

Incidence of Hepatitis C Virus in Chronic Kidney Disease Patients on Long Term Hemodialysis

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Abstract

Objectives: The objective of the study was to find the frequency of hepatitis C virus in patients with chronic kidney disease on long term hemodialysis and its associated factors.

Methodology: Descriptive cross-sectional study was done in Pakistan Institute of Medical Sciences (PIMS), department of Nephrology, from September to December 2021. All patients on regular hemodialysis aged more than 12 years, having at least 20 cycles of hemodialysis were included in the study by consecutive sampling. Qualitative detection of Anti-HCV antibodies was carried out/to detect hepatitis C-infection. A self-structured questionnaire was designed and all the data was entered on that questionnaire. Data was analyzed on SPSS version 25.

Results: Total 200 patients were enrolled in the study, and males were 121 (60.5%), females 79 (39.5%) and the mean age was 57.6±9.8 years. Out of 200 patients, 36% patients were seropositive for hepatitis C. It was significantly associated with duration of hemodialysis, surgery history and blood transfusion ($p \leq 0.05$).

Conclusion: Hepatitis C virus prevalence is very high among patients on long term hemodialysis and it is associated with dialysis duration, surgery history and blood transfusion.

Keywords: Hepatitis C, chronic; Kidney failure, chronic; Renal dialysis.

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Introduction

The most common viral infection in developing countries is Hepatitis C in hemodialysis patients, causing significant morbidity and mortality.¹ Hepatitis C virus is a blood borne in nature, transmitted by introduction to small volume of blood which results in acute as well as chronic infections. A small percentage of patients are diagnosed during the initial phase of hepatitis C-infection as it is usually asymptomatic.² Likewise, in chronic patients, Hepatitis C virus stands undiagnosed as it remains asymptomatic until years subsequent to getting infected primarily due to development of symptoms, typically as a result of damage to liver parenchyma.³ In the early 1990s, diagnostic testing for HCV became available. This was the period when the hepatitis C virus referred as non-A, non-B hepatitis.⁴ In

developing countries, hepatitis C virus is an important cause of interstitial nephritis and glomerulonephritis, resulting in chronic kidney disease (CKD).⁵ According to DOPPS (Dialysis Outcomes and Practice Patterns Study) report 1996–2015, the trends in the incidence, risk factors and prevalence for hepatitis C virus were assessed as per the definition stated by positive antibodies or a documented diagnosis. Hepatitis C virus prevalence was observed to be approximately 10% among prevalent hemodialysis patients.⁶ Documented anti HCV antibodies are the basis for diagnosis of HCV. A major factor that leads to infection with hepatitis C virus is long term hemodialysis. In Pakistani population, 28% of hepatitis C was reported to be caused by dialysis, having an annual incidence of 4 million cases (3%) globally.⁷ The high risk of seroconversion is a considerable issue in hemodialysis patients (appearance of anti-HCV antibody after exposure), due

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to multiple factors, such as frequent needling, multiple blood transfusions, extracorporeal circulation, blood sampling and decreased cellular immunity. HCV infection, although slow progression, seems to have an atypical course in this population as a result of delayed seroconversion which is secondary to poor immunity and nutrition. Therefore, a seronegative picture is observed in most of such patients. ELISA (enzyme linked immunosorbent assay) is the most common method used in a dialysis center which usually misses patients who are seronegative but are PCR positive.⁸ The objective of the study was to find the frequency of hepatitis C virus in patients with chronic kidney disease on long term hemodialysis and its associated factors.

Material and Methods

Descriptive cross-sectional study was done in Pakistan Institute of Medical Sciences (PIMS), department of Nephrology, from September to December 2021. All patients on regular hemodialysis aged more than 12 years, having at least 20 cycles of hemodialysis were included in the study by consecutive sampling after informed verbal consent from the patients. Patients having history of chronic hepatitis C infection before commencement of hemodialysis either treated or untreated were excluded. Ethical approval was taken from hospital research ethics committee.

After necessary aseptic precautions, 5cc of blood was collected by venipuncture and transferred to a clean sterilized tube and allowed to clot (non-hemolyzed sample). For further testing, serum was separated and stored in two labeled Eppendorf tubes in equal amounts. One Eppendorf stored at -20°C for long-term stock storage if repeat testing is required. The second Eppendorf was stored at 2-8°C and tested within one hour. Qualitative detection of Anti-HCV antibodies was carried out to detect hepatitis C-infection. Test was performed on MK Bio GmbH Robert-Bosch-Breite 23, 37079 Gottingen Germany, commercially available kits were used to measure antibodies by enzyme-linked immunoassay (EIA). A self-structured proforma was designed and all the data was entered including sociodemographic variables.

Data was entered and analyzed on SPSS version 25. Descriptive statistics were used to describe data such as for quantitative variables mean and standard

deviation, while for qualitative variables frequencies and percentages. Chi-square test was used to study the association of HCV with different variables. A p value ≤ 0.05 was considered significant.

Results

Total 200 patients were recruited in this study, and males were 121 (60.5%), females 79 (39.5%) and the mean age was 57.6 ± 9.8 years. Major cause of renal failure was chronic glomerulonephritis, followed by diabetic nephropathy and hypertension, however a massive percentage of patient's cause was unknown (Table I). Details of basic characteristics of patients like cause of renal failure, dialysis duration, history of surgical procedures, blood transfusion, dialysis schedule and hepatitis B vaccination is given (Table I).

Study outcomes	Number	Percent
Renal failure		
Chronic glomerulonephritis	46	23%
Diabetic nephropathy	43	21.5%
Hypertension	22	11%
Polycystic kidney	7	3.5%
Chronic pyelonephritis	4	2%
Calculus	8	4%
Not known	70	35%
Dialysis duration		
≤ 1 year	61	30.5%
1.1 – 2.0 years	47	23.5%
2.1 – 3.0 years	17	8.5%
3.1 – 4.0 years	36	18%
≥ 4 years	39	19.5%
Surgery history		
Blood transfusion	71	35.5%
Whole blood	27	13.5%
Fresh frozen plasma	7	3.5%
Pack cells	37	18.5%
Dialysis schedule		
Twice a week	189	94.5%
Thrice a week	11	5.5%
Vaccinated for HBV		
	49	24.5%

Out of 200 patients, 36% (n=72) patients were seropositive for hepatitis C. It was significantly associated with duration of hemodialysis, history of surgery and blood transfusion (Table II). Hepatitis C seroprevalence was significantly higher in patients with longer duration of hemodialysis, having history of surgery and blood transfusion. Hepatitis B vaccination status and schedule of dialysis was insignificant associated with seropositivity for hepatitis C (Table III).

Table II: Association of HCV infection (seroprevalence) with dialysis duration, surgery history and blood transfusion, (n=200)			
Study Parameters	Positive cases (n = 72)	Negative cases (n = 128)	p value
Duration of dialysis			
≤ 1 year	7 (11.5%)	54 (88.5%)	0.001
1.1 – 2.0	9 (19%)	38 (81%)	
2.1 – 3.0	11 (64.7%)	6 (35.3%)	
3.1 – 4.0	20 (55.6%)	16 (44.4%)	
≥ 4 years	25 (64.1%)	14 (35.9%)	
History of surgery			
Yes	17 (85%)	3 (15%)	0.001
No	55 (30.6%)	125 (69.4%)	
Blood transfusion			
Yes	45 (63.4%)	26 (36.6%)	0.001
No	27 (21%)	102 (79%)	

Table III: Association of seroprevalence of HCV infection with vaccination status and schedule of dialysis, n=200			
Study Parameters	Positive cases (n = 72)	Negative cases (n = 128)	p value
Vaccinated against Hepatitis B			
Yes	17 (34.7%)	32 (65.3%)	0.826
No	55 (36.4%)	96 (64.6%)	
Schedule of dialysis			
1-2 / week	66 (35%)	123 (65%)	0.187
3 / week	6 (54.5%)	5 (45.6%)	

Discussion

We found that seroprevalence of anti-HCV antibodies was 36% in our population, which is quite high. Patients on hemodialysis for more than one year, having history of surgical procedures and history of blood transfusion were found to have significantly higher seroprevalence for hepatitis C virus.

Glomerulonephritis (23%), diabetes mellitus (21.5%) and hypertension (11%) were most common causes of chronic kidney disease leading to dialysis in our study. No cause was found in 35% patients. This is in accordance with previous literature as diabetes, hypertension, vascular disease and glomerulonephritis are the common causes of chronic kidney disease worldwide.¹ Hypertension and diabetes were found as most common of CKD in dialysis patients in a study conducted by Malekmakan et al, comparable with our results but glomerulonephritis was found as cause in just 3.7% patients in contrast with our results.⁹ This difference may be due to geographic difference in the study population because this study was conducted in Iran.

In hemodialysis patients the prevalence of HCV infection varies from 1.4%–28.3% in developed countries and

4.7%–41.9% in developing countries depending upon the region,⁵ higher in developing world as compared to developed world. As Pakistan is a developing country our findings are in accordance with these results, prevalence was 36% in our study.

Previous studies from Pakistan also show high prevalence of HCV in dialysis patients. A study shows that, the prevalence of chronic hepatitis C in patients undergoing dialysis was 25.5% in Pakistan.⁷ Another observational study conducted in Punjab showed 53.4% seroconversion rate among patients on chronic hemodialysis,⁸ these findings are almost comparable with our results, showing that HCV prevalence is still very high in Pakistan while it is decreasing with time in other countries,⁷ this situation is alarming. No difference was found in prevalence in Pakistan from 2006 (32.3%) to 2019 (36.4%) in a meta-analysis also, rather it showed that prevalence has increased over the years,¹ it was 36% in our study as well comparable with this meta-analysis. This indicates that there is a lack of education and awareness regarding HCV transmission among health care workers and patients. There is also non-adherence or gaps in the implementation of practices required to decrease the incidence and prevalence of HCV in hemodialysis patients, like use of unsterilized instruments, adequate use of erythropoietin, adequate screening of HCV for donated blood and use of separate dialysis machines for HCV positive patients leading to increased prevalence.

Literature review shows that prevalence was quite high in our study as compared to neighboring countries. Prevalence is around 11% in Iran as shown by a meta-analysis.¹⁰ If we compare our results with India, again situation is disturbing because prevalence is two times higher in our study, it was found 18.8% in India.¹¹ These results demand urgent measures to control increasing prevalence of HCV among dialysis patients in Pakistan.

Long term hemodialysis was significantly associated with the prevalence of HCV in our study. Longer duration of hemodialysis was linked with increased prevalence of HCV in a study conducted in Kosovo supporting our results.¹² A study from Pakistan also shows that history of dialysis for more than two years was significant risk factor for HCV seroprevalence.¹³ All these results support our findings. Long term hemodialysis exposes the patients to infected

equipment, dialysis machines and blood products leading to increased chance of HCV infection.

Surgery history and blood transfusion were also linked with the increased prevalence of HCV in our study. These two are the risk factors even in the general population.¹⁴ Unsterilized surgical instruments and infected blood products are responsible for the increased prevalence in patients with history of surgery and blood transfusion. In developed countries, improved healthcare conditions, sterilization measures, use of screened blood and blood products have reduced the incidence of iatrogenic hepatitis C, but the virus is still transmitted through uncontrolled blood transfusions and non-sterile injections and instruments, where spread from epidemic continues to developing countries.¹⁵ An estimated 40% of blood transfusions are still not screened for any infectious diseases in Pakistan.¹⁶ Many studies evaluating the risk factors for HCV in hemodialysis patients have shown that patients having surgery history and blood transfusion are at increased risk of HCV infection supporting our findings.^{17,18}

Our study has some limitations, firstly it was a small sample size and single center study and secondly, we studied few risk factors associated with HCV infection. Future multi center studies required to confirm our findings.

Conclusion

The study concluded that hepatitis C virus prevalence is very high among patients on long term hemodialysis and it is significantly associated with duration of dialysis, history of surgery and blood transfusion.

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