Evaluation the validity of Interleukin-17 in Nephrotic Syndrome patients

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Abstract. Background: The Nephrotic Syndrome (NS) is a clinical condition characterized via severe proteinuria, which causes hyperlipidemia, hypoalbuminemia, and edema, and other problems. It is produced by basement membrane is more permeable as a result of the damage of the renal glomerulus. Essentially, it occurs when there is an abnormality in glomerular permeability, which can be due to an intrinsic renal disease or secondary to congenital infections, diabetes, systemic lupus erythematosus, or neoplasia. Materials and methods: The research study was conducted on 70 randomly selected participants (35 Females and 35 Males) with autoimmune disease and nephrotic syndrome attending the kidney disease center in AlSadder Teaching City in AlNajaf province, Iraq. It was carried out from December 2022 to July 2023. The age of patients was range of 1-50y. Results: show a significant escalation (P≤ 0.05) in Interleukin level in nephrotic patients in comparing with control groups also a significant rise (P≤ 0.05) in Interleukin (IL)-17 level in nephrotic patients at Various ages groups in comparison to the various age groups of control groups and results moreover demonstrate significant effect (P≥ 0.05) in Interleukin (IL)-17 level between groups of ages. reveal no significant effect (P≥ 0.05) in Interleukin (IL)-17 level in females and males in nephrotic patients furthermore show a significant increase (P≤ 0.05) in Interleukin level in nephrotic patients in rural groups than urban groups. Conclusion: concluded that Interleukin-17 highly elevated and in patients with nephrotic syndrome, this factor is also linked to disease severity.

1 Introduction

Nephrotic Syndrome (NS) is one of the most prevalent kidney diseases and one of the main factors that leads to end-stage renal disease in both adults and children [1]. As a result, kidney function may be altered because of a rise in the permeability Basement membranes of the glomeruli to plasma proteins, including albumin. This disorder manifests as edema, hypoalbuminemia, and chronic proteinuria [2]. It is a chronic kidney An illness that is characterized by a large loss of urinary protein as a result of damage to the basement membrane of the glomerulus [3]. Nephrotic syndrome is a disease with a heterogeneous
etiology, basement membranes, and podocytes [4]. Based on the morphology, pathogenesis and it is one of the greatest prevalent glomerular disorders amongst children. There are multiple etiologies for this condition, and it can lead to end-stage kidney disease and the requirement for kidney replacement treatment. It is characterized by a malfunctioning glomerular filtration barrier containing endothelial cells, glomerular, or the disease's clinical presentation, it is classified into Minimal change disease, diabetic nephropathy, IgA nephropathy and Focal segmental glomerular sclerosis occur in the kidneys., Renal amyloidosis, and Membranoproliferative glomerulonephropathy [5].

Interleukin (IL)-17 has a mass of 17 kDa and is a transmembrane protein. There are six members in this cytokine family: IL-17A through IL-17F [6], and are engaged in a variety of immunological responses, including those that occur in inflammatory, autoimmune, and infectious diseases. As the family's archetypal member, IL-17 was first discovered to be a cytokine secreted by a subset of CD4+ T cells known as Th17 [7]. Interleukin 17 plays a significant function in the immune response against specific infections, especially fungi and bacteria (such Candida albicans, Citrobacter rodentium, and Klebsiella pneumoniae) [8]. Additionally, IL-17 has been associated with a number of autoimmune diseases conditions, counting systemic sclerosis, inflammatory bowel disease, rheumatoid arthritis, and SLE, especially when it comes to cutaneous involvement and serositis [9]. Strong pro-inflammatory effects of interleukin 17 are observed, along with other pro-inflammatory cytokines involved in the process as well, including the recruitment of neutrophils, macrophages, and lymphocytes, and the facilitation of the infiltration of T cells [10].

2 Materials and Methods

Seventy patients were chosen at random to participate in the clinical study (35 Males and 35 Females) with autoimmune disease and nephrotic syndrom attending the kidney disease center in Al-Sader Teaching City in AlNajaf province, Iraq. It Carrying out from December 2022 to July 2023. The age of patients was range of 1-50y. Patients was identified by medical consultants. A questionnaire was used to collect patient data, which included name, sex, age, and weight. A groups of 30 apparently control subjects (15 Males and 15 Females) included in a healthy groups. the ages ranges were similar to those of the patients. Each patient and control participant provided 5ml of venous blood samples, which were drawn using plastic syringes and a disposable needle. After 10 minutes of clotting at room temperature, the blood was separated and placed into fresh, disposable tubes after centrifuging it for 10 minutes at 6000 rpm. Human Interleukin 17 was determined using the sandwich enzyme immunoassay technique [11].

3 Results

3.1 Interleukin (IL)-17 level between nephrotic patients and control groups

The outcomes in figure (1) indication a significant elevate (P≤ 0.05) in Interleukin level in nephrotic patients in comparing with control groups.
Fig. 1. Interleukin levels (ng/ml) in nephrotic patients and control groups.

* Statistically significant difference at (P≤0.05)

3.2 Comparison levels of Interleukin-17 between nephrotic patients and control groups according to age

The outcomes in figure (2) show a significant increase (P≤ 0.05) in Interleukin (IL)-17 level in nephrotic patients at different age groups (0-10y,11-20y, 21-30y, 31-40y and 41-50y) in comparison to the control group at different age groups (0-10y,11-20y, 21-30y, 31-40y and 41-50y) respectively and Furthermore, the data show a significant impact(p≥ 0.05) in Interleukin (IL)-17 level between groups of ages.

Fig. 2. Interleukin levels (ng/ml) in nephrotic patients according to age.

* Statistically significant difference at (P≤0.05)
3.3 Comparison levels of Interleukin-17 between nephrotic patients and control groups according to gender

The outcomes of figure (3) expose no significant effect (P≥ 0.05) in Interleukin (IL)-17 level in females and males in nephrotic patients and significant rise (P≤ 0.05) in Interleukin (IL)-17 level in both nephrotic patients in comparing with control groups.

**Fig. 3.** Interleukin levels (ng/ml) in nephrotic patients according to gender.

* Statistically significant difference at (P≤0.05)

3.4 Interleukin (IL)-17 level between nephrotic patients according to place of living

The consequences in figure (4) demonstrate a significant elevate (P≤ 0.05) in Interleukin level in nephrotic patients in rural groups than urban groups.

**Fig. 4.** Interleukin levels (ng/ml) in nephrotic patients according to place of living.

* Statistically significant difference at (P≤0.05)
4 Discussion

The results show a significant increase in Interleukin (IL)-17 level in nephrotic patients and this agree with study of Abbas et al., [2] that work showed higher level of IL-17 in patients with nephrotic patients than healthy control. Also the work of Zhai et al., [12] indicate the increased levels of Interleukin (IL)-17 in nephrotic patients than in normal persons. IL 17 is a crucial cytokine that Th17 cells secrete and has been linked to the development of coronary heart disease [13] [14], multiple sclerosis [15], inflammation and autoimmune diseases [16]. In kidney diseases, discovered the elimination of IL 17 in urine throughout the slightly active phase was considerably more than that during the remission phase, and that this excretion was correlated with the elimination of urinary protein [17]. Furthermore, in patients with PNS [18], experimental glomerulonephritis [19], and the IgA nephropathy severity [20], IL 17 was moreover linked to renal tissue damage. The expression of IL 17 was shown to be much higher in the renal tissues of PNS patients than in normal kidney tissues in the Zhai et al., [12] study. This finding was also linked to the severity of the disease in PNS patients. Additionally, it was discovered that IL 17 [21] [22]. Podocytes are a type of terminally differentiated cells that are glomerular visceral epithelial cells. Podocytes that sustain damage separate from the basement membrane because the injured podocytes disrupt the normal organization of the foot processes. As a result of IL 17 treatment, podocytes undergo apoptosis in addition to mRNA expression of podocyte specific markers, including WT1, nephrin, synaptopodin, and podocalyxin, being reduced in vitro. This is because the integrity of the glomerular filtration membrane is compromised, resulting in proteinuria, which is difficult to repair due to the limited proliferation of podocytes [21]. This compromises proteinuria. In fact, investigations have shown that the progress of FSGS and familial nephrotic syndrome is caused by the harm or mutation of podocalyxin, and the expression of these indicators was strongly correlated with podocyte integrity [23] [24]. Furthermore, fluvastatin therapy, which is primarily used to treat primary mixed dyslipidemia and hypercholesterolemia, activates synaptopodin, nephrin, and WT1 expression to protect podocytes from HIV-associated nephropathy [25] [26]. In cultured podocytes, changes in protein expression are observed after IL 17 administration were investigated in order to learn more about the molecular mechanism by which IL 17 causes podocyte apoptosis. Concurrent management with the NF-κB inhibitor helenalin reduced the enhanced expression of Fas, FasL, active caspase 8, active caspase 3, and phosphorylation of p65 resulting from IL 17 therapy. An earlier work shown that the activation of the Fas/FasL caspase 8 caspase 3 pathway by inflammatory stimuli might cause muscle cell death [27]. Numerous genes linked to inflammation, such as TNF α and IL 1β, are transcriptionally regulated by NF κB signaling, which can then intensify NF κB signaling even more [28]. Thus, it's possible that IL 17 activated the NFκB pathway in podocytes, which in turn triggered the Fas/FasL caspase 8 caspase 3 pathway, increasing podocyte death. This would have raised the secretion of IL 1β and TNF α [29].

5 Conclusions

The present study concluded that Interleukin-17 highly elevated and Also linked to illness severity in people with nephrotic syndrome.

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References

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