JOURNAL OF CRITICAL REVIEWS

ISSN- 2394-5125 VOL 7, ISSUE 15, 2020

A PLASMA CONCENTRATION OF VASCULAR ENDOTHELIAL GROWTH FACTOR-A (VEGF-A) IN INFLAMMATORY BOWEL DISEASE (IBD) PATIENTS IN BABYLON PROVINCE

Heba Sajad Al – Esawy[1], Oruba K.Al-Bermani[2], Noran Jameel Ibraheem[3]

[1]College of Science for Women, University of Babylon, Iraq.
[2]College of Science for Women, University of Babylon, Iraq.
[3]College of Science for Women, University of Babylon, Iraq.

Accepted: 21.06.2020 Revised: 24.05.2020 Received: 23.04.2020

ABSTRACT: Background: Inflammatory bowel disease (IBD) is a term that involves some bowel disorders of chronic inflammation in the gastrointestinal (GI) tract. The pathogenesis of IBD is a complex process, involving environmental, genetic, bacterial and immune causes, involving Ulcerative Colitis UC and Crohn's Disease CD. Vascular Endothelial Growth Factor (VEGF) is a powerful activating factor for angiogenesis and vascular penetrability, is formed by endothelial cells, macrophages, smooth muscle cells, and fibroblasts. is an elect capability gene to IBD, together from a useful add to genetic view. **Method:** This disease diagnosis by physician after endoscopy for IBD patients, 5 ml of venous blood collected from 60 patients and 25 healthy group, for getting plasma to evaluated concentration of VEGF, during the period September 2018 to first February 2019. Used the (Human VEGF-AELISA Kit) to detected the concentration of VEGF. **Results:** Our study data explained that evaluated levels of plasma VEGF in IBD patients, the means were 72.92 pg/ml, and 63.79 pg/ml for (UC and CD patients) respectively compression with means of control were 51.57 pg/ml. **Conclusions:** high concentration of (VEGF) associated with the IBD, may be sign of angiogenesis in this state.

KEYWORDS: Plasma concentration and Inflammatory Bowel Disease (IBD).

 DOI: http://dx.doi.org/10.31838/jcr.07.14.208

I. INTRODUCTION

The Inflammatory bowel disease, is chronic inflammatory diseases, including ulcerative colitis and crohn's disease, that emerge from a complicated immunological interaction (Lange et al., 2017), hereditary, and ecological factors (Chang et al., 2018). IBD influence about 1 million patients in the United States has a significant clinical and economic effect (Floyd et al., 2015). The clinical symptoms manifestations of IBD are abdominal pain, diarrhea, bloody feces and weight loss (Berrill et al., 2013).

VEGF a powerful vasculogenesis regulator and angiogenesis of the tumor plays role in abnormal tissue growth, encompassing embryogenesis, the skeletal development, repetition and wound therapeutic. Additionally it is too main in pathological angiogenesis, which commonly occurs in carcinogenesis, rheumatoid arthritis, diabetic and several other diseases (Harmanci et al., 2018). In the early phase of mucosal therapeutic and tissue reparation process in the infection gut, angiogenesis, the development and production of new blood-vessels, is vital. There are number of angiogenic variables that can be significant in neovascularization, comprising VEGF and TGF-β transforming growth factor (Lan et al.,, 2012).

VEGF promotes the movement and production of endothelial cells and these physiological special effects are interceded by linking to binary homologous VEGF receptors, VEGF receptor-1(Flt-1) and VEGF receptor-2 (KDR or Flk1), which are displayed on vascular endothelial cells (Palmer et al., 2015). VEGF joins on endothelial cells to a surface receptor, leading in intracellular signal transduction via tyrosine kinases, thus increasing endothelial mitosis and replication, increasing vascular permeability and capillary angiogenesis (Nakayama et al., 2013). VEGF links to monocytes and stimulates migration to inflamed tissue across endothelial cells.

It's also stimulates the gene expression of the connective tissue growth factor in retinal endothelial cells that may induce fibrosis (Sankar et al., 2018). The IBD patient's colonic mucosa shows increased epithelial cell turnover.

ISSN- 2394-5125 VOL 7, ISSUE 15, 2020

Mutation attack with continuous DNA injury induced via variables in an infection cell-wealthy microenvironment show toward drive the carcinogenic process in the environment of increased epithelial cell turnover (Claesson et al., 2016). Aim: determine if the concentration of (VEGF) is increasing in IBD patients, and how can it be as indictor for the development of this disease.

II. MATERIALS AND METHODS

Healthy control and patients

Our study include (25) healthy persons and IBD patients (ulcerative colitis No. 30 and crohn's No.30 patients), enrolled to in gastrointestinal tract unit of Marjan hospital, Babylon, Iraq, during the period from 1September 2018 to 1 February 2019. The IBD cases were diagnosed by specialist doctors. Specimens collected and handling, in EDTA tubes five ml were collected, from healthy control and patients, blood was centrifuge at 3300 x g for 10 mit to separate the plasma and it stored in microfuge tubes and kept at -20 (Wang et al., 2016). To evaluated the level of VEGF-A in plasma we used "Human VEGF A ELISA Kit" as of Elabscience /USA, the procedure was direct according to the of the manufacturer's company. Concentrations of VEGF-A in patient's plasma were determined by plotting the absorbance of each sample against a standard curve of recombinant VEGF-A, was measured at 450 nm (primary wavelength).

Typical data

Since the standard curve OD values may vary depending on the real test performance situations (e.g. operator, pipetting method, washing method, or temperature effects), the operator would set a standard curve for all test. Typical standard curve and information for reference only are given below, shown in figure (1)

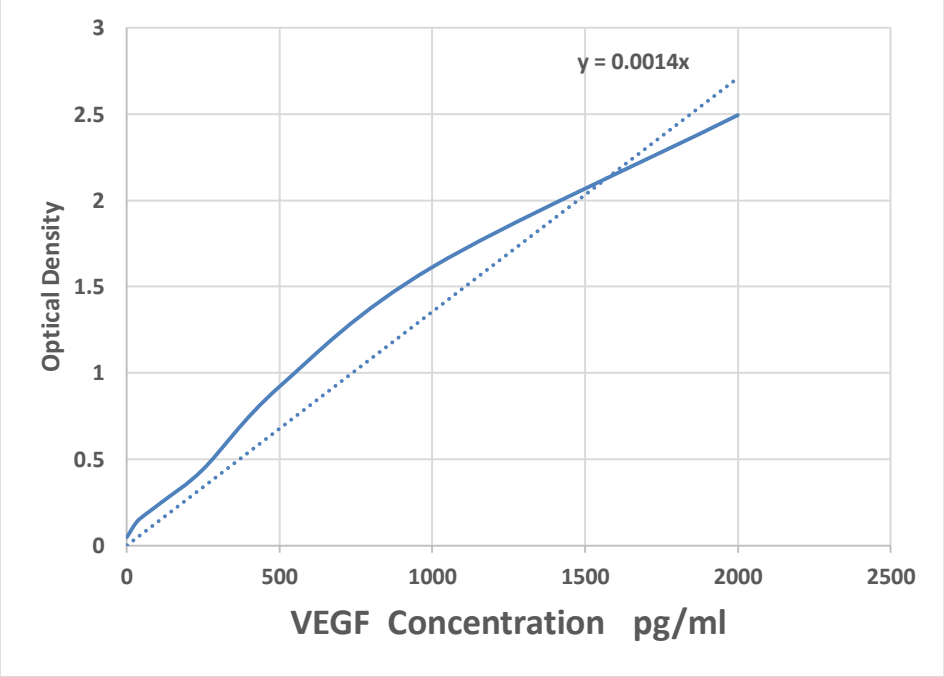

Figure 1: Correlation between the Concentration pg/ml of Plasma (VEGF-A) and the Optical Density Grades

Statistical Analysis (Babbie et al., 2018)

Data statistical analysis were used the Social Science Statistical Package (SPSS) version 24 for Windows. For continuous variable the mean and standard deviation (SD) were calculated as well as compared by student's t-test 5 values < 0.05 were regarded to show statistical significance.

III.RESULTS

ISSN- 2394-5125 VOL 7, ISSUE 15, 2020

Our results showed that the concentration levels of plasma VEGF-A in both UC and CD patients were high significant, the means (72.92 and 63.79 pg/ml) respectively, compared with control, It's means was 51.57 pg/ml, as is shown in table (1) and in figure (2).

The statistical analysis for estimation the difference between the concentration in patients and control was significant P≤0.05.

Table 1: Means of Concentration and P Value of VEGF-A in Patients and Control

Groups	Mean and ±SD (pg/ml)	P value
Ulcerative colitis No.30	72.92±21.08	0.0001
Crohn's disease No.30	63.79±6.91	0.006
Control No.25	51.57±17.68	

Significant P≤0.05, SD: standard deviation

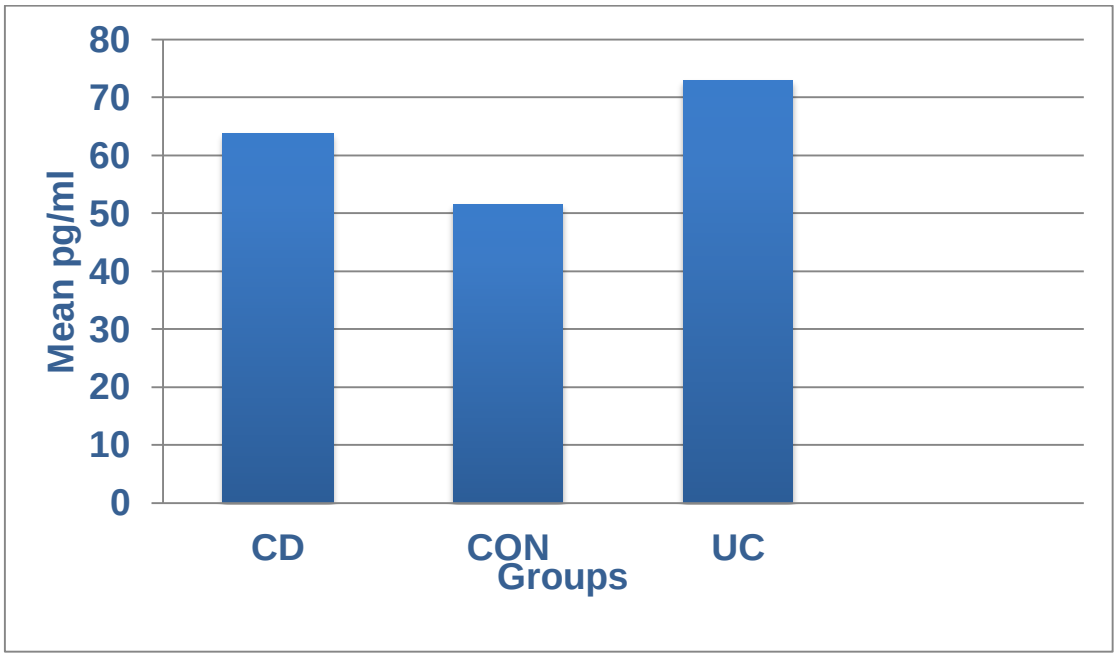

Figure 2: Comparison between the Concentration pg/ml of (VEGF-A) in Groups (UC & CD Patients) and Control

IV. DISCUSSION

There are little studies intended to measure the concentration of VEGF plasma comparison with It's in serum, our study similar with those studies (Smith et al., 2017) found VEGF concentration of (CD, UC and asthma patients) were high significant compared with healthy. Other studies such as (De Souza et al., 2016) appeared the causes of high level VEGF in those patients with arise intramuscular blood that VEGF probably formation new blood vessel a marker in this case.

However more studies such as (Francescone et al., 2015) shown, Serum levels of VEGF relationship with disease activity in more number of autoimmune disease. It is well-known that evaluated level of VEGF is a rise in serum and inflamed tissues and lead increasing activity of endothelial cells for formation of new vessels in autoimmune diseases, such as rheumatoid arthritis (Jiang et al., 2016).

It is also known that the source of the circulating VEGF is the bowel mucosa of patients with IBD (Wen et al., 2017) and the researcher found significantly higher production of VEGF in mucosa for (CD and UC patients) compared with normal mucosa of the healthy.

So the inflamed gut mucosa is a origin of inflammatory, different disease position, in both CD and UC patients, might affected VEGF concentrations, VEGF is produced and released by both the inflamed bowel mucosa and peripheral blood mononuclear cells through inflammatory processes, (Li et al., 2016). And (Karaman et al., 2016) found the high level of VEGF for together serum and plasma in (UC and CD patients) was probably reflected overexpression in intestinal inflammatory tissue and While (D'alessio et al., 2014) suggested that VEGF play an important role in the inflammation process in the tissue , but it role in the angiogenesis in IBD has not been proven.

V. REFERENCES

[1] Babbie, E., Wagner III, W. E., & Zaino, J. (2018). Adventures in social research: *Data analysis using IBM SPSS statistics. Sage Publications.*

[2] Berrill, J. W., Green, J. T., Hood, K., & Campbell, A. K. (2013). Symptoms of irritable bowel syndrome in patients with inflammatory bowel disease: examining the role of sub-clinical inflammation and the impact on clinical assessment of disease activity. *Alimentary pharmacology & therapeutics*, 38(1), 44-51.

[3] Chang, M., Chang, L., Chang, H. M., & Chang, F. (2018). Intestinal and extraintestinal cancers associated with inflammatory bowel disease. *Clinical colorectal cancer*, 17(1), e29-e37.

[4] Claesson-Welsh, L. (2016). VEGF receptor signal transduction–A brief update. *Vascular pharmacology*, 86, 14-17.

[5] D'alessio, S., Correale, C., Tacconi, C., Gandelli, A., Pietrogrande, G., Vetrano, S., ... & Fiocchi, C. (2014). VEGF-C–dependent stimulation of lymphatic function ameliorates experimental inflammatory bowel disease. *The Journal of clinical investigation*, 124(9), 3863-3878.

[6] de Lange, K. M., Moutsianas, L., Lee, J. C., Lamb, C. A., Luo, Y., Kennedy, N. A., ... & Heap, G. (2017). Genome-wide association study implicates immune activation of multiple integrin genes in inflammatory bowel disease. *Nature genetics*, 49(2), 256.

[7] De Souza, H. S., & Fiocchi, C. (2016). Immunopathogenesis of IBD: current state of the art. *Nature reviews Gastroenterology & hepatology*, 13(1), 13.

[8] Floyd, D. N., Langham, S., Séverac, H. C., & Levesque, B. G. (2015). The economic and quality-of-life burden of Crohn's disease in Europe and the United States, 2000 to 2013: *a systematic review. Digestive diseases and sciences*, 60(2), 299-312.

[9] Francescone, R., Hou, V., & Grivennikov, S. I. (2015). Cytokines, IBD, and colitis-associated cancer. *Inflammatory bowel diseases*, 21(2), 409-418.

[10] Harmanci, K., Akan, O. Y., Pirildar, T., Ortan, P., & Ulman, C. (2018). The Evaluation of the Relationship between sTREM-1, VEGF-B, and VEGF Gene Expression Levels with Disease Activity of Behçet's Patients. *Disease markers, 2018.*

[11] Jiang, S., Li, Y., Lin, T., Yuan, L., Li, Y., Wu, S., ... & Lu, J. (2016). IL-35 inhibits angiogenesis through VEGF/Ang2/Tie2 pathway in rheumatoid arthritis. *Cellular Physiology and Biochemistry*, 40(5), 1105-1116.

[12] Karaman, S., Hollmén, M., Yoon, S. Y., Alkan, H. F., Alitalo, K., Wolfrum, C., & Detmar, M. (2016). Transgenic overexpression of VEGF-C induces weight gain and insulin resistance in mice. *Scientific reports, 6, 31566.*

[13] Lan, H. Y. (2012). Transforming growth factor-β/S mad signalling in diabetic nephropathy. *Clinical and Experimental Pharmacology and Physiology*, 39(8), 731-738.

[14] Li, Y. L., Zhao, H., & Ren, X. B. (2016). Relationship of VEGF/VEGFR with immune and cancer cells: staggering or forward?. *Cancer biology & medicine*, 13(2), 206.

[15] Nakayama, M., Nakayama, A., Van Lessen, M., Yamamoto, H., Hoffmann, S., Drexler, H. C., ... & Cooper, J. A. (2013). Spatial regulation of VEGF receptor endocytosis in angiogenesis. *Nature cell biology*, 15(3), 249.

[16] Palmer, K. R., Kaitu'u-Lino, T. U. J., Hastie, R., Hannan, N. J., Ye, L., Binder, N., ... & Tong, S. (2015). Placental-specific sFLT-1 e15a protein is increased in preeclampsia, antagonizes vascular endothelial growth factor signaling, and has antiangiogenic activity. *Hypertension*, 66(6), 1251-1259.

[17] Sankar, M. J., Sankar, J., & Chandra, P. (2018). Anti-vascular endothelial growth factor (VEGF) drugs for treatment of retinopathy of prematurity. *Cochrane Database of Systematic Reviews*, (1).

[18] Smith, C. J. F., Friedlander, S. F., Guma, M., Kavanaugh, A., & Chambers, C. D. (2017). Infantile hemangiomas: an updated review on risk factors, pathogenesis, and treatment. *Birth defects research*, 109(11), 809-815.

[19] Wang, J., Yan, Y., Song, D., & Liu, B. (2016). Reduced plasma miR-146a is a predictor of poor coronary collateral circulation in patients with coronary artery disease. *Bio Med research international*, 2016.

ISSN- 2394-5125 VOL 7, ISSUE 15, 2020

[20] Wen, Z., Shen, Y., Berry, G., Shahram, F., Li, Y., Watanabe, R., ... & Weyand, C. M. (2017). The microvascular niche instructs T cells in large vessel vasculitis via the VEGF-Jagged1-Notch pathway. *Science translational medicine*, 9(399), eaal3322.