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A BIOCHEMICAL STUDY OF A ROLE OF FIBROBLAST GROWTH FACTOR (FGF-2) IN IRAQI BLADDER CANCER PATIENTS

Zinah Abbass Ali and Hiba Resheed Behayaa*

Department of Clinical Biochemistry, College of Medicine, University of Babylon, Hilla, Iraq.
*e-mail : hiba_resheed80@yahoo.com

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ABSTRACT : To evaluate the level of Fibroblast Growth Factor-2 in the serum of Iraqi bladder cancer patients, eighty Iraqi subjects were enrolled in this revision; 40 with bladder cancer and 40 healthy subjects (as a control group) with age ranged between (45-75) years. Serum level of Fibroblast Growth Factor-2 was measured by enzyme-linked immunosorbent assay (ELISA) technique. The levels of Fibroblast Growth Factor-2 showed significantly increased in bladder cancer patients in comparison with control group (p<0.01).

Key words : Fibroblast Growth Factor 2, bladder cancer.

INTRODUCTION

Bladder tumor is one of the most common tumors worldwide. Bladder tumor incidence in men are more common than women and typically affects old age subjects, yet it can happen at any age (Shahrokh F. Shariate *et al*, 2009).

Urothelial carcinoma, Squamous cell carcinoma, Adenocarcinoma is the main type of bladder tumor. But one of the most common types of bladder tumor is the urothelial tumor also known as the Transitional Cell Carcinoma, in this case the tumor stars in the cells in the bladder's internal lining. Stages of bladder cancer depend on the degree of tumor attack within the bladder wall (Michael Schulster, 2019).

Bladder tumor is the 9th most common form of cancer in the world, though globally ranking 7th in men.Even bladder cancer diagnose at early stage it may recur in the bladder. For this reason, subjects have bladder cancer needed follow-up tests for several years to look for returns or spreads of the disease (Witjes Chair *et al*, 2018).

Patients with Bladder cancer may have hematuria, aching with urination, Pelvic pain, Back pain and recurrent urination but, these sign and symptoms may occur as a result of disease other than bladder cancer (Marcus G K Cumberbatch *et al*, 2019). Smoking, contact with chemicals compound, previous exposure to radiation, irritation in the lining of the bladder and parasitic infections may contribute as the main reason of bladder cancer (Lotan, 2017).

One member of a family of cell signaling proteins is fibroblast growth factors (FGF) that have basic role in different process, especially in normal development. Dysfunction of FGF lead to disturbance in the development. Fibroblast growth factor stimulates cell surface receptors by acting as extracellular molecules that circulate systemically or locally (Keiji Inoue *et al*, 2000). FGFs are capable of binding to heparin and heparan sulfate and sequestered in the extracellular matrix of tissues containing proteoglycans of heparan sulfate, allowing FGFs released locally after damage or tissue transformation (Darren C Tomlinson *et al*, 2009).

Basic growth factor for fibroblasts (bFGF) and FGF-β is another name of FGF2, which functions as growth factor and signaling protein encoded by the gene FGF2. 155 Polypeptide amino acid is synthesized and 18 kDa proteins are produced (Chaffer, 2006).

The four start codons that supply N-terminal extensions of 41, 46, 55, or 133 amino acids, resulting in 22 kDa (196 aa total), 22.5 kDa (201 a total), 24 kDa (210 aa total) and 34 kDa (288 aa total) proteins, respectively. InGeneral, the 155 aa/18 kDa low molecular weight (LMW) form is present in the cytoplasm and can be secreted from the cell, whereas the high molecular weight (HMW) forms are release to thenucleus of the cells (Erica di Martino, 2012). bFGF have wide mitogenic

and cell survival activities - Like other FGF family members- and have different biological processes, like embryonic development, growth of cell, morphogenesis, wound healing and growth oftumor (Witjes Chair *et al*, 2011).

MATERIALS AND METHODS

Ethical issues

Depending on the local ethics group the revision was agreed, all patients in this study given an idea about the purpose of the review, agree and signed permission were informed.

Study design

This revision designated as a studyof case-control.

Collection of samples

The sample size was determined according to the equation of Daniel sample size formula. The participants in the recent study include forty Iraqi patients with bladder cancer, the history from them was taken, which involve: age, residence, smoking, personal history, therapeutic and medication history and forty apparently healthy subjects therapeutically free were serve as healthy control group. The age of these groups from 45 to 80 years. The statistical analysis was done with version 18 of SPSS. The findings have been expressed as Mean ± SD and P values below 0.05 are considered significant.

Chemicals and methods

Serum FGF2 concentration was determined by the sandwich-ELIZA kit. An antibody specific to Human b FGF /FGF2 was pre-coated to the micro- ELIZA plate supplied with the kit.

RESULTS

The study groups consist of 60 adults designate on two categories :

1. Patients with bladder cancer(n=40)
2. Healthy control group (n=40)

The mean ± SD of FGF2 in the bladder cancer group and control group as shown in Table 1.

Table 1 : Sample characteristics of bladder cancer.

Parameters	Bladder cancer n=40	Control group n=40	P value
FGF2pg/ml Mean± SD Range	655.2 ± 25.4 (599.1-675.3)	3500 ±22.3 (312.6-394.7)	P <0.01

SD= standard deviation, FGF2= fibroblast growth factors 2

DISCUSSION

Around 45,000 men and 17,000 women are diagnosed with Bladder cancer each year at the National Institutes of Health (Marcus *et al*, 2019).

Transitional cell carcinoma occurs in the transitional cells inside the bladder's inner lining, making the more prevalent form of bladder cancer. At this time when the tissue is prolonged transitional cells changes there shape without becoming damaged (Seiler, 2017). Most people with bladder cancer may reach advance stage without apparently symptom these subjects required more attention for the presence of blood in urine without pain, fatigue, loss of weight and bone tenderness (Efstathiou, 2012).

There are 5 isoforms for human FGF2, all of them are biologically active, but they differ in function, molecular weight and the location inside the cell (Seema Nayak *et al*, 2015). LMW FGF2 motivates growth ofcell, proliferation, migration and differentiation through FGFR signaling and complex internalization of the ligand receptors. While the mitogenic response of FGF2 is regulated either directly or indirectly by nuclear kinase factor of regulation and transcription activity for ribosome biogenesis by differentiation and growth of cell (Murraykorc *et al*, 2009).

The main target for cancer therapy is the control of cell growth. The FGF signaling system shows a universal role in normal cell growth and survival (Elizabeth A McNiel *et al*, 2017), but also associated in tumor development.

Table 1 shows a significant rise in FGF2 levels in the serum of bladder cancer as opposed to control group (p>0.01). Similarly, in this revision the high level of fibroblast growth factor-2 in bladder cancer group give an idea about the role of FGF2 in tumor development. These result is reliable with Gazzaniga *et al* (1999) and Gazzaniga (1999).

CONCLUSION

Among Iraqi patients with bladder cancer, elevated the level of FGF2 indicate significant associated between FGF 2 and bladder cancer.

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