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# Evaluation of Syndecan-1 Expression in Iraqi Patients with Papillary Thyroid Carcinoma

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**Abstract**

Papillary thyroid carcinoma (PTC) represents the most prevalent kind of thyroid gland cancer, making up around 80% of all occurrences of thyroid cancer. Evidence shows that Syndecan-1 (SDC-1) expression is lost in a number of benign and malignant epithelial neoplasms, although its expression profile in thyroid gland neoplasms is yet unknown. Therefore, the aim of this study was to assess SDC-1 expression in papillary thyroid carcinoma patients, as well as the relationship between age and gender and SDC-1 expression. To undertake a detailed investigation of SDC-1 in normal and malignant tissues, tissue sections were used to examine SDC-1 expression in 70 tissue samples, 50 distinct PTC (6 males and 44 females) and 20 normal tissue types (10 from each gender) as control. Ages in each group ranged from 20 to 60 years. The results showed a statistically different level of SDC-1 expression in patients and control. There was no significant relationship between SDC-1 expression and gender or age, in accordance with recent research findings which suggest that SDC- 1 might be exploited as a prognostic indicator or a target in cancer treatment in the future.

**Keywords**:Syndecan-1,CD138,Papillary thyroid carcinoma, Immunohistochemistry, Iraqi patients

# تقييم تعبير Syndecan-1 في المرضى العراقيين المصابين بسرطان الغدة الدرقية الحليمي

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**الخلاصة**

يعد سرطان الغدة الدرقية الحليمي اكثر انواع سرطان الغدة الدرقية انتشارا، و يشكل حوالي 80% من جميع حالات سرطان الغدة الدرقية. تشير الدلائل الى ان تعبير Syndecan 1 قد فقد في عدد من الاورام الظهارية الحميدة والخبيثة، على الرغم من ان ملف تعريف تعبيره في اورام الغدة الدرقية غير معروف حتى الان. لذلك، كان الهدف من هذه الدراسة هو تقييم تعبير Syndecan 1 في مرضى سرطان الغدة الدرقية الحليمي وكذلك العلاقة بين العمر والجنس وتعبير SDC-1. لإجراء بحث مفصل لـ Syndecan 1 في النسج الطبيعية والخبيثة، استخدمنا مقاطع نسجية لفحص تعبير Syndecan 1 في 70 عينة من النسج ، 50 عينة لمرضى سرطان الغدة الدرقية الحليمي (6 ذكور و 44 أنثى) و 20 عينة من النسج الطبيعية (10 من كل جنس). تراوحت الاعمار في كل مجموعة من 20 إلى 60 عاماً. أظهرت النتائج مستوى مختلف

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احصائياً لتعبير Syndecan 1 في المرضى ومجموعة التحكم (الاصحاء)، لم تكن هناك علاقة ذات دلالة إحصائية بين تعبير الSyndecan 1 والجنس أو العمر، بما يتفق مع الأبحاث الحديثة التي تشير إلى أنه قد يمكن استخدام Syndecan 1 كمؤشر تنبؤي أو هدف في علاج السرطان في المستقبل.

## Introduction

Papillary thyroid carcinoma (PTC) is the most common kind of malignant thyroid tumor in countries with adequate iodine diets [1]. Despite the prevalence of lymph node metastases, it is categorized as low-grade neoplasia and is included in the group of well-differentiated thyroid carcinomas [2]. Nuclear characteristics such nuclear overlaps, optically transparent nuclei, nuclear grooves, and pseudo inclusions are present in this type of carcinoma. Papillary architecture and the presence of psammoma bodies are additional PTC diagnostic indicators [3]. However, the localized morphologic overlap of these characteristics in other thyroid tumors creates a diagnostic problem, making the differentiation from PTC challenging. In these situations, immunohistochemistry tests provide support for the diagnosis of these challenging patients.

Syndecan-1 (SDC-1or CD138) is a heparin sulfate proteoglycan found on the surface of all adherent cells, as well as many nonadherent cells [4, 5] that plays a role in cell-cell adhesion processes and the cell-extracellular matrix [6]. Syndecan-1 is an external cell surface protein with three structural domains that interact to heparin and chondroitin sulfates [7]. As a cell surface receptor, Syndecan-1 demonstrates a substantial participation in both pathological and healthy processes. It has been discovered that it is expressed on plasma cells and a number of epithelial cell types in normal tissues and that it impacts cell proliferation, migration, and cytoskeleton structure [8]. Hepatocytes, goblet and columnar cells of the digestive tract, as well as the normal squamous epithelium of several organs, expressed SDC-1 particularly strongly. A tumor ranking order based on the frequency and intensity of SDC-1 expression was produced following the extremely methodical examination of the majority of human cancer types. Squamous cell carcinomas and adenocarcinomas have the greatest levels of SDC-1 immunostaining, whereas germ cell tumors, sarcomas, endocrine tumors, including thyroid cancer, and neuroendocrine tumors have the lowest levels or none [7]. Altered SDC-1 expression has been reported in several malignant tumors. For instance, overexpression of SDC-1 has been observed in several cancers including those of the breast, bladder, gallbladder, pancreas, ovary, endometrium, and prostate [8]. In contrast to the nearby normal epithelium, SDC-1 or CD138 expression was shown to have decreased in different cancer types, including lung, head/neck, gastric, renal, and colorectal cancer [8]. Reduced or enhanced SDC-1 expression in numerous of these tumor types has been associated with a poor patient prognosis and an undesirable tumor phenotype [9–13].

Bologna-Molina *et al.* [14] revealed that SDC-1 is expressed in both neoplastic epithelial cells and the stroma, and that the stromal expression of SDC-1 is greater and more intense in PTC with extracapsular extension than in PTC without extracellular extension. There is no information on the association between SDC-1 expression and the age and gender of patients with papillary thyroid cancer.

The aim of this study was to evaluate SDC-1 expression in Iraqi patients with papillary thyroid cancer, as well as investigate the association between gender, age and SDC-1 expression.

## Materials and Methods

The research was carried out during the period between 2022 and 2023 at the Biology Department of the College of Science at Baghdad University and the Pathology Department of the College of Medicine at Al-Nahrain University. The thyroid gland tissue samples used

in this study were paraffin blocks and were collected from the labs of Al-Kindi Teaching Hospital, Baghdad Teaching Hospital, Teaching Laboratories of Medical City, Forensic Medicine of Medical City, and Al-Shariqa private laboratory for the years 2019-2022. A total of 70 paraffin blocks containing thyroid gland tissues were used in this research, including 20 thyroid gland tissues that were used as positive controls (10 males and 10 females), and 50 papillary thyroid carcinomas to identify the Syndecan-1 using immunohistochemistry staining (6 males and 44 females). Each group age ranged from 20 to 60 years. Positive control and thyroid tissues samples were sectioned as 5 μm thickness and stained with Harris hematoxylin and alcoholic eosin stain [15] for histopathology detections and immunohistochemistry stain (Syndecan-1) by using abcam data sheet to identify the malignancy respectively.

**Statistical Analysis**

Numeric data was shown as the mean and standard deviation (SD), whereas categorical variables were presented as numbers and percentages. The Chi-square test was used to analyze the relationship between categorical variables, and any necessary corrections were made. The Iindependent samples-t test or the Mann Whitney U Test was used to compare the mean values between the two groups [16].

**Result and Discussion**

**Thyroid Morphology**

The general histological structure of the thyroid gland in healthy group stained with hematoxylin and eosin showed normal structure of thyroid tissues that involved normal follicular epithelial cells which were lined by simple cuboidal epithelium tissues with small round regular nuclei, normal thyroid follicle filled with colloid substance (Figureure 1A). In patients with papillary thyroid carcinoma, the cross-section examination revealed large and crowded nuclei of malignant cells, clearing chromatin with irregular nuclear membranes, appearance of nuclear groves and papillary fronds with fibrovascular cores (Figureure1 B, C). According to Xu's research, PTC is the most prevalent form of thyroid cancer and is distinguished by a set of typical nuclear features such as nuclear morphology changes include nuclear expansion, elongation and overlap, chromatin clearing, margination and glassy nuclei, as well as irregular nuclear membrane, nuclear groove and nuclear pseudo inclusion [17]. These results agree with the findings of present study.

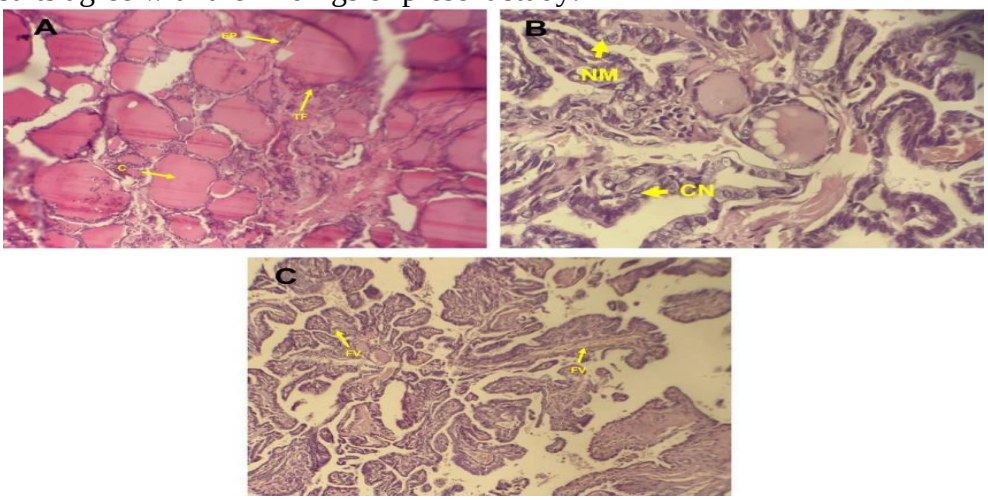


**Figure1:** Showing cross section of thyroid gland tissue in (A) healthy control group revealed normal structure of follicular epithelial cells with small round regular nuclei (EP), and normal thyroid follicle (TF), filled with colloid (C); (B) and (C) in patients with papillary thyroid carcinoma revealed large and crowded nuclei (CN) of malignant cells with irregular nuclear membranes (NM) and clearing chromatin, as well as appearance of nuclear groves; papillary fronds with fibrovascular cores (FV). Stained H&E. 40X

**Scores of SDC-1**

When compared to healthy controls, Syndecan-1 expression in papillary thyroid cancer patients exhibited significant values, but at varied intensities (Table 1; Figure. 2). A total of five cases (10% of the patients) with high expression (Figure. 2D), 27 cases (54% of the patients) with moderate expression (Figure. 2C), and 18 cases (36% of the patients) with weak expression (Figure. 2B) were examined. Twenty healthy controls, representing 100% of the samples, showed the negative expression (Figure. 2A). The differentiation of tumor cells and prognosis may be correlated with Syndecan-1 expression in patients with papillary thyroid carcinoma.

According to several research, Syndecan-1 expression in cancer is closely related to tumor cell differentiation and prognosis [7, 18]. Kind *et al.*'s [7] findings that CD138 expression is frequently low or nonexistent in germ cell cancers, sarcomas, endocrine malignancies (including thyroid cancer), and neuroendocrine tumors provide support for the data presented here. Heparan sulfate transmembrane proteoglycans called Syndecans are important for cell adhesion, proliferation and signaling. Their precise function in the development and control of tumors has been the subject of several studies [19].

Depending on the environment, Syndecan-1 is expressed on the cell surface of tumor tissue in different ways. In contrast to normal epithelial cells, prostate cancer cells that have undergone the malignant transformation, have been found to have lower Syndecan-1 expression, and decreased cell-membrane. Syndecan-1 immunoreactivity has been found in many epithelial malignancies linked to various stages of tumor progression [20]. Syndecan-1 expression in PTC neoplastic epithelial cells is associated with extracapsular invasion and tumor development as claimed by Bologna-Molina *et al.*[14].

Several biological processes, including growth and differentiation, cell adhesion [21], cell migration, cytoskeletal architecture [22], infiltration, and angiogenesis [23, 24] are influenced by Syndecans-1 expression.

**Table 1:** Comparison of studied scores between patients and healthy control.

| Score | | Patients N=50 | Control N=20 | *p*-value |
|---|---|---|---|---|
| Syndecan-1 | Intense; N (%) | 5 (10.0) | 0 (0.0) | **<0.001*** |
| | Moderate; N (%) | 27 (54.0) | 0 (0.0) | |
| | Weak; N (%) | 18 (36.0) | 0 (0.0) | |
| | Negative; N (%) | 0 (0.0) | 20 (100) | |

***** *p* value by Yates chi square test

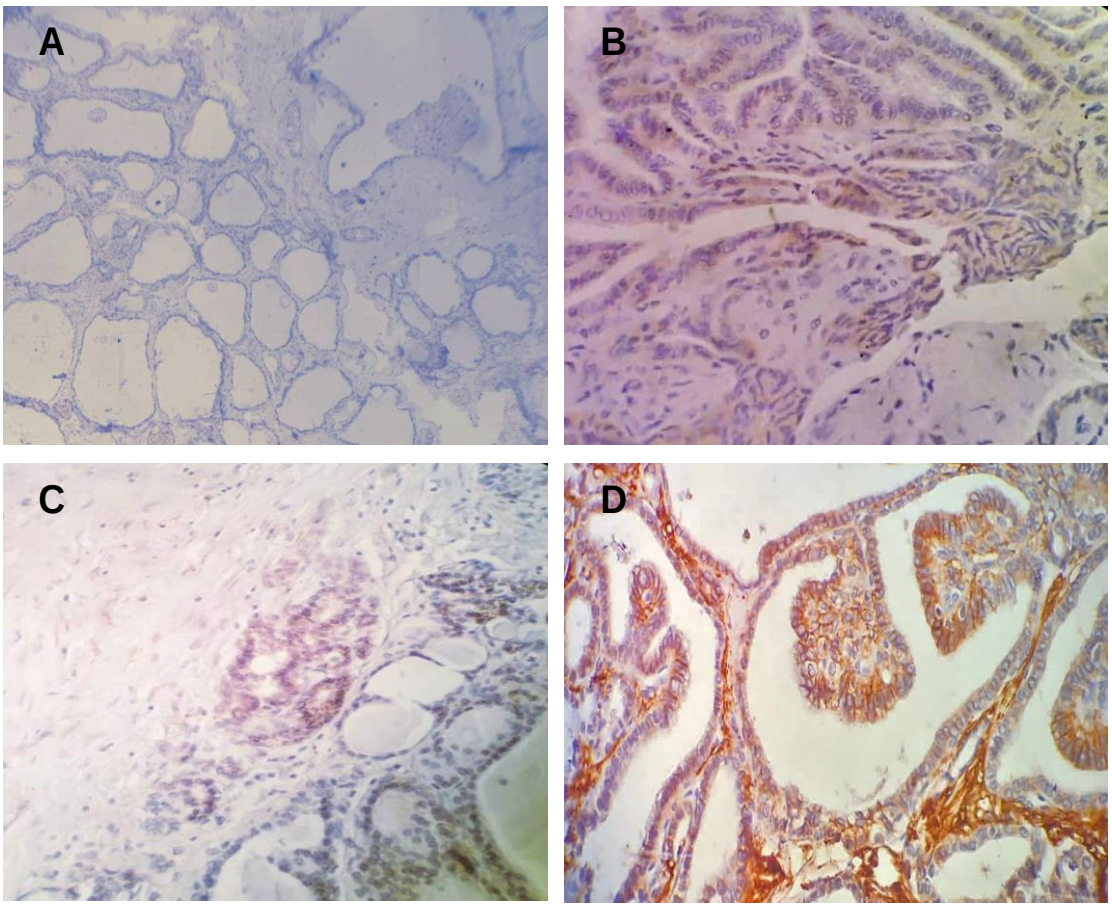


**Figure 2**: Showing cross section images of Syndecans-1 immuno-staining in normal and tumors thyroid tissue. (A) showed negative expression of Syndecan-1 in healthy control. 10X
(B) Shows weak expression of Syndecan-1 in PTC. 40X
(C) Shows moderate expression of Syndecan-1 in PTC.10X
(D) Shows intense expression of Syndecan-1 in PTC. 40X

**Syndecan-1 Expression According to Age**

The age of PTC patients and the degree of Syndecans-1 expression are not significantly correlated (Table 2). Patients 25 years of age had moderate intensity in 5 cases. Patients aged between 26-35 showed moderate intensity in 13 cases and weak intensity in seven cases. The expression expanded to all levels of intensity between 36 and 45 years which showed in four cases for each moderate and very strong intensity and nine were weak. The expression was detected in all intensities in those over 45 years old, with 1 being intense, 5 being moderate, and 2 being low (Table 2). Even though SDC-1 expression intensity was positive at all ages, there was no link between these two parameters. Miše and Vučić [25] demonstrated that SDC-1 was negatively correlated with a patient's age, estrogen receptors (ERs) and PRs in the primary tumors. This result is in line with the results of the present study.

**Table 2:** Comparison of studied scores according to age groups in patients' group.

| Score | | Age (yr) | | | | *p*-value |
|---|---|---|---|---|---|---|
| | | ≤25 N=5 | 26-35 N=20 | 36-45 N=17 | >45 N=8 | |
| Syndecan-1 | Intense; N (%) | 0 (0.0) | 0 (0.0) | 4 (23.5) | 1 (12.5) | 0.177* |
| | Moderate; N (%) | 5 (100) | 13 (65.0) | 4 (23.5) | 5 (62.5) | |
| | Weak; N (%) | 0 (0.0) | 7 (35.0) | 9 (52.9) | 2 (25.0) | |

* *p*-value by Yates chi square

### Syndecan-1 Expression According to Sex

Although the fact that there was no statistically significant difference between male and female patients, the degree of Syndecan-1 expression differed (Table 3). Females displayed varying degrees of intensity. Female PTC patients expressed themselves strongly in 5 cases, moderately in 26 cases, and weakly in 13 cases. Males, on the other hand, showed just one case of moderate intensity expression and five cases of weak intensity expression (Table 3). The current results agree with the results of a study by Solbu *et al.* [26] that SDC-1 was not associated with gender.

**Table 3:** Comparison of studied scores according to sex in patients' group.

| Score | | Male N=6 | Female N=44 | *P*-value |
|---|---|---|---|---|
| Syndecan-1 | Intense; N (%) | 0 (0.0) | 5 (11.4.0) | 0.138* |
| | Moderate; N (%) | 1 (16.7) | 26 (59.1) | |
| | Weak; N (%) | 5 (83.3) | 13 (29.5) | |

***** p value by Yates chi square

## Conclusions

Syndecan-1 was linked to incident PTC, and this link was more pronounced in women than in men and in various age groups, suggesting a link between endothelial glycocalyx shedding and PTC disease in women. Further research is required on the use of Syndecan-1 as a risk marker in clinical settings.

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