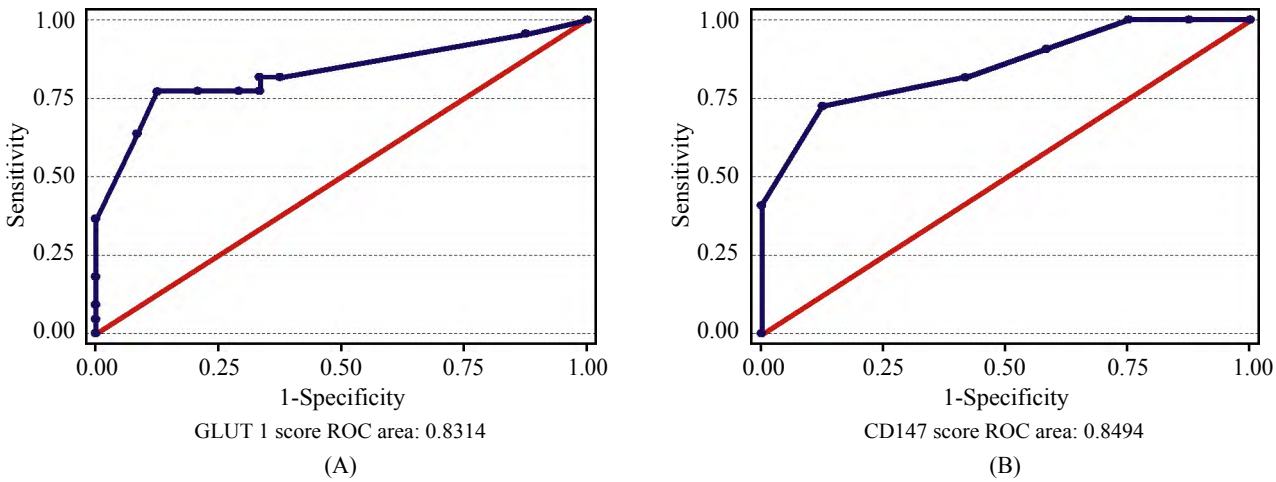

Fig. (2): Receiver operating characteristics curve for the validity of GLUT1 and CD147 to predict high Gleason score group from low Gleason score group (A) GLUT1 with AUC=0.8314. (B) CD147 with AUC=0.8494.

Discussion

It is well acknowledged that tumor cells require a high level of glucose to meet the energy needs of rapidly proliferating cells and to provide a carbon source for the building blocks that generate nucleotides, proteins and cell membrane lipids [13].

Glucose Transporter 1 (GLUT 1) facilitates cellular glucose uptake and is overexpressed in many tumors. Many studies have been conducted to investigate the prognostic value of GLUT 1 in tumors. However, contrasting results have been found in several tumors [14].

CD 147 (EMMPRIN) is a transmembrane glycosylated protein that belongs to the Immunoglobulin (Ig) superfamily. Many studies indicated that CD147 plays a central role in tumor progression [15].

This retrospective study aimed for assessment of the degree of GLUT1 and CD147 expression in 46 prostatic carcinoma with comparison to BPH and HGPIN as well as their correlation with different clinicopathological parameters in addition to detect the correlation between two markers.

Our study showed that GLUT1 positively expressed in (54.3%) of prostatic carcinoma cases. The GLUT1 positive expression rate in prostate cancer cells was significantly higher in BPH and HGPIN ($p<0.05$). This could highlight the role of GLUT1 in carcinogenesis of prostate cancer.

This pattern of GLUT-1 expression was similar to the results declared by previous studies as [16] and [17] who reported that GLUT 1 was highly expressed in prostate cancer cells than benign prostatic hyperplasia. Similarly, this finding was in accordance with [11] who analyzed GLUT1 expression in several tumor types and reported that the highest frequency of GLUT 1 expression was noticed in prostate (47%) and thyroid cancers (29%).

The study of [18] stated that Androgen Receptor (AR) signaling has an apparent role in GLUT1 expression in prostatic carcinoma as nuclear translocation of AR was upregulated at low glucose concentration correlating with increased level of GLUT 1.

However, inconsistent results have also been reported by other studies as [19] who found that GLUT1 was lowered in prostatic carcinoma rather than BPH. They studied the expression of Glut-1 and GLUT-12 proteins in only three specimens of cancer prostate. These analyses were deficient in recognizing the molecular pathways (transport systems) which involved in hexose uptake in benign human prostate cells and possibly regulating the expression of these transporters during prostate tumorigenesis.

This study revealed that GLUT1 positive expression showed a statistically significant correlation with high Gleason score ($p<0.01$), advanced tumor stage ($p<0.01$), lymph node metastasis ($p<0.01$), distant metastases ($p<0.05$) and TNM stage ($p<0.01$). However, no statistically significant correlation was detected between GLUT1 positive expression and patient age ($p=0.095$), pre-operative PSA level ($p=0.069$) and perineural invasion ($p=182$). Our results suggest that upregulation of GLUT 1 may be linked to increased invasive ability and progression of prostatic carcinoma.

This is parallel to results provided by [16] who reported that GLUT-1 expression increases with higher grades of prostatic carcinoma and [20] who reported that higher expression of GLUT1 significantly associated with tumor aggressiveness, short survival, and tumor recurrence.

A recent meta-analysis of [21] has been revised the prognostic significance of GLUT1 in twenty-seven different studies including 4079 cancer patients and demonstrated that abnormal expression of GLUT1 was significantly associated with poorly differentiated tumors, lymph node metastases and the shorter overall survival in different types of human cancer.

The mechanism that clarifies the role of GLUT1 in oncogenesis remains unclear. Li et al., [22] stated that GLUT1 overexpression increases significantly with expression of NF κB-p65.

GLUT1 overexpressed in cancer cells is believed to be linked to the abnormal activation of PI3KC1-AKT pathway secondary to mutagenic activation of PI3KC1, as described by [23]. In addition, many molecules and signaling mechanisms were believed to be involved in regulating the expression of GLUT1, as hypoxia induced Factor 1, Ras, C-Myc and p53 signaling pathway as reported by [14].

This current study showed that CD147 was expressed positively in (63.0%) of prostatic carcinoma cases. The positive expression rate of CD 147 in prostatic carcinoma tissues was significantly higher than BPH and HGPIN ($p<0.01$).

This pattern of CD147 expression was similar to the results declared by other previous studies

as [24,25] who reported that CD 147 was overexpressed in prostatic carcinoma than BPH.

Prostate cancer tissues showed a decline in DNA methylation in the CD 147 promoter in contrast to adjacent non-tumor prostate tissues, and the methylation intensity was inversely correlated with CD147 mRNA levels, elucidated by [26]. This could suggest a possible mechanism that causes the abnormal expression of CD147 on PC. Therefore, it is highly suggestive that the expression of CD147 may be considered a marker closely related to the pathogenesis of prostate cancer.

However, inconsistent results have also been declared by other studies as [27] who have reported that CD147 expression reduced in prostate cancer, benign prostatic hyperplasia than normal prostate tissue, and this was against the conclusion that we have achieved. Since CD147 was quantitatively assessed in their study, this difference in interpretation may lead to different results.

This present study revealed that positive CD 147 expression was statistically correlated with high Gleason score (p<0.05), advanced tumor stage (p <0.01), lymph nodes metastasis (p<0.01), distant metastasis (p<0.01), TNM stage (p<0.01) and perineural invasion (p<0.01). This is parallel to results provided by [25,28-30].

Similar results were reported in other cancers as [31] who reported that CD147 high expression was correlated with age, tumor size, location, depth of invasion, TNM stage, Lauren's classification, vascular invasion, lymph node and distant metastasis of tumor in gastric carcinoma and [32] who stated that the positive rate of CD147 expression was higher in renal cell carcinoma tissue than non-cancer tissues and was associated with lymph node metastases, TNM stage, and larger tumor size.

The current study showed no significant association between CD147 and pretreatment PSA and patient age in agreement with [27].

CD147 was reported to be involved in tumor invasion and metastasis through stimulation of MMP synthesis in adjacent fibroblasts and malignant cell growth by activation of ERK1/2 and p38 mitogen-activated protein kinases, in stimulating angiogenesis through vascular endothelial growth factor induction and in involvement in resistance of tumor cells to chemotherapy via the production of hyaluronan [28].

The current study found a high positive significant correlation between GLUT 1 and CD 147 (p<0.001). To our best knowledge, this the first study examining the correlation between GLUT 1 and CD147 in prostatic carcinoma.

Recently, a direct correlation between CD147 and GLUT-1 expression in melanoma was reported by [33] who also stated that CD 147 blockage could inhibit the growth of melanoma by lowering the expression of GLUT-1 via PI3K/Akt pathway.

A significant positive correlation between CD147 and GLUT-1 expression (p<0.001) in cervical squamous cell carcinoma and that combined expression of CD147 and GLUT-1 was obviously related to radioresistance, this conclusion was also declared by [34].

Hypoxia induces the expression of CD147 by transcriptional activation of both HIF-1 α and Sp1 in the promoter region of CD147 and so this significantly activate glycolysis in both tumor cell lines and tumor xenograft model through interaction with Monocarboxylate Transporter 1 (MCT-1) and MCT-4, this was demonstrated by [35]. They concluded that tumor cells can adapt to hypoxia by activating the interaction between CD 147 and MCTs to induce glycolysis that leads to tumor progression.

A study by [36] demonstrated that CD 147 significantly connected to the change in glucose metabolism in hepatocellular carcinoma and that increased CD147 induced glycolysis mediated through not only the upregulation of GLUT 1 in a p53-dependent manner but also through activation of liver type phosphofructokinase (PFKL) in HCC lines.

This work suggests that further studies are needed to declare the interaction between GLUT1 and CD 147 in prostatic carcinoma to clarify CD 147 enhanced glycolytic activity.

Conclusion:

GLUT 1 and CD 147 may have a role in carcinogenesis, progression, and aggressiveness of prostate cancer. A significant association between GLUT1 and CD147 may emphasize the cross talk between CD147 and glycolytic transporters. CD147 enhanced glycolytic activity of cancer cells may be a new effective therapeutic target. Further studies may be recommended to confirm these results.

References

1- FORMAN D. and FERLAY J.: The global and regional burden of cancer Organization WH: World Cancer Report. Chapter 1.1. ISBN 9283204298, 2014.

2- YE Y., LI S.L., WANG Y., et al.: The role of CD147 expression in prostate cancer: A systematic review and meta-analysis. Drug design, development and therapy. 10: 2435. http://doi.org/10.2147/DDDT.S111155, 2016.

3- FURUTA E., OKUDA H., KOBAYASHI A., et al.: Metabolic genes in cancer: Their roles in tumor progression and clinical implications. Biochimica et Biophysica Acta (BBA)-Reviews on Cancer, 1805 (2): 141-52, 2010.

4- LIBERTI M.V. and LOCASALE J.W.: The Warburg Effect: How Does it Benefit Cancer Cells? Trends in biochemical sciences, 41 (3): 211-8. Doi:10.1016/j.tibs.2015.12.001, 2016.

5- WANG J., YE C., CHEN C., et al.: Glucose transporter GLUT1 expression and clinical outcome in solid tumors: A systematic review and meta-analysis. Oncotarget, 8 (10): 16875-86. Doi:10.18632/oncotarget.15171, 2017.

6- De WIT M., JIMENEZ C.R., CARVALHO B., et al.: Cell surface proteomics identifies glucose transporter type 1 and prion protein as candidate biomarkers for colorectal adenoma-to-carcinoma progression. Gut., 61: 855-64. [PubMed], 2012.

7- GUNNINK L.K., ALABI O.D., KUIPER B.D., et al.: Curcumin directly inhibits the transport activity of GLUT1. Biochimie, 125: 179-85. Doi: 10. 1016/j.biochi.2016.03. 014, 2016.

8- YANG M., YUAN Y., ZHANG H., et al.: Prognostic significance of CD147 in patients with glioblastoma. J. Neurooncol., 115 (1): 19-26, 2013.

9- WEIDLE U.H., SCHEUER W., EGGLE D., KLOSTERMANN S. and STOCKINGER H.: Cancer-related issues of CD147. Cancer Genomics Proteomics, 7 (3): 157-69, [PubMed], 2010.

10- SEGAWA A., NAGAMORI S., KANAI Y., et al.: L-type amino acid transporter 1 expression is highly correlated with Gleason score in prostate cancer. Molecular and Clinical Oncology, 1 (2): 274-80. http://doi.org/10.3892/mco.2012.54, 2013.

11- CARVALHO K.C., CUNHA I.W., ROCHA R.M., et al.: GLUT1 expression in malignant tumors and its use as an immunodiagnostic marker. Clinics, 66 (6): 965-72, Doi: 10.1590/S1807-59322011000600008, 2011.

12- PÉRTEGA-GOMES N., VIZCAÍNO J.R., MIRANDA-GONÇALVES V., et al.: Monocarboxylate transporter 4 (MCT4) and CD147 overexpression is associated with poor prognosis in prostate cancer. B.M.C. Cancer, 11 (1): 312. Doi:10.1186/1471-2407-11-312, 2011.

13- YIN C., QIE S. and SANG N.: Carbon Source Metabolism and Its Regulation in Cancer Cells. Critical Reviews in Eukaryotic Gene Expression, 22 (1): 17-35, 2012.

14- SZABLEWSKI L.: Expression of glucose transporters in cancers. Biochim Biophys Acta (BBA)-Reviews on Cancer, 1835 (2): 164-9, 2013.

15- XIONG L., EDWARDS C.K. and ZHOU L.: The Biological Function and Clinical Utilization of CD 147 in Human Diseases: A Review of the Current Scientific Literature. International Journal of Molecular Sciences, 15 (10): 17411-17441. http://doi.org/10.3390/ijms151017411, 2014.

16- EFFERT P., BENIERS A.J., TAMIMI Y., et al.: Expression of glucose transporter 1 (GLUT-1) in cell lines and clinical specimens from human prostate adenocarcinoma. Anticancer Res., 24 (5A): 3057-63, 2004.

17- STEWART G.D., GRAY K., PENNINGTON C.J., et al.: Analysis of hypoxia-associated gene expression in prostate cancer: Lysyl oxidase and glucose transporter-1 expression correlate with Gleason score. Oncology Reports, 20 (6): 1561-7. https://doi.org/10.3892/or_00000180, 2008.

18- GONZALEZ-MENENDEZ P., HEVIA D., RODRIGUEZ-GARCIA A., et al.: Regulation of GLUT Transporters by Flavonoids in Androgen-Sensitive and-Insensitive Prostate Cancer Cells. Endocrinology, 155 (9): 3238-50. Doi: 10.12 10/en.2014-1260, 2014.

19- CHANDLER J.D., WILLIAMS E.D., SLAVIN J.L., et al.: Expression and localization of GLUT1 and GLUT12 in prostate carcinoma. Cancer, 97 (8): 2035-42, 10.1002/cncr.11293 [PubMed], 2003.

20- JANS J., VAN DIJK J.H., VAN SCHELVEN S., et al.: Expression and Localization of Hypoxia Proteins in Prostate Cancer: Prognostic Implications After Radical Prostatectomy. Urology, 75 (4): 786-92, 2010.

21- YU M., YONGZHI H., CHEN S., et al.: The prognostic value of GLUT1 in cancers: A systematic review and meta-analysis. Oncotarget, 8 (26): 43356-67. Doi: 10. 18632/oncotarget. 17445, 2014.

22- LI S., YANG X. and WANG P.: The Effects of GLUT1 on the Survival of Head and Neck Squamous Cell Carcinoma. Cell Physiol. Biochem., 32 (2): 624-34, 2013.

23- PHADNGAM S., CASTIGLIONI A., FERRARESI A., et al.: PTEN dephosphorylates AKT to prevent the expression of GLUT1 on plasmamembrane and to limit glucose consumption in cancer cells. Oncotarget, 7 (51): 84999-5020. http://doi.org/10.18632/oncotarget.13113, 2016.

24- HUANG J., ZHUANG X. and ZHEN Y.: Expression and clinical significance of extracellular matrix metalloproteinase inducer in human prostatic carcinoma tissues [J]. Guangxi Medical Journal, 37 (5): 640-2, 2015.

25- WANG Q., ZHANG J.G. and WANG W.: Expression and significance of S100P, CD147, and OCT4 in different prostate cancer tissue TNM stages. Genet. Mol. Res., 14 (2): 6844-51, 2015.

26- LIANG Y.X., MO R.J., HE H.C., et al.: Aberrant hypomethylation-mediated CD147 overexpression promotes aggressive tumor progression in human prostate cancer. Oncology Reports, 33 (5): 2648-54. https://doi.org/10.3892/or.2015.3870, 2015.

27- BAUMAN T.M., EWALD J.A., HUANG W., et al.: CD147 expression predicts biochemical recurrence after prostatectomy independent of histologic and pathologic features. B.M.C. Cancer, 15: 549. Doi: 10.1186/s12885-015-1559-4 [PMC free article] [PubMed], 2015.

28- ZHONG W.D., LIANG Y.X., LIN S.X., et al.: Expression of CD 147 is associated with prostate cancer progression. Int. J. Cancer, 130 (2): 300-8. Doi: 10.1002/ijc.25982, 2012.

29- CAI C., WU C., YANG Y., et al.: Expression and Clinical Significance of CD 147 Protein in Human Prostate Cancer [J]. Journal of Clinical Research, 32 (11): 2088-90, 2015.

30- WU B., WEI J., HU Z., et al.: Slug silencing inhibited perineural invasion through regulation of EMMPRIN expression in human salivary adenoid cystic carcinoma. Tumor Biology, 37 (2): 2161, 2016.

31- SHOU Z.X., JIN X. and ZHAO Z.S.: Upregulated Expression of ADAM17 Is a Prognostic Marker for Patients With Gastric Cancer. Ann. Surg., 256: 1014-22, 2012.

32- LI H., WU D., SHI S., et al.: Expression and clinical significance of CD147 in renal cell carcinoma: A meta-analysis. Oncotarget, 2017.

33- SU J., GAO T., JIANG M., et al.: CD 147 silencing inhibits tumor growth by suppressing glucose transport in melanoma. Oncotarget, 7 (40): 64778-84. http://doi.org/10.18632/oncotarget.11415, 2016.

34- HUANG X.Q., CHEN X., XIE X.X., et al.: Co-expression of CD147 and GLUT-1 indicates radiation resistance and poor prognosis in cervical squamous cell carcinoma. International Journal of Clinical and Experimental Pathology, 7 (4): 1651-66, 2014.

35- KE X., FEI F., CHEN Y., et al.: Hypoxia upregulates CD147 through a combined effect of HIF-1 α and Sp1 to promote glycolysis and tumor progression in epithelial solid tumors. Carcinogenesis, 33 (8): 1598-607. Doi: 10.1093/carcin/bgs196, 2012.

36- HUANG Q., LI J., XING J., et al.: CD147 promotes reprogramming of glucose metabolism and cell proliferation in HCC cells by inhibiting the p53-dependent signaling pathway. J. Hepatol., 61: 859-66. [PubMed], 2014.

تحديد دور دلالات الآورام (GLUT 1) و (سى دى 147) فى تكوين وتطور سرطان البروستاتا: دراسة كميائية مناعية

تعد زيادة معدل تحلل السكر واحدة من أهم السمات المميزة للآورام الخبيثة يلعب ناقل الجلوكوز (GLUT 1) دورا محوريا فى نقل وتحلل الجلوكوز داخل الخلايا السرطانية. كما تعتبر الدلالة (سى دى ١٤٧) من البروتينات السكرية متعددة الوظائف والتى يزيد معدلات ظهورها فى العديد من الآورام السرطانية.

طريقة الدراسة: قد قام هذا البحث على دراسة ٤٦ حالة مصابة بسرطان البروستاتا وذلك لدراسة مستوى كل من (GLUT 1) و (سى دى ١٤٧) بواسطة إستخدام الكيمياء المناعية وتحديد علاقتهم وإرتباطهم بالعوامل الإكلينيكية–الباثولوجية المختلفة فى سرطان البروستاتا.

نتائج الدراسة: فى خلال هذه الدراسة قد تبين وجود دلالات الآورام (GLUT 1) فى ٢٥ حالة و (سى دى ١٤٧) فى ٢٩ حالة من إجمالى حالات الدراسة البالغ عددهم ٤٦ حالة كما تبين وجود علاقة إحصائية طردية بينهما وبين كل من إرتفاع درجة التميز (جليسيون) وتقدم مراحل السرطان وإنتشار السرطان فى الغدد الليمفاوية وتكوين الثاناويات البعيدة وأخيرا غزو الخلايا السرطانية للأعصاب المحيطة.

ومن ثم يمكن إستنتاج أن دلالات الآورام (GLUT 1) و (سى دى ١٤٧) قد يكون لهما دورا رئيسيا فى تكوين سرطان البروستاتا وأيضا دورا فى تطور وتقدم هذا الورم السرطانى ويمكن أن يتم إعتبارهما من أحد العوامل المهمة فى التنبؤ بالمدة المتوقعة لحياة المرضى.