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KIF20A immunohistochemical expression in urothelial carcinoma of urinary bladder in Egyptian patients

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Abstract:

Introduction: Urothelial bladder cancer, a prevalent malignancy worldwide, poses significant challenges in diagnosis and prognosis due to its complex and multifactorial etiology.

Aim of the study: This article comprehensively studies the production of Kinesin family member 20A (KIF20A), a well-established oncogene implicated in various human cancers, within the context of urothelial bladder carcinoma. Furthermore, we sought to study potential correlations of KIF20A production to a range of clinicopathological parameters to evaluate its utility as a diagnostic or prognostic biomarker.

Subjects and Methods: Immunohistochemical analysis of KIF20A was conducted on a cohort of 60 archived paraffin-embedded bladder cancer tissue samples.

Results: Our findings revealed high KIF20A expression in 60% (36/60) of the cases, exhibiting both cytoplasmic and membranous staining patterns. KIF20A expression showed significant correlations with several clinicopathological factors. A strong association was observed with tumor grade (p=0.001) and pathological T stage (p=0.001). Vascular embolism also correlated significantly with KIF20A expression (p=0.000), as did perineural invasion (p=0.025). Furthermore, KIF20A expression levels were significantly associated with tumor location within the bladder (p=0.027).

Conclusion: These results introduces KIF20A as a valuable biomarker for bladder cancer, potentially aiding in risk stratification and treatment decision-making.

Keywords: KIF20A; Immunohistochemistry; Bladder carcinoma.

1. Introduction

Within Western societies, bladder cancer persists as a major health challenge, holding its position as the fifth most frequently diagnosed cancer. Patients diagnosed with advanced-stage bladder cancer face a particularly dismal

prognosis, with high mortality rates. Despite significant research efforts, advancements in treatment strategies and improvements in overall survival have remained limited over the past three decades. [1] Kinesin 20A (KIF20A), classified within the kinesin-6 superfamily, has a pivotal influence in fundamental cellular processes, including intracellular transport of organelles and the intricate machinery of cell division. [2,3] Numerous studies have documented KIF20A overexpression across a spectrum of human cancers, implicating it as a key driver of oncogenesis. [4] Conversely, research suggests that experimental downregulation of KIF20A effectively disrupt and inhibit cellular division, further solidifying its role in cancer progression. [5] Given its involvement in mitotic processes, KIF20A has a critical function in regulating cell cycle progression. [6] Consequently, aberrant KIF20A expression can disrupt normal cell division, potentially leading to chromosomal aneuploidy and genomic instability, hallmarks of cancer development and progression. [7] The possibility of suppressing KIF20A protein expression through the action of specific microRNAs (miRNAs) presents an exciting avenue for the development of novel and precise cancer therapies. [8] This present study specifically investigates KIF20A expression within urothelial carcinoma and analyzes its correlation with relevant clinicopathological variables, aiming to assess its diagnostic and prognostic implications.

2. Subjects and Methods

This retrospective investigation examined sixty archival formalin-fixed, paraffin-embedded (FFPE) tissue specimens. The specimens are obtained from patients had undergone radical cystectomy for the treatment of transitional cell carcinoma (TCC). These samples were sourced from the Pathology Department archives at Cairo University. Ethical considerations were paramount, with all participating patients providing written informed consent before inclusion in the study. For each patient, a detailed clinicopathological profile was compiled, incorporating information on age, gender, tumor dimensions, histological grade, the specific location of the tumor within the bladder, and the status of lymph nodes.

2.*1 Histopathological and Immunohistochemical Examination*:

Three one-micrometer-thick sections were meticulously prepared from tissue specimens. Sections were subjected to staining for histological assessment. hematoxylin and eosin (H&E) was used. This staining technique allowed for a detailed assessment of the tissue architecture, including the arrangement of cells and their morphological characteristics. The remaining two sections were mounted on positively charged glass slides to ensure optimal adherence and prevent tissue loss during subsequent processing. These sections underwent deparaffinization and rehydration procedures to remove the paraffin wax and restore tissue hydration, preparing them for immunohistochemical staining. Antigen retrieval, a crucial step in immunohistochemistry, was then

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performed. This process unmasks epitopes, making them more accessible to the antibody, thereby enhancing antibody binding and improving the sensitivity of the staining. Then the sections were exposed to antibody specifically targeting human KIF20A. This incubation allowed the antibody to bind to the KIF20A protein present within the tissue. To ensure standardized and reproducible staining results across all samples, an automated immunohistochemical staining platform was utilized. Skin epidermis served as the positive control tissue, confirming the efficacy of the KIF20A antibody staining and providing a reference point for KIF20A expression.

2.2 Immunohistochemical Assessment

Immunohistochemical staining revealed KIF20A localization within cells. Positive tumor cell percentages were categorized as: 0 (no staining), 1 (1-25%), 2 (25-50%), 3 (50-75%), and 4 (75-100%). Staining intensity was scored as: 0 (negative), 1 (weak), 2 (moderate), and 3 (intense). A composite score (percentage x intensity, range 0-12) was calculated. Scores of 6 or higher defined high KIF20A expression, in line with established standards [9].

2.3 Statistical Analysis

All data were rigorously reviewed, coded, and entered into IBM SPSS Statistics (version 20) for analysis. Descriptive statistics were calculated to summarize data distribution and central tendencies. Inferential statistical tests were applied for comparison between variables. These test included Chi-square, Fisher's exact test, or independent samples t-tests. A significance level was detected at p value less than 0.05

3. Results

In this study of 60 urothelial carcinoma patients KIF20A, KIF20A expression did not show a noticeable link to patient demographics like age or sex. Similarly, no apparent connection was observed between KIF20A expression levels and tumor size or overall appearance.

However, KIF20A expression showed a clear relationship with tumor location within the bladder (p=0.027), as depicted in Figure 1. Furthermore, stronger relationships were identified between KIF20A expression and several key histopathological features.KIF20A show strong relationship with tumor histological grade (p=0.001 Figure 2), high grade tumors (Figure 5) KIF20A expression displayed a strong positive trend with them (Figure 9 & 10) versus low or negative with low grade tumors (Figure 11&12) and the presence of lymphovascular embolism (Figure 6) KIF20A show positive relationship with it (p=0.000, Figure 3, Table 3). A pronounced positive trend was also evident between KIF20A expression and pathological T stage (p=0.001, Table 1), suggesting a possible role in tumor advancement. Perineural invasion (Figure 7) also exhibited a clear relationship with KIF20A expression (p=0.025, Figure 4, Table 2), hinting at a potential involvement in local tumor invasion. In contrast, no discernible link was found between KIF20A expression and lymph node metastasis (p=0.180), implying it may not be a dependable marker for lymphatic spread. Similarly, bilharzial infestation (Figure 8) KIF20A expression showed no relationship with it (p=0.825),

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suggesting its role in bladder cancer may be unrelated to this parasitic infection.

T	High KIF20A expression		Low KIF20A expression		Total	P-value
	Number	Percent	Number	Percent		
T2	1	11.1%	8	88.9%	9	**0.001**
T3	28	63.6%	16	36.4%	44	
T4	7	100%	0	0%	7	

Table 1: Relation between KIF20A and tumor T status

Perineural invasion	High KIF20A expression		Low KIF20A expression		Total	P-value
	Number	Percent	Number	Percent		
No	24	52.2%	22	47.8%	46	**0.025**
Yes	12	85.7%	2	14.3%	14	

Table 2: Relation between KIF20A and tumor perineural invasion

Vascular embolism	High KIF20A expression		Low KIF20A expression		Total	P-value
	Number	Percent	Number	Percent		
No	16	42.1%	22	57.9%	38	**0.000**
Yes	20	91%	2	9%	22	

Table 3: Relation between KIF20A and tumor vascular embolism

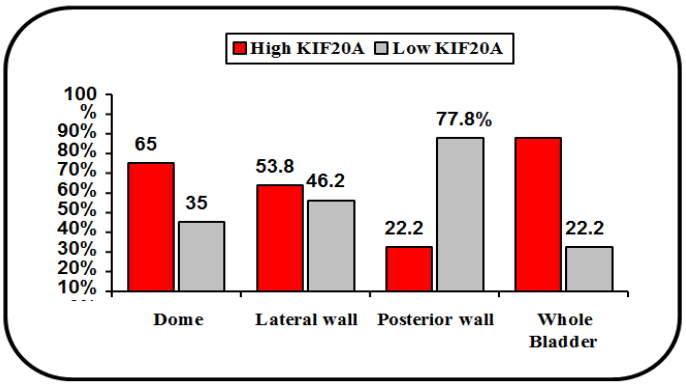

Figure1: Relation between KIF20A expression & tumor site

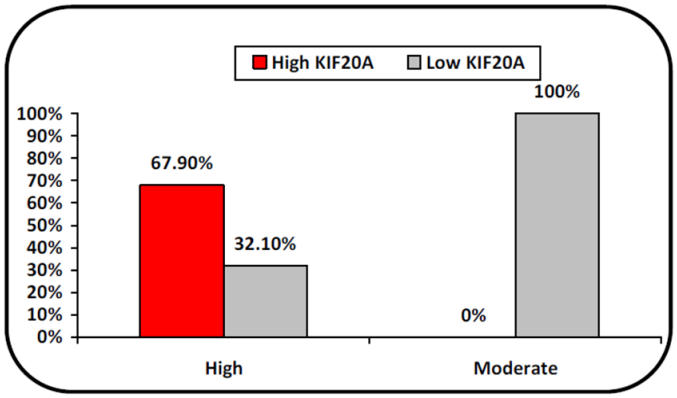

Figure 2: Relation between KIF20A expression & tumor grade

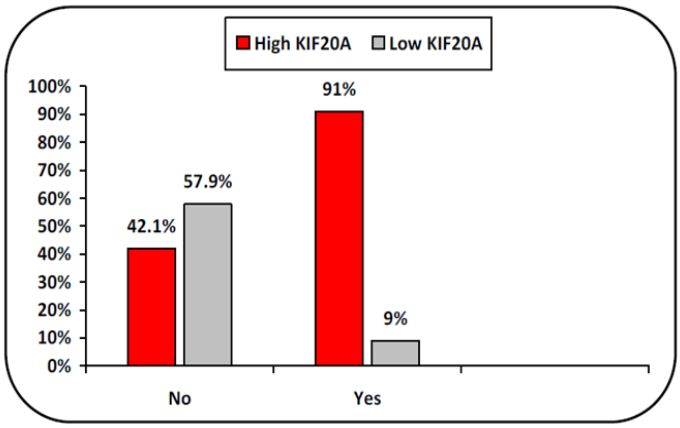

Figure3: Relation between KIF20A and tumor vascular invasion

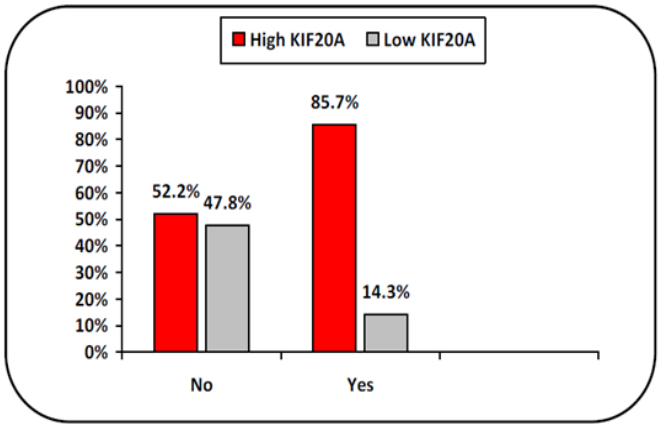

Figure 4: Relation between KIF20A and tumor perineural invasion

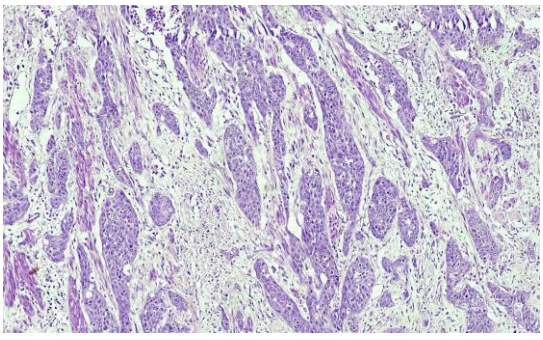

Figure 5: High-grade invasive Urothelial Carcinoma (UC) (H&E, 100x)

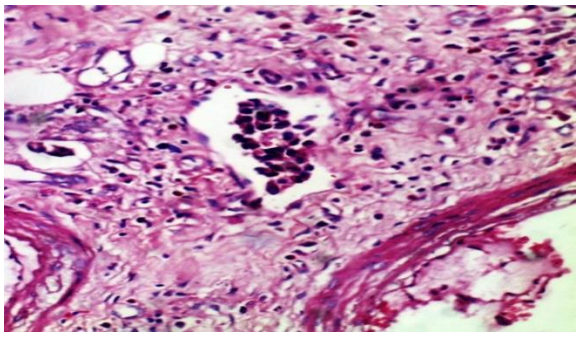

Figure 6: High grade invasive UC showed lymphovascular emboli (H&E ×400)

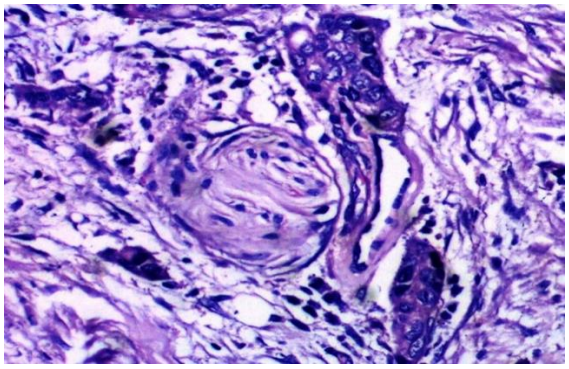

Figure 7: High grade invasive UC showed perineural invasion (H&E ×400)

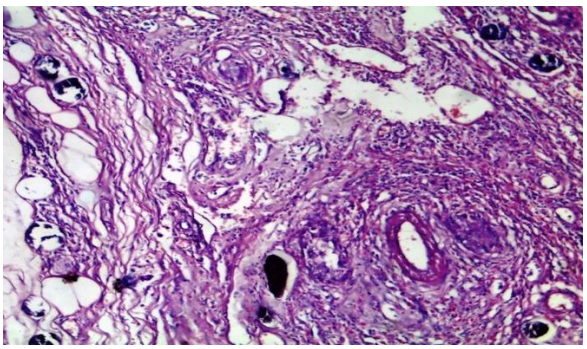

Figure 8: High grade invasive UC showed bilharzia ova (H&E ×200)

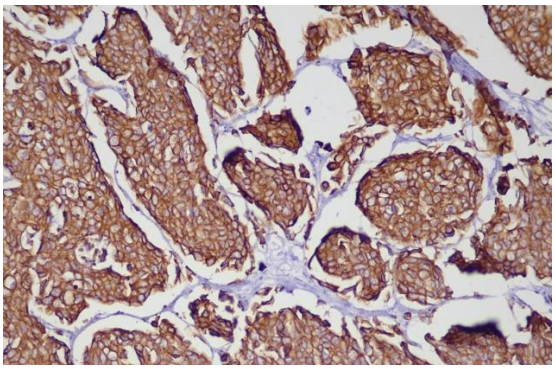

Figure 9: Elevated expression of KIF20A in high grade UC ×100

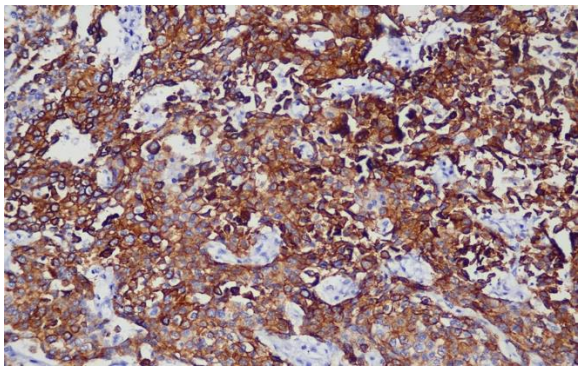

Figure 10: Elevated expression of KIF20A in high grade UC ×100

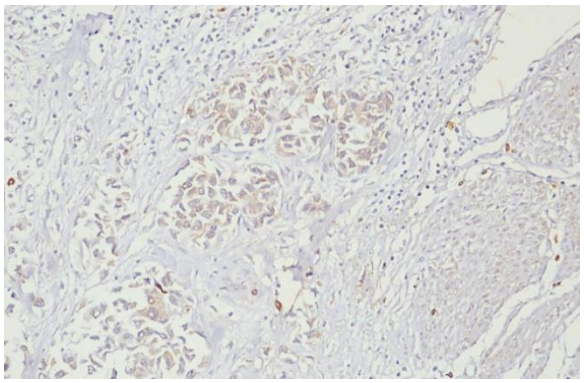

Figure11: Low expression of KIF20A in low grade UC ×100

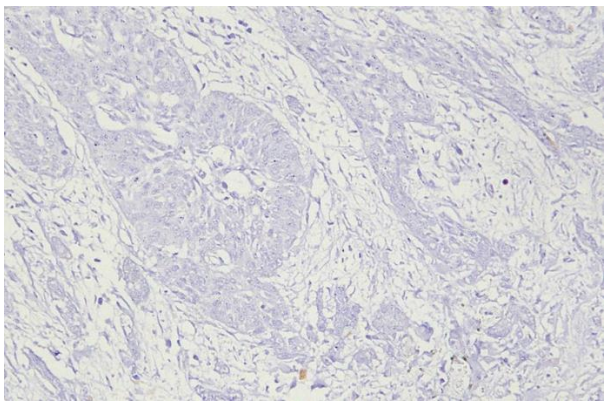

Figure12: Negative expression of KIF20A in low grade UC ×100

4. Discussion

Urothelial carcinoma is a prevalent malignancy within the urogenital system. [9] The kinesin family, encompassing KIF20A, is integral to vital cellular processes, particularly mitosis and intracellular trafficking. [10] Emerging evidence suggests that KIF20A could be exploited in immunotherapy. [11] Increasingly, KIF20A expression has been linked to aggressive phenotypes in multiple malignancies, implicating it as a crucial driver of tumor progression. [12]

This study investigated KIF20A expression patterns in bladder carcinoma using immunohistochemistry and explored its correlations with a spectrum of clinicopathological parameters. We conducted a retrospective analysis of sixty pathologically confirmed bladder carcinoma cases. Our analysis revealed strong statistically significant correlations between KIF20A expression and several critical clinicopathological characteristics, including tumor location, histological subtype and grade, pathological T stage, vascular embolism, and perineural invasion (p=0.000). nonetheless, KIF20A level wasn't related to patient age or sex, tumor size, gross morphology, lymph node metastasis, or bilharzial infestation.

KIF20A's molecular function involves interacting with microtubules, harnessing energy from ATP hydrolysis to generate mechanical force. This facilitates essential cellular activities such as intracellular transport and chromosomal segregation during mitosis. [13] Our findings are consistent with existing research on KIF20A in urothelial bladder carcinoma by Shen et al (2019), which has shown its role in increased proliferation and metastatic capability of bladder cancer cells. Moreover, high KIF20A expression has been associated with poorer tumor differentiation and a worse prognosis. [14]

In summary, our study reinforces the evidence for substantial KIF20A overexpression in urothelial bladder carcinoma. The observed correlations between KIF20A expression and various clinicopathological characteristics, combined with its established role in cellular proliferation and metastasis, strongly indicate that KIF20A may be an independent prognostic marker influencing patient outcomes in bladder cancer. Further investigations are necessary to evaluate KIF20A as a potential therapeutic target and to develop strategies for modulating its expression to improve bladder cancer management.

Ethical approval and consent to participate:

The study was conducted with the approval of the ethical committee of Faculty of Medicine, Fayoum University, all subjects were submitted to an informed consent

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Conflicts of Interest: No author has disclosed any conflicts of interest.

The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript, nor for the creation of images, graphics, tables, or their corresponding captions.

Authors' contributions: DGEA: Protocol development, Data collection and management, Manuscript writing. **HME:** Data analysis, Manuscript editing. **HMK:** Protocol development, Data analysis, Manuscript editing. **DNA:** Data management, Manuscript editing. **All authors have read and approved the manuscript.**

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