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ROLE OF INTERLEUKIN-35 IN RENAL FAILURE PATIENTS WITH HEPATITIS C VIRUS

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ABSTRACT

Background: Chronic Renal Failure is a condition where there is a loss of kidney function over a period of months or years.Hepatitis C virus (HCV) is a hepatotropic virus that infects people and causes liver disease. It is a potential source of significant morbidity and death throughout the globe. patients with acute hepatitis C become chronically infected. Therefore, the high, acute HCV infection and chronicity rates after acute infection contribute to the high prevalence of HCV infection in End Stage Renal Disease patients.In patients with CRF, renal problems are caused by an imbalance between the oxidant and antioxidant systems, as well as the depletion of the protective antioxidant system and the production of reactive oxygen species (ROS). T lymphocytes are then attracted into the kidney as a consequence. T cells infiltrating the body may induce tissue damage, iTr35 cell generation, IL-35 expression, and iTr35 regulatory T cell conversion, indicating that these cells may be involved in the development of renal failure.

Objective: Evaluate the levels of IL-35Renal Failure Patients with Hepatitis C.

Methods and Results: Collected 46 patients with Hepatitis C Virus and 45 control. This sandwich kit is used to detect human Interleukin-35 in a quantifiable manner. The identification of HCV-specific IgM and IgG was accomplished using a third-generation ELISA method. Study population an age ranging between (14-73) years old. The present study showed that the female group had the highest percentage and constituted 26/46 (56.52%) patients, while the male group constituted 20/46 (43.48%). The first age group is 14-33 years, n = 15 (32.6%). The second age group, 34-53, 24 (52.1), was the oldest group of renal failure patients infected with the hepatitis C virus. The third age group, 54-73 years, n=7 (15.21%), had the fewest renal failure patients infected with the hepatitis C virus. the mean level of Interleukin-35 (IL-35) in Renal Failure patients with Hepatitis C Virus (RF-HCV) (11.48) was significantly higher than in control group (2.30).

Key words: Renal Failure Patients with Hepatitis C, Interlukin-35, ELISA.

I. INTRODUCTION

Chronic Renal Failure is a condition where there is a loss ofkidney function over a period of months or years. CRF can be diagnosed by measuring serumcreatinine levels, which are a degradative product of muscle protein. Creatinine levels indicate the glomerular filtration rate (GFR) and in CRF, its activities are raised, indicating a loweredGFR[1].

Hepatitis C virus (HCV) is a hepatotropic virus that infects people and causes liver disease. It is a potential source of significant morbidity and death throughout the globe [2].

Cirrhosis, portal hypertension, hepatic decompensation with encephalopathy, and hepatocellular cancer are among side consequences of hepatitis C virus infection [3].

patients with acute hepatitis C become chronically infected.Therefore, the high, acute HCV infection and chronicity rates afteracute infection contribute to the high prevalence of HCV infectionin End Stage Renal Disease patients. The reported prevalence rates of chronic HCVinfection among ESRD patients ranges from 3.4%to 80% withgreat geographic variationThe higher incidenceand prevalence rates of HCV infection among

ESRDpatients suggest the possible routes of nosocomial transmission,such as contamination of the hands of staff members, sharing itemsbetween patients, dialyzer reuse, and contamination of dialysismachines[4].

Furthermore, it has been shown that IL-35 has a greater expression level in chronic hepatitis patients, and that its expression level has a positive relationship with infection severity [5].In addition, both in vivo and in vitro, IL-35 has been shown to inhibit liver regeneration and hepatocyte proliferation [6].

In patients with CRF, renal problems are caused by an imbalance between the oxidant and antioxidant systems, as well as the depletion of the protective antioxidant system and the production of reactive oxygen species (ROS). T lymphocytes are then attracted into the kidney as a consequence. T cells infiltrating the body may induce tissue damage, iTr35 cell generation, IL-35 expression, and iTr35 regulatory T cell conversion, indicating that these cells may be involved in the development of renal failure [7].

II. MATERIALS AND METHODS:

- **Samples Collection:** Blood samples were taken from patients at the Dialysis Centers in Al-Sadr Teaching Hospital and Al-Hakim General Hospital in the governorate of Al-Najaf. It was carried out between the first of November 2020 and the last day of February 2021, and 46 patients renal failure with Hepatitis C Virus and 45 with control.

- **Detection of Hepatitis C Virus**: The identification of HCV-specific IgM and IgG was accomplished using a third-generation ELISA method. Plasmatic provided Anti-HCV IgM and IgG ELISA kits, and the test was performed according to the manufacturer's instructions.

- **Detection of Serum Interleukin-35 by ELISA Kits:** This sandwich kit is used to detect human Interleukin-35 in a quantifiable manner. It's an E.L.I.A. (Enzyme-Linked Immunosorbent Assay) (ELISA). The Human IL-35 antibody has been pre-coated on the plate. When IL-35 is introduced to the sample, it binds to antibodies coated in the wells. The biotinylated human IL-35 Antibody is then added to the sample and binds to IL-35.

- **Ethical Approval:** The consent of all patients included in the research study was taken.

- **Results and Discussion:** This study was conducted composed of two groups. 46 patients seropositive results for anti-HCV antibodies by using (ELISA) included renal failure with hepatitis C virus (HCV). The second group included 45 control.

The researchers believe that prolonged vascular access and the potential for exposure to infected patients and contaminated equipment are the factors that put patients with renal disease at risk of contracting HCV. There are also a number of risk factors linked to the spread of hepatitis C infection, including: the patient's age, hemodialysis length, family history of hepatitis C, blood transfusion history, kidney transplant history, and dental treatments, among other considerations [8].

- **Distribution of renal failure patients with hepatitis C virus according to sex:**

The gender of the renal failure patients with hepatitis C virus was divided into two groups: male and female. The present study showed that the female group had the highest percentage and constituted 26/46 (56.52%) patients, while the male group constituted 20/46 (43.48%) patients, as shown in the figure (1).

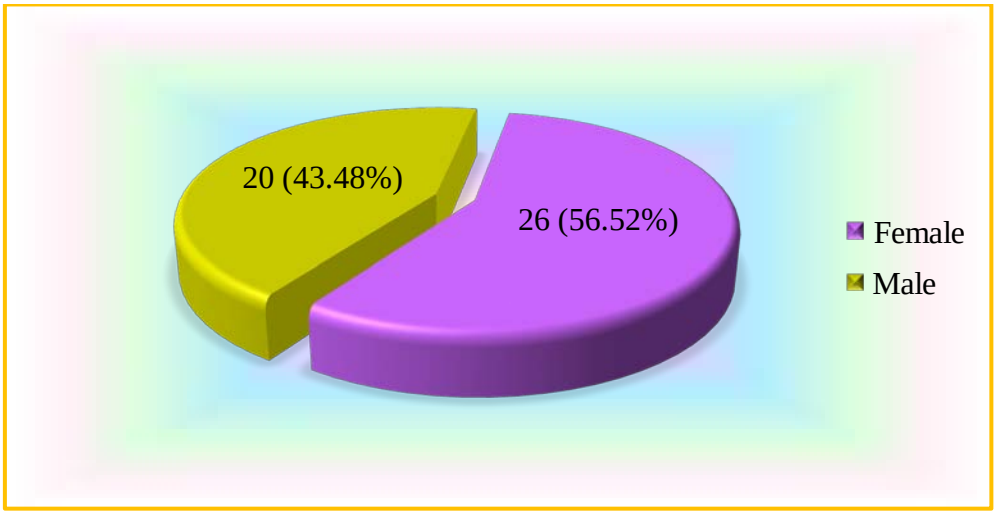

Figure (1): Distribution of hepatitis C patients with renal failure according to sex.

Females made up the bulk of the research sample in this study. This finding is consistent with the findings of [9].

And[12], who discovered that the majority of research subjects are females. While our findings differed from those of [10],[11]. They noted in their research that the majority of the study participants were males.

Anti-HCV positive rates differ by risk category, with greater rates of HCV reported in those at risk for STDs and lower rates in long-term heterosexual partners. This disparity in HCV infection rates might be due to variations in sexual risk behaviors (frequency or type of sexual activities). On the other hand, different rates of exposure to nonsexual sources of HCV, such as injectable drug use, as well as other possible risk factors, including intranasal cocaine use and tattooing, or sharing of razors and toothbrushes, might explain the variations between risk groups [12].

•Distribution of renal failure patients with hepatitis C virus according to age groups:

The age parameters of renal failure patients with hepatitis C virus were divided into three groups in the current study. The first age group is 14-33 years, n = 15 (32.6%). The second age group, 34-53, 24 (52.1), was the oldest group of renal failure patients infected with the hepatitis C virus. The third age group, 54-73 years, n=7 (15.21%), had the fewest renal failure patients infected with the hepatitis C virus. As shown in the figure (2).

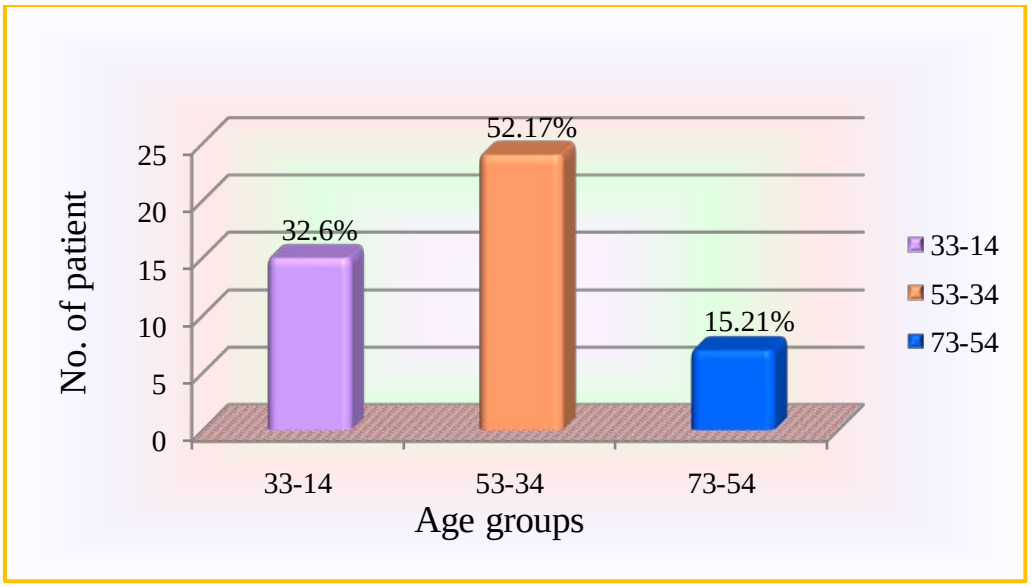

Figure (2): Distribution of HCV patients with renal failure according to age groups.

[9]who highlighted that the majority of the study subjects who are infected with HCV are within the (31-35) age group.

Patients who are older at the time of infection and have a weakened immune system are more likely to acquire chronic HCV infection [13].

•**Interleukin-35:** As shown in the table (1) and figure (3), the mean level of Interleukin-35 (IL-35) in Renal Failure patients with Hepatitis C Virus (RF-HCV) (11.48) was significantly higher than in control group (2.30).

Table (1): Comparison the mean, standard error and p-value of Interlukin-35 among Renal Failure patients with HCV and control.

parameter	Group	Mean	Std. Error	P.value
IL-35	RF with HCV	11.48	0.60	0.0001**
	Control	2.30	0.17	

P > 0.05 = Non Significant (NS)

P < 0.05 = significant (*)

P < 0.01 = Highly significant (**)

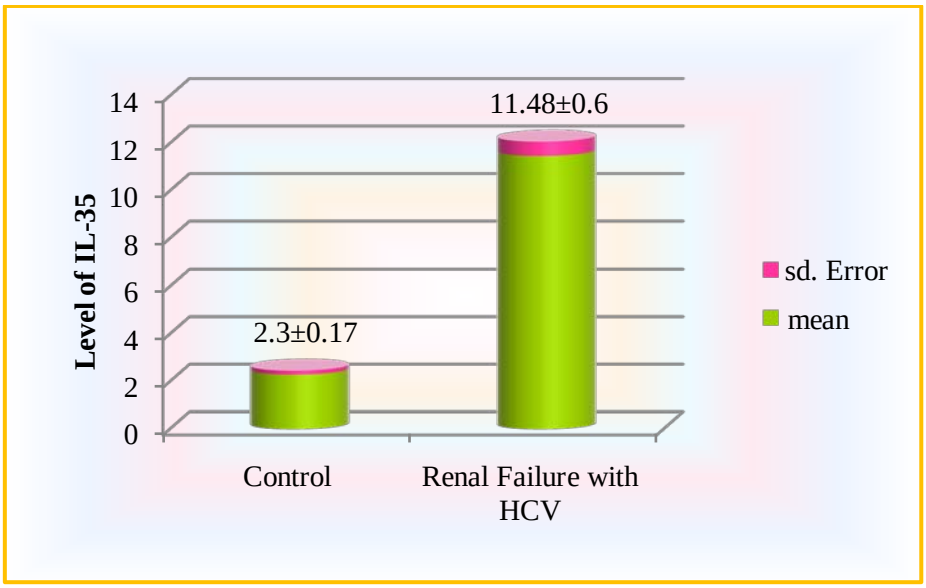

Figure (3): Graphical comparison of Interlukin-35 mean levels of Renal Failure patients with HCV and control.

IL-35 had a greater expression level in Hepatitis C Virus patients, according to [14],and its expression level showed a positive relationship with the severity of infection.

According to [15],IL-35 may have a critical role in the progression of liver disorders through immunosuppressive modulation. Furthermore, several evident advantages suggest that IL-35 might be used as a novel therapeutic target to slow the course of liver disorders, albeit its mechanism of action remains unknown. The role of IL-35 in kidney damage has received very little attention thus far.

IL-35 has selective actions on various T-cell subsets to generate its suppressive effects; it promotes T-regulator cell proliferation while suppressing Th17 cell activity [16].Renal disorders are caused by an imbalance between the oxidant and antioxidant systems, as well as the depletion of the protective antioxidant system and the generation

of reactive oxygen species (ROS) in patients with CRF. As a result, T lymphocytes are recruited into the kidney. Infiltrating T cells can cause tissue damage, iTr35 cell production, IL-35 expression, and iTr35 regulatory T cell conversion, indicating that these cells may play a role in causing renal failure [17].

In the renal viscera, a podocyte is a differentiated cell type. The podocyte foot process is broken when it is damaged, and the podocyte detaches from the Glomerular Membrane Base (GMB). Because a mature podocytes proliferation is restricted, it is unable to repair itself, resulting in protein leakage from the GMB. As a result, the quantity and functional integrity of podocytes are critical for proper renal function.Podocyte damage is a common nephrotic syndrome complication. Th17-IL17 expression is considerably elevated in the peripheral blood and kidney tissue of patients with nephritic syndrome, according to a prior study. There have been no findings on whether Il-17 can harm podocytes or what the mechanism is [18].

Because Th17 cells are a common kind of T cell capable of generating IL-17, researchers have discovered that IL-17 increases podocyte death. The mechanism by which IL-17 causes podocyte apoptosis, on the other hand, is unclear. Previous research has linked podocyte death or loss from the GMB to a reduction in podocyte quantity [19],[20]as well as the development of kidney disorders [21].

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