Comparison of hemoglobin levels between hepatitis positive and negative patients in dialysis unit of a tertiary care hospital.

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INTRODUCTION

Hepatitis C virus status has an impact on hemodialysis patients with end-stage renal illness who have low Hemoglobin and Hematocrit levels. The most frequent haematological anomaly in chronic renal failure is anaemia. Patients with renal failure frequently have an iron deficiency, and treatment with erythropoietin (EPO) increases this demand. It is unclear whether higher iron storage influences to hepatitis C virus (HCV) infection or whether HCV infection helps iron accumulation, making the Hepatitis C virus infections are chronic in over 170 million people globally (HCV). HCV infection is widespread in hemodialysis (HD) facilities around the world, mostly in the Mediterranean and developing nations of the Middle and Far East, and is persistently more common among patients receiving dialysis than in the general population. In contemporary hospital dialysis facilities, nosocomial transmission of HCV infection has been documented to be a significant pathway, particularly during outbreaks of HCV. [1–4]. The most effective way to treat renal anaemia in the past was blood transfusions, its no longer required due to the use of erythropoietin (EPO).Renal anaemia must be treated with iron replacement since erythropoietin therapy increases the need for iron.

A significant route reportedly exists in modern hospital dialysis units, As it is unclear whether increased iron storage predisposes to HCV

infection or whether HCV infection facilitates iron accumulation, it is known that there is a contentious association between iron stores and HCV infection[5,6]. In addition, despite the frequent reports, the impact of HCV infection on possible iron and erythropoietin therapy is debatable.

Patients with HCV infection have elevated blood ferritin levels and hepatosteatosis, which may impair their response to treatment.[7] However, it has been noted that erythropoietin needs and levels in HCV-positive and -negative individuals differ in those with end-stage renal disease (ESRD). [8,9] and erythropoietin therapy increases the need for iron; as a result, iron supplementation is crucial in the treatment of renal failure.

LITERATURE REVIEW

Renal structural and physiological traits, as well as the theories of renal tissue injury and healing, should be taken into account while examining the pathophysiology of CKD. The kidney, ureters, and urethra make up the renal system. The system as a whole filters about 200 liters of fluid each day from renal blood flow, enabling the excretion of toxins, metabolic waste products, and excess ions while maintaining the blood's necessary components. The rate of renal blood flow, which is roughly 400 ml/100g of tissue per minute, is significantly higher than that seen in other well-perfused vascular beds including the heart, liver, and brain. Glomerular hypertension and hyperfiltration were noted by Brenner and colleagues as two key factors in the development of chronic renal illness. Thirdly, anionic macromolecules are resisted by negatively charged molecules in the glomerular filtration membrane, which act as a barrier. Plasma protein enters the glomerular filtrate through the rupture of this electrostatic barrier, which occurs in many types of glomerular damage. Fourthly, the glomerular convolute and peritubular capillary network's sequential arrangement within the nephron's microvasculature, as well as the tubuli's position downstream of the glomeruli, not only preserve theglomerulo-tubular balance but also make it easier for glomerular injury to spread to the tubulointerstitial compartment during disease.[7,8,11]. Providing abnormal ultrafiltrate to tubular epithelial cells. Because peritubular vasculature forms the foundation of glomerular circulation, some mediators of glomerular inflammatory reaction may overflow into the peritubular circulation, contributing to the interstitial inflammatory reaction typically observed in glomerular illness. Additionally, any reduction in peritubular blood flow—which, depending on the severity of hypoxia, results in tubulointerstitial damage and tissue remodeling—is caused by a drop in preglomerular or glomerular perfusion. Thus, the idea of the nephron as a functional unit is relevant to both renal pathology and renal physiology. Fifth, each of the glomerulus' distinct components, including the endothothelial, bases, visceral, and parietal epithelial cells, podocytes, and tubulointerstitial compartment in illness, should be viewed as a functional unit.[7]

Chronic kidney disease is characterised by renal fibrosis, including glomerulosclerosis and tubulointerstitial fibrosis, regardless of the aetiology. At least equally significant to the deterioration of the glomeruli is that of the tubulointerstitium (tubulointerstitial fibrosis and tubular atrophy) (glomerulosclerosis). In underprivileged neighbourhoods, where maternal health is also subpar and risk factors for unfavourable pregnancy outcomes are prevalent, hypertension and chronic renal disease are widespread. [10]

The most significant risk factor for renal programming is being tiny for gestational age, although other risk factors include being born prematurely, having a low birth weight, being large for gestational age, or having gestational diabetes and preeclampsia. This programmed risk could be reduced by improving maternal health prior to conception, promoting healthy lifestyles, and screening people who may have had developmental programming to enable early detection and intervention. A large number of newborns are born prematurely and too tiny,[9] ,[16]. Renal insufficiency or reduced renal reserve are the earliest symptoms of chronic kidney

disease (CKD), which can eventually lead to renal failure (end-stage renal disease). Decline of kidney function for 3 months or more ANDEvidence of kidney damage (e.g. albuminuria or abnormal biopsy) OR GFR <60 mL/min/1.73 m2.

HEPATITIS C VIRUS INCIDENCE: Hepatitis C virus (HCV) infection affects around 71 million individuals globally, and it is the leading cause of cirrhosis and hepatocellular carcinoma (HCC) in over 399,000 fatalities[1]. Because the research mostly focuses on liver-related consequences including cirrhosis and HCC, HCV-related morbidity and death are frequently underestimated. A sizable percentage of HCV patients experience a variety of extrahepatic symptoms [2]. These include cardiovascular disease events, mixed cryoglobulinemia/cryoglobulinemia vasculitis, B-cell non-lymphoma Hodgkin's (NHL), type 2 diabetes mellitus, glomerulonephritis, renal insufficiency, lichen planus, and porphyria cutaneatarda. The connection between chronic HCV infection and chronic renal disease is the main topic of this review (CKD).

HCV and CKD: Since the moment of its discovery, HCV has been linked to CKD [5]. The viral infection could contribute to or result from CKD [6]. Although the HCV virus has been connected to CKD in a number of additional ways [6, 7], the characteristic HCV-induced glomerulonephritis symptom has been widely reported [7]. The relationship between HCV infection and initial CKD, as well as the quick progression of CKD to end-stage renal disease (ESRD) requiring a transplant or hemodialysis, is becoming increasingly clear.

Prevalence of HCV infection in patients on dialysis: Compared to the general population, those receiving chronic hemodialysis have a greater prevalence of HCV infection [8]. HCV prevalence rates range from 4% to 9% in the majority of high-income nations, although they are substantially higher and vary greatly among other nations in the Middle East, North and Sub-Saharan Africa, Asia, and Eastern Europe [9]. The mean HCV prevalence in the Dialysis Outcomes and Practice Patterns Study (DOPPS) study, a prospective observational study of HCV prevalence and seroconversion rates among dialysis patients in high-income countries, was 13.5%, ranging from 2.6% to 22.9% between different participating countries. Longer dialysis stays were linked to higher HCV prevalence. Male gender, black race, diabetes, hepatitis B virus (HBV) infection, previous kidney transplant, and drug or alcohol addiction. Human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS), HBV infection, and recurrent cellulitis or gangrene were linked to extended dialysis stays, HCV seroconversion, and these conditions. [10]

The study discussed the variations in HCV prevalence and rate of seroconversion across countries and hemodialysis facilities on three continents.HCV spreads via the parenteral route, primarily through percutaneous contact with blood, making dialysis patients more susceptible to infection. In reality, the primary mode of HCV transmission in dialysis centres is nosocomial transmission, and patient to patient transmission of HCV infection has been seen [11]. Current guidelines recommend screening all patients initiating chronic hemodialysis as well as those who transfer between dialysis facilities or dialysis modalities and routine surveillance testing every 6 months thereafter [9].

HCV prevalence and seroconversion rates have declined significantly following routine implementation of infection control practices and regular screening and follow up of dialysis patients for HCV infection [12,13]. Lapses in standard infection control practices, including sharing contaminated hemodialysis machines and multidose vials and breaches in cleaning and disinfection practices, are responsible for outbreaks of infection [14].

HCV Transmission in CKD Patients: HCV spreads via parenteral route, primarily through percutaneous exposure to blood, making dialysis patients more prone to acquiring infection. In fact, nosocomial transmission is the main method of spread of HCV in dialysis units and patient to patient spread of HCV infection has been documented [11]. Current guidelines recommend screening all patients initiating chronic

hemodialysis as well as those who transfer between dialysis facilities or dialysis modalities and routine surveillance testing every 6 months thereafter [9].

HCV prevalence and seroconversion rates have declined significantly following routine implementation of infection control practices and regular screening and follow up of dialysis patients for HCV infection [12,13]. Lapses in standard infection control practices, including sharing contaminated hemodialysis machines and multidose vials and breaches in cleaning and disinfection practices, are responsible for outbreaks of infection [14]. The identification of acute HCV infection in a patient on hemodialysis should be reported to the appropriate public health authorities and all patients in the same center must be screened again. Adherence to currently recommended infection control practices can effectively control this problem [9].

HCV infection is independently associated with microalbuminuria, and a higher risk and shorter time to development of CKD [11,14]. Studies have shown that HCV infection is associated with up to 2.2 fold higher mortality [10], and a progressive loss of kidney function leading to higher risk of developing ESRD [1]. The risk of developing CKD is higher in the younger population (age <50 years), men, and those with co-existing diabetes, hypertension (HTN),hyperlipidemia, or cirrhosis [19,20]. Multiple meta-analyses have confirmed these associations, with HCV infection being associated with up to 51% increase in the risk of proteinuria and 43% increase in incidence of CKD. Longer duration of infection and lower estimated glomerular filtration rate (eGFR) at baseline are associated with a higher risk [12]

The association of HCV with CKD is also evident among other patient groups. Co-infection with human immunodeficiency virus (HIV) increases the risk of CKD [14,15], with the risk linearly associated with HCV viral load [4,5]. Among patients with primary glomerulonephritis, HCV infection is associated with increased risk of progression of CKD [14], and in persons with diabetes, HCV is a predictor of poor renal survival leading to early ESRD development. This association is independent of age, race, sex, blood pressure, proteinuria, diabetes duration, and diabetic nephropathy [7,8].HCV GENOTYPE DISTRIBUTION A total of 6 different genotypes and multiple subtypes of HCV, each with a different geographic distribution have been identified. Genotype 1 is the most prevalent qgenotype worldwide. Subtype 1b is more frequent in Europe and Japan while subtype 1a in the United States. Genotype 2 is prevalent in North America, Europe, Japan (Subtypes a and b) and in northern Italy (subtype c). Genotype 3a is frequently seen in India and in European and American drug abusers while genotype 4 is encountered in North Africa, Middle East and among European drug abusers. Genotype 5 has been found in South Africa, genotype 6 in Hong Kong, genotypes 7, 8, 9 in Vietnam and genotypes 10 and 11 in Indonesia[6-8]. There are no firm data concerning the distribution of HCV genotype among HD patients. In studies conducted in the Netherlands, France, Morocco, Mexico and Turkey, there was a predominance of genotype 1b among patients on HD[9,10]. In a study from the United States, subtype 1a was the most frequent among dialysis patients while in Italian HD patients subtypes 2a and 3a predominated. Some of these studies showed a different genotype distribution in dialysis patients than in the general population, some others did not. In general,subtype 1a seems to be more frequent among HD patients than in the general population[9].An interesting point is that dialysis patients are susceptible to mixed genotype infections attributed to multiple exposures in the dialysis environment. Mixed infections are not often identified due to their short duration and to the lack of sensitivity of the molecular techniques. When more sensitive techniques were applied, 13% of HCV infected HD patients were diagnosed with a mixed infection. In these patients, one of the transmitted subtypes usually prevails in the course of the disease and it is in general subtype 1a[9,11]

A higher incidence and progression of chronic kidney disease (CKD), as well as higher mortality in CKD and renal transplant patients, are all linked to hepatitis C virus (HCV) infection. Direct acting

antiviral drugs (DAAs) have completely eradicated the HCV virus in 90–100% of patients who have received treatment. In patients with CKD and renal transplants, DAAs exhibit outstanding safety and tolerability profiles.[9]

The availability of newly available direct acting anti-viral agents has revolutionized the treatment of HCV in persons with advanced CKD and undergoing dialysis. With these regimens, viral eradication can be attained in 90–100% of the treated patients. The safety, tolerability, and efficacy of these drugs in renal transplant patients have also made it possible to use HCV-infected grafts and successful virus eradication at a later stage.[6,9,14]

HCV and Anemia in CKD: In some patients, bone marrow failure and aplastic anemia develop after an episode of hepatitis. Interferon and ribavirin are two drugs that have been used to treat hepatitis C for many years. They've been proven to increase the likelihood of developing anemia in people who take them.

Some of the newer drugs used to treat hepatitis C also have this side effect. Finally, anemia is a recognized complication of treatment of chronic hepatitis C with a combination of interferon and ribavirin: anemia in this context is predominantly caused by ribavirin-induced hemolysis[4].Interferon and ribavirin are two drugs that have been used to treat hepatitis C for many years. They've been proven to increase the likelihood of developing anemia in people who take them. Some of the newer drugs used to treat hepatitis C also have this side effect.

Material s and Methods

It is a Case control Study and was conducted at Department Of Nephrology AIMS Muzaffarabad AJ&K. Total 102 Samples were analyzed over a period of 6 months, results were calculated via SPSS Softwar.

DATA ANALYSIS &RESULTS

Case Processing Summary

	Cases					
	CKD HCV positive		CKD HCV Negative		Total	
	N	Percent	N	Percent	N	Percent
Hb levels CKD HCV Positive *and Hblevels CKD HCV Negative	29	28.2%	73	72%	102	100.0%

HCV Positive CKD Patients Treatment and PCR Results

On Anti HCV treatmen	**No Anti HCV Treatment**	**PCR positive after treatment**	**PCR Negative after treatment**	**Total**
29	00	11	18	29

Hb		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	7.5 to 8.5 g/dL	6	20.6	20.7	20.6

10 to 11.5g/dL	8	27.5	27.6	41..3
8.5 to 10.5g/dL	12	41.3	41.4	10.3 27.6
>11.5g/dl	3	10.3	10.3	100.0
Total	29	41.4	100.0	
Total	29	100.0		

Hb wise Complications (HCV Positive)

	Cramps	**Nausea**	**Chest pain**	**Clotting Set**	**Hypotension**
7.5 to 8.5 g/dL	02	----	01	01	02
10.5 to 11.5 g/dL	01	01	01	01	04
8.5 to 10.5 g/dL	05	02	02	01	02
> 11.5 g/dL	01	----	----	01	01

Hb wise Complications (HCV Negative)

	Cramps	**Nausea**	**Chest pain**	**Clotting Set**	**Hypotension**	**Total No of patients**
7.5 to 8.5 g/dL	03	01	01	01	---	06
10.5 to 11.5 g/dL	12	04	02	----	02	20
8.5 to 10.5 g/dL	10	06	02	02	04	24
> 11.5 g/dL	03	02	----	10	08	23

Hb wise Duration of Dialysis (HCV Positive

	<1 to 2 years	**3 to 6 years**	**7 to 12 years**	**Total Patients (29)**
7.5 to 8.5 g/dL	**02**	**03**	**01**	**06**
10.5 to 11.5 g/dL	**04**	**02**	**02**	**08**
8.5 to 10.5 g/dL	**05**	**03**	**04**	**12**
> 11.5 g/dL	**01**	**01**	**01**	**03**

Hb wise Duration of Dialysis (HCV Negative)

	<1 to 2 years	**3 to 6 years**	**7 to 12 years**	**Total Patients(73)**
7.5 to 8.5 g/dL	**03**	**02**	**01**	**06**
10.5 to 11.5 g/dL	**04**	**12**	**04**	**20**
8.5 to 10.5 g/dL	**04**	**06**	**14**	**24**
> 11.5 g/dL	**03**	**09**	**11**	**23**

Discussion:

Total **102** patients were included in this study, from which 29 CKD patients were Hepatitis C

positive and 73 CKD patients were Hepatitis C Negative. From Hepatitis C Positive CKD patients which are **28.2%6** patients whose Hemoglobin levels are between 7.5 and 8.5 g/dL (about 20%) Total **12** patients (about 41%)having Hemoglobin levels between 8.5 and 10.5g/dL. Also **8** patients (27%) having Hemoglobin levels were between 10.5 and 11.5g/dL and 4 patients (about 10%) having Hemoglobin levels greater than 11.5g/dL . **70%** CKD Patients were Hepatitis C Negative in our study tenure.

Anti HCV therapy is the main cause of low Hb levels in Hepatitis C positive CKD patients. Hepatitis C can lower the red blood cell count. This is most likely due to the side effects of the medications being used to treat hepatitis, however it is possible that associated kidney damage or more rare instances of anemias can be caused by hepatitis. Hematological changes occurred in Patients such as mechanism of hematopoiesis is deadly effected and also Iron deficiency Anemia most prevalently in CKD HCV positive patients due to depletion of iron stores in the body. Idiopathic thrombocytopenia **(ITP)** is also observed in overall cases of CKD

CONCLUSION:

Hemoglobin levels in CKD Hepatitis C Positive Patients comparatively low as compared to Hepatitis negative CKD Patients due to Hepatitis C treatment in CKD patients and most patients of CKD were suffered by Iron deficiency Anemia and Idiopathic Thrombocytopenia. Hemoglobin levels in CKD can be improved by Iron therapy and Transfusion.

SUGGESTIONS/RECOMMENDATIONS

- Effective Iron therapy is mandatory to avoid anemia.
- Safe and healthy blood transfusions
- Avoid extra anti HCV drugs
- Maintain Biosafety controls and avoid from hazards
- There is minimum direct contact of HCV and Non HCV CKD patients.
- Health department should arrange awareness sessions regarding HCV & CKD.
- Hospital Administration should provide PPEs to
- Use of WHO approved SOPs & protocols can minimize the risk of developing Hep C.
- Safety of staff and patients should be at top priority.
- Training of staff is mandatory
- Workshops should be held for Health care providers.

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