

## Research Article

# Prevalence of hepatitis B and C viruses among hemodialysis patients in Southern West Bank, Palestine

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### ABSTRACT

**Background:** In addition to severe renal impotence and decline of immune status, the high prevalence of hepatitis B and C virus's infection represents one of the most critical clinical problems that are implicated in the progression of severe complication among hemodialysis patients. This study was performed to estimate the prevalence of hepatitis B and C viruses among hemodialysis patients and to recognize the pattern of chronic disease that will access to the renal failure.

**Methods:** In this retrospective cohort study, data were collected from 252 hemodialysis patients for the presence of HBsAg, anti-HCV antibody, and the primary chronic disease that causes renal failure, in March 2013 from three governmental hospitals in southern West Bank in Palestine.

**Results:** From 252 HD patients, 59% were male and 41% were female. 78% of them ranged between 15 and 65 years. 6.7% of all patients were HBsAg positive and 8.7% were anti-HCV antibodies are positive. Diabetes mellitus (33.7%), hypertension (23.7%), and chronic nephritis (6.0%), represent the most known primary chronic diseases that causes end stage renal disease.

**Conclusions:** The role of the chronic diseases in accession to the renal failure, and the high prevalence of hepatitis B and C virus infection among hemodialysis patients compared to the normal healthy population indicate a causative relation between hemodialysis and hepatitis virus transmission.

**Keywords:** Hemodialysis, HD, CKD, HBV, HCV, HBsAg, GFR, DM, NSAIDs, ESRD, Renal

### INTRODUCTION

Infections by hepatitis C virus (HCV) and hepatitis B virus (HBC) are the major problem in hemodialysis (HD) patients.<sup>1-3</sup> The prevalence of HCV and HBV infection in patients undergoing dialysis is greater than that in general population. This is because these patients are at high risk of acquisition of this infection and also because they are monitored monthly by laboratory examinations that permit early diagnosis of the infection.<sup>5</sup>

Hemodialysis patients are at high risk for viral hepatitis infections, the high level of prevalence have been related

to several factors including; the duration of dialysis treatment, the number of blood units and blood products from non-tested blood donors transfused, organ transplantation from infected donors, administration of drugs with contaminated syringes, occupational exposure to blood, perinatal infection, sexual transmission, and the great variety of human activities with potential exposure to blood. Several possible biological transmission models exist, such as from tattoos, barber shops, circumcisions, acupuncture, prolonged vascular access, the potential for exposure to infected patients and contaminated equipment, and impaired cellular immunity.<sup>1,3,5,6</sup>

The incidence of HBV infections among HD patients is less than that with HCV infections. This is due to the following of standard precautions, isolation, blood product screening and the availability and implementation of an effective vaccination. In case of HCV infections the prevalence in HD units has been progressively increasing. The larger increase is due to lack of effective vaccine, inadequate infection control policies, inadequate isolations of infected patients, limited resources available to treat rapidly growing HD population, contamination of dialysis machine, improper sterilization, inadequate training staff and limited numbers of dialysis machines and overcrowding of HD units.<sup>3</sup>

The prevalence of hepatitis C and B infections among hemodialysis patients are contrastive worldwide. In the Arab countries, the prevalence of chronic hepatitis C infections among HD patients ranged from 27% in Lebanon, to 75% in Syria, but the prevalence of chronic HBV infections ranged from 2% in Morocco, to 11.8% in Bahrain.<sup>7</sup> In Palestine there was no documented data or previous studies reported on the prevalence of hepatitis B or C in West Bank. In Gaza the prevalence of HCV and HBV among HD patients was 22% and 8.1% respectively.<sup>7</sup>

The main objectives of this retrospective study is to estimating the prevalence of HCV and HBV infections among hemodialysis patients in Southern West Bank, major risk factors for transmission of these viruses among HD patients, and the approach and protocol used in hospitals to prevent viral infection transmission.

#### **Litreture review**

##### **Hepatitis B virus (HBV)**

Approximately 3 billion people have been exposed to hepatitis B virus and there are an estimated 350 to 400 million chronic carriers worldwide, hepatitis B virus (HBV) is a member of the hepadnavirus group, partial double-stranded DNA viruses which replicate unusually, by reverse transcription.<sup>8-10</sup> Hepatitis B virion is a 42-nm particle comprising an electron-dense core (nucleocapsid) 27 nm in diameter surrounded by an outer envelope of the surface protein (HBsAg) embedded in membranous lipid derived from the host cell.<sup>11,12</sup> The nucleocapsid of the virion consists of the viral genome surrounded by the core antigen (HBcAg).<sup>13</sup> The specificity of HBV for liver cells is based on two properties: viral specific receptor on hepatocyte cell membrane (facilitate entry), and transcription factors found only in the hepatocyte, that enhance viral mRNA synthesis (act post entry).<sup>12</sup>

Hepatitis B virus produce hepatitis B core antigen (HBcAg), hepatitis B envelope antigen (HBsAg), hepatitis B x antigen (HBxAg), and hepatitis B surface antigen (HBsAg) that could contribute to the HBV life cycle.<sup>9</sup> In contrast the host immune system produce

antibodies to these viral antigen. Anti-HBc and anti-HBs, and so different combinations of markers are used to identify different phases of HBV infection.<sup>14</sup> The detection of viral DNA in the serum is strong evidence that infectious virions are present.<sup>12</sup>

##### **HBV vaccination and CKD**

According to the unfortunate effect of HBV infection, hepatitis B vaccination in early stage of (chronic kidney disease) CKD is an obligation to avoid exacerbation of patient conditions. In early stage of CKD patients have less severe immune abnormalities, low chance of viral sero-conversions, stronger immune response to vaccination, avoidance of post dialysis infection, and prevention of viral transmission to healthy staff and individuals.<sup>15</sup>

##### **Hepatitis C virus (HCV)**

Approximately 160 to 170 million people are infected with HCV, hepatitis C is enveloped, small (55–65 nm), positive sense, single stranded, RNA virus. It is a member of the hepacivirus genus, in the family of Flaviviridae, There are seven HCV genotypes, with many subtypes: a, b, c, and about 100 different strains: 1, 2, and 3, based in the sequence of the HCV genome. Genotype 4 is characteristics for the Middle East, Egypt and central Africa, and genotype 5 is almost exclusively found in South Africa.<sup>8,16-18</sup>

Diagnosis of acute infection is often missed because a majority of infected people have no symptoms. The presence of antibodies against the hepatitis C virus indicates that a person is or has been infected. The hepatitis C virus recombinant immuno blot assay (RIBA) and hepatitis C virus RNA testing are used to confirm the diagnosis (Figure 1).<sup>19</sup> However, a new entity of HCV infection was first described in 2004 in patient with persistently elevated liver function tests and who were anti-HCV and serum HCV RNA negative.<sup>20</sup>

Occult HCV infection is related to the persistence of necro-inflammation activity in the liver of sustained patient of either, anti-HCV positive individuals with normal value of liver enzymes, or anti-HCV negative patients with abnormal level of liver enzymes. In this way HCV RNA can be detected in liver biopsy or it could be present in peripheral blood mononuclear cell (PBMCs).<sup>20</sup>

##### **Chronic kidney disease (CKD)**

According to kidney disease outcome Quality Initiative (KDOQI), chronic kidney disease (CKD) defined as irreversible loss of renal function, or persistence of kidney damage for at least 3 months duration caused by structural or functional abnormalities with or without a decreased glomerular filtration rate (GFR).<sup>4,21</sup> CKD is usually asymptomatic until its most advanced state.<sup>22</sup> CKD has been categorized into five stages based on level

of glomerular filtration rate (Table 1), the presence or absence of evidence of renal injury, and screening for proteinuria.<sup>4,23,24</sup>

**Primary disease cause ESRD**

End stage renal disease (ESRD) is the last stage of CKD or dialysis, in which the GFR is less than (15 ml/min/1.73m<sup>2</sup>) (Table 1).<sup>4</sup> Diabetes mellitus, and hypertension are the most primary diseases that are implicated in the ESRD.<sup>6,21-23,25</sup> In addition, polycystic kidney disease, pyelonephritis, in many unknown causes, patient without primary renal disease comes to hospital with complete or partial renal interstitial fibrosis result from long-term use of medicines that can damage the kidneys, such as; (NSAIDs), and certain antibiotics.<sup>4,25,26</sup>

**METHODS**

In this retrospective cohort study, HD patient’s data were obtained from the patients records in the intended hospital, and HD patient’s files from Palestinians Ministry of Health in March 2013. The data were includes all 252 HD patients in Southern West Bank (Hebron and Bethlehem ), 155 patients at HD department in Hebron Hospital, 30 patients at HD department in Yatta Hospital, and 72 HD patients at Beit Jala Hospital in Bethlehem. Clinical data such as age, gender, HBsAg and anti-HCV antibody, and the primary cause of renal disease in the end stage of kidney disease (ESKD) were obtained after obtaining permission from the concerned hospitals through the provision of papers on research and obtain approval.

All patients had serological testing for HBV surface antigen and antibodies to HCV at the time of initiation of hemodialysis and routinely every three months. The HBsAg and anti-HCV antibodies titers were performed using enzyme linked immunosorbent assay (ELISA). The positive anti-HCV antibody test was confirmed by using recombinant immunoblot assay (RIBA), detecting of HBV-DNA and HCV-RNA by polymerase chain reaction (PCR) technique, and real time PCR (RT-PCR) for viral load to follow-up treatment of infection.

**RESULTS**

From 252 HD patients, 149 (59%) of them were male and 103 (41%) were female (Table 1). The age ranged between 13 to 85 years. 3 (1.2%) less than 15 years, 196 (77.8%) between 15 to 64 years, 53 (21.0%) years over 65 years.

In this study, 39 (15.4%) patients were either hepatitis B virus, or hepatitis C virus are positive, 22 (8.7%) patients were HCV positive, and 17 (6.7%) patients were HBV positive.

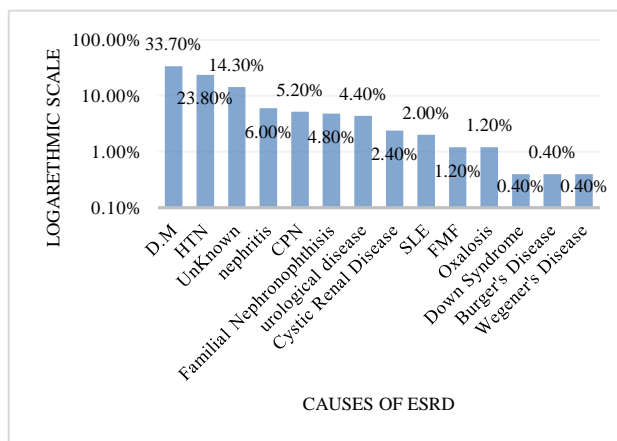
Diabetes mellitus, hypertension, and chronic nephritis are the most common causes of renal failure (dialysis) with

33.7%, 23.8%, 6.0% respectively. 14.3% of 252 patients were unknown causes (Figure 1).

**Table 1: National kidney foundation’s kidney disease outcomes quality initiative (NKF-K/DOQI) stages of chronic kidney disease.<sup>4</sup>**

Stage	Description	GFR (ml/min/1.73m <sup>2</sup> )
1	Kidney damage with normal or increased GFR	>90
2	Kidney damage with mild decrease in GFR	60-89
3	Moderate decrease in GFR	30-59
4	Severe decrease in GFR	15-29
5	Kidney failure	<15 or dialysis

GFR: glomerular filtration rate



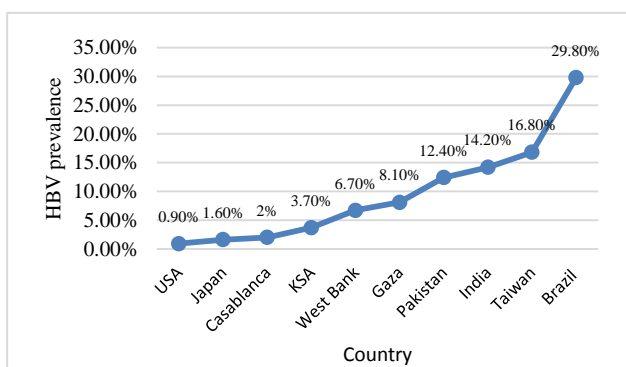
**Figure 1: Bar chart represent the frequency of primary renal diseases that causes end stage renal disease (dialysis).**

**DISCUSSION**

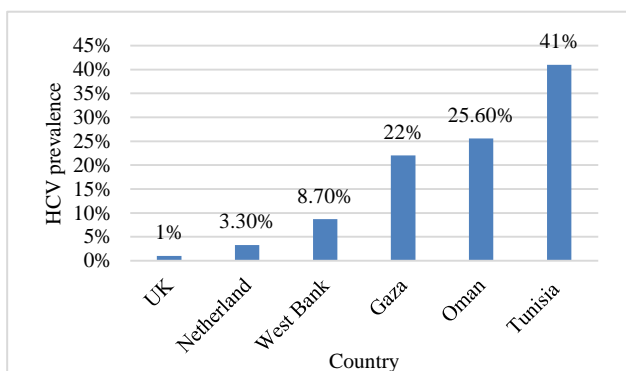
Viral Hepatitis remains a major hazard for the patients in HD units.<sup>27</sup> HCV become the major form of viral hepatitis among HD patients specially after the decline in incidence of HBV infection due to several factors including vaccination and screening of transfused blood for HBV.<sup>7</sup> In West Bank especially southern part, the prevalence of hepatitis B and C among HD patients was not previously investigated and their related risk factors were not assessed. This study evaluate the prevalence of hepatitis B and C among HD patients and risk factor that may associated with transmission of viral hepatitis among them.

In this study, the overall prevalence of HBV in HD patients in southern West Bank was 6.7 % compared with a prevalence rate of HBV among healthy blood donors in Nablus 0.81%, and 2.3% the prevalence of HBV among healthy blood donors in Gaza according to last report of MOH.<sup>7,28</sup> This prevalence is higher than that in the USA (0.9%), Japan (1.6%), Casablanca (2%), Saudi Arabia

(3.7%), Jordan (5.9%), but lower than Gaza (8.1%), Kenya (8%), Italy (9.2%), Bahrain (11.8%), Pakistan (12.4%), India (14.2%), Taiwan (16.8%), and Brazil (29.8%).<sup>7,28,30</sup> The prevalence of HCV among hemodialysis patient in southern west bank in this study was (8.7%), this prevalence is higher than that in Mortimer in UK (1%), and Schmeerberger in Netherlands (3.3%). But lower than that in Gaza strip (22%), Al-Dahnry in Oman (25.6%), Hachicha in Tunisia (41%) (Figure 2 and 3).<sup>7,28</sup>



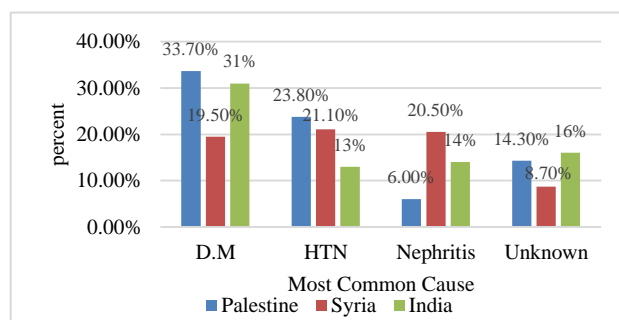
**Figure 2: Line chart represent HBV prevalence among hemodialysis patients in different region and country worldwide.**



**Figure 3: Bar chart represent prevalence of HCV among hemodialysis patient in different region and country worldwide.**

The relatively high prevalence rate of hepatitis viral infection between hemodialysis patients in Palestine according with datum about viral hepatitis infection between healthy blood donors and workers suggest that HD patients is more exposed to infection than those peoples who is away from direct contact with hospitals departments, medical equipment and medical staff. Several recent studies have reported nosocomial patient to patient transmission of viral hepatitis infections among HD patients. Thus, lack of strict adherence to standard precautions by the staff and sharing of articles such as instruments or multi-dose drugs might be the main mode of nosocomial spread of viral hepatitis among HD patients.<sup>27</sup>

Diabetes mellitus (DM), hypertension (HTN), nephritis and hereditary are considered to be the most primary disease that causes end stage renal disease with (33.7%), (23.8%), (6%), and (7.8%) respectively. This epidemiology of ESRD causes distribution is somewhat differ than that in Aleppo in Syria, DM (19.5%), HTN (21.1%), nephritis (20.5%), and hereditary (6.2%).<sup>31</sup> In another study done at 2012 in India the most common cause of ESRD as well as most study is DM (31%), undetermined etiology (16%), nephritis (14%) and hypertension (13%) (Figure 4).<sup>31,32</sup>



**Figure 4: Clustered column chart represent distribution of most common cause of primary renal diseases that causes end stage renal disease (dialysis) in different situation (Southern West Bank in Palestine, Aleppo in Syria, and India).**

The following are the recommendations from this study are protection of HD patient from viral hepatitis infection from both recognized and unrecognized sources require implementation of a comprehensive infection control program. This should include specific infection control practices, vaccination, periodic serology testing, surveillance, staff vaccination, education, and training.

Centers for disease control and prevention in United State suggest a popular recommendation for limitation and prevention of viral infection among hemodialysis patient includes: isolation of positive hepatitis viral infection HD patient in an single floor, or parts in dialysis unit, hand washing, gloves are required whenever caring for a patients, medication preparation and storage in special rooms, housekeeping staff should aware of infection transmission, use of disinfection, routine investigation of viral serological markers for all staff, patient and housekeeping staff, hepatitis B virus vaccination is recommended for all chronic susceptible HD members, and check of viral titer either HBV or HCV, hepatitis HD patient and staff should be treated, check of viral serotype and seroconversion, monitoring of viral positive hepatitis, and infection control training and education for all employees at risk for occupational exposure to infection.<sup>33</sup>

## CONCLUSION

Hepatitis B and C viruses infection are very frequent between HD patients in Southern West bank 6.7% and

8.9% respectively, these viruses are implicated in several disease includes hepatitis, liver cirrhosis, and hepatocellular carcinoma, these percent is higher than the positive of virus in general population, prevention remain a priority, and vaccination of non-immune renal patients, specially before the develop advanced renal failure.

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