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PREVALENCE OF HEPATITIS B VIRUS (HBV), HEPATITIS C VIRUS (HCV) AND OCCULT HBV IN HEMODIALYSIS PATIENTS IN THE ARMED FORCES HOSPITAL AT AL HADA- TAIF, SAUDI ARABIA.

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ABSTRACT

Introduction

The prevalence of HBV and HCV in the general community and in hemodialysis population differs between countries and even in the same country. The wide implementation of HBV vaccination in Saudi Arabia and the adoption of new control and prevention measures had contributed significantly to low prevalence rates reported recently. The aim of this study is to determine seroprevalence for HBV and HCV for hemodialysis patients in our hospital. **Materials and Methods:** Demographic and biomedical data were collected via questionnaires from the electronic files of patients undergoing hemodialysis. Third generation ELISA and polymerase chain reaction were used to look for serology, DNA and RNA of HBV and HCV. Data were analyzed and discussed. **Results:** We included 164 patients in this study, all were Saudi. Their ages ranged between 11 and 103 years. Only five of these patients were tested positive for HBs Ag (seroprevalence of 3.0%). PCR for HBV was tested in 49 patients, only one turned to be positive. None of tested patients had occult HBV infection. HCV was tested for in 156 of our patients. Six of the patients were positive for both HCV Ab and HCV PCR (seroprevalence of 5.1%.). Only four patient had daul infection. **Conclusion:** The prevalence of Hbs Ag positivity in this study is very low (3%) compared to previous studies. No occult HBV infection was found in the tested patients. The prevalence of HCV was also low (5.1%).

KEYWORDS: seroprevalence, HBs Ag, HBV PCR, HCV Ab, HCV PCR.

INTRODUCTION

Chronic viral hepatitis is a notorious disease especially in patients with other comorbidities and presents a challenge to many governments and health authorities. Patients on chronic hemodialysis are particularly at increased risk of getting both hepatitis B and hepatitis C (HBV&HCV) infections, which represent the third most common complication of hemodialysis. As these patients are immunocompromised they are potentially prone to have chronic disease with permanent viremia and consequently acquire the complications.[1-2]

Serological markers are usually used for diagnosis of HBV and HCV infection. These markers may be negative for different reasons and detection of DNA of HBV or RNA of HCV may be the only indicator for the virus denoting occult infection. Although the prevalence of HBV and HCV differs between countries and even in the same country, it is generally higher among hemodialysis population. Nevertheless, the adoption of new control and prevention measures- including HBV vaccination before starting dialysis, better screening of transfused blood, isolation of HBV and HCV infected patients to separate machines, and regular screening for the viruses in other patients- had significantly reduced the prevalence of the disease.[1, 3,4]

The prevalence of overt HBV, HCV as well as the presence of occult HBV infection in hemodialysis patients in Armed Forces Hospital -Al Hada (KSA) is not yet known. The infection with either HBV and or HCV adds to the challenges in this population. The prevention, early detection, and treatment are among the major goals for the medical authorities.

We are studying here the seroprevalence of HBV, occult HBV and HCV among hemodialysis population in our institute to see and compare the prevalence of the infection and evaluate our preventive measures.

MATERIALS AND METHODS

This study was carried in Armed Forces Hospital at Al Hada- Taif, which is located in the western part of Saudi Arabia. It is a five hundred bedded general hospital that

serves military individuals and their families. The hospital is composed of different medical departments including the major ones (surgery, medicine, pediatrics, obstetrics with their different subunits). There is a well-equipped dedicated hemodialysis unit. There are 164 patients receiving regular dialysis (88 males). All the patients were included in this cross-sectional study which was conducted in July 2017. Viral screening (HBs Ag, HBs Ab, HBc Ab and HCV Ab) -using third generation ELISA –were done routinely before the start of dialysis and on regular basis (every three months) for the patients without obligations. Other related investigations including polymerase chain reaction (PCR) for HBV DNA and HCV RNA, liver function tests, ultrasound and CT were requested when needed. Patients who turn negative for HBs Ag and HBc Ab were offered free vaccination before the start of hemodialysis. Patients with evidence of previous or current infection with HBV (HBs Ag positive/anti-HBc positive or positive PCR) or HCV infection were referred to the gastroenterology unit in the hospital for assessment and appropriate management.

After getting the permission from the authorities and ethical clearance, demographic and biomedical data, including age, sex, nationality, viral serology and PCR results, duration of dialysis and blood transfusions were collected from the electronic files of the patients using questionnaires.

RESULTS

All the164 hemodialysis patients were included in this study, all were Saudi, 76 of them were females. Their ages ranged between 11 and 103 years (mean 56.44), the majority (108) lie between 41 and 80 years of age, only five of the patients were 20 years or less. (Table 1).

Table 1: Age and sex distribution of 164 patients on hemodialysis at Armed Forces Hospital, Al Hada-Taif.

Age in Years	Males	Females	Total
< 20	3	2	5
21-40	19	16	35
41-60	25	21	46
61-80	29	33	62
81-100	11	4	15
>100	1	0	1
Total	88	76	164

Almost all the patients have three sessions of dialysis per week. The duration of hemodialysis ranged between one month and 22 years. Only 24 of our patients had blood transfusion (12 had one unit, nine had two units and three had three units).

All the patients (164) were tested for HBs Ag, HBs Ab and HBc Ab. Only five of these patients were tested positive for HBs Ag giving a seroprevalence of 3.0%. Out of these five patients; two were also positive for HBs Ab, four positive for HBc Ab and one was positive for HBV PCR. Those who were HBs Ag negative (159) had 147 positivity to Hbs Ab and 52 were also positive to HBc Ab. Hbc Ab was found in 56 of our patients, two of them were HBs Ab negative and one had PCR positive. HBs Ab and HBc Ab were simultaneously positive in 52 of our patients indicating that these patients had acquired immunity via natural HBV infection. The majority of HBs Ab positive patients (95) tested negative for both HBs Ag and HBc Ab showing that they had probably acquired immunity through vaccination. HBs Ag, HBs Ab and HBc Ab were all negative in ten of the patients indicating clear liability to infection and the need for vaccination. HBV DNA was tested for by PCR in 49 of our patients; one of them turned to be positive and he is also positive for HBs Ag, another four patients were also positive for HB s Ag, while the other 44 patients were negative for HBs Ag. Out of these 44 patients; 21 were also negative for HBc Ab.

The majority (115) of our patients do not have PCR test for HBV, out of these; ten tested negative for HBs Ag, HBs Ab and HBc Ab; 29 were negative for Hbs Ag and positive for both HBs Ab and HBc Ab. None of the 49 patients who had PCR test, had occult HBV infection.(Table 2).

Tabe 2: Serology and PCR for HBV of 164 patients on hemodialysis at Armed Forces Hospital, Al Hada- Taif.

		HBsAg +ve	HBsAg -ve	HBsAb +ve	HBsAb -ve	HBcAb +ve	HBcAb -ve	HB PCR +ve	HB PCR - ve
HBs Ag test (n*=164)	HBs Ag +ve	5	0	2	3	4	1	1	4
	HBs Ag -ve	0	159	147	12	52	107	0	44
HB s Ab test (n*=164)	HBs Ab +ve	2	147	149	0	54	95	0	45
	HBs Ab-ve	3	12	0	15	2	13	1	4
HBc Ab test (n*= 164)	HBc Ab +ve	4	52	54	2	56	0	1	27
	HBcAb -ve	1	107	95	13	0	108	1	21
HB PCR test (n*= 49).	HB PCR +ve	1	0	0	1	1	1	1	0
	HB PCR -ve	4	44	45	4	27	21	0	48

n*= number of tested patients.

HCV was tested for in 156 of our patients (we could not trace the test in eight patients). Eight of these patients were positive for HCV Ab indicating seroprevalence of HCV of 5.1%. Six of these eight patients were also positive for HCV PCR, the other two have no PCR testing. Five of these six patients were tested negative for HBs Ag and all were positive for HBs Ab. Only four patient had daul infection (positive HBs Ag and positive HCV Ab). (Table 3)

Table 3: Serology and PCR for HCV of 164 patients on hemodialysis at Armed Forces Hospital, Al Hada – Taif.

		HC Ab +ve	HC Ab - ve	HC PCR +ve	HC PCR - ve
HC Ab test (n*= 156)	HC Ab +ve	8	0	6	0
	HC Ab -ve	0	148	0	82
HC PCR test (n*= 88)	HC PCR +ve	6	0	6	0
	HC PCR -ve	0	82	0	82

n*= number of tested patients

DISCUSSION

The average seroprevalence of HBs Ag differs significantly in the Saudi adult population depending on the location and the population of the study.[5] Around 3.0% of healthy Saudi blood donors in Tabuk region were positive for HBs Ag. In southwestern region and in the eastern region, 5.4% and 6.7% prevalence were reported respectively.[6,7] Some other higher rates (10%%) were also reported. Generally, we can state that the seroprevalence of HBs Ag in Saudi Arabia ranges between 3.0 % and 10%.[8] These figures were taken mainly from old studies. The wide implementation of HBV vaccination in all parts of Saudi Arabia in the last four decades has definitely and significantly reduced the incidence and prevalence of the infection in different parts of the country.[9]

Due to the underlying impaired cellular immunity, patients on hemodialysis are more prone to acquire viral infection. Beside that these patients are exposed more to infectious material through the extracorporeal circulation in the process of hemodialysis pointing to hemodialysis itself as a risk factor. The frequent visits to hospitals and repeated blood transfusions will add more to the chances of infection.[10]

HBV prevalence of 0-6.6% in dialysis population was seen in Western Europe, Japan and the USA according to Dialysis Outcomes and Practice Patterns Study.[11] Higher prevalence rate of 14.6% was reported from Asia-Pacific countries.[12] Reports from elsewhere have indicated similar high prevalence of HBs Ag positivity in Turkey (13.3%) and Brazil (2.4-10%).[13,14] In Arab countries similar rates were reported earlier from Saudi Arabia and Bahrain (11.8%), however, lower rates came from some other Arab countries e.g. 2% in Moracco and 2.2% in UAE and 5% in Sudan.[15-18]

The low seroprevalence (3.0%) of HBs Ag positivity found in this study that goes with reports from Western Europe – compared with the 11.8% reported before elsewhere in Saudi Arabia - confirms rapid decline of HBV prevalence, probably reflecting the effect of wide implementation of vaccination in the country. It is interesting to note that all the patients who were HBs Ag positive in this study were born before the wide implementation of HBV vaccination. The meticulous standard precautions taken currently in our dialysis unit, the lesser need for blood transfusion due to appropriate usage of erythropoietin and the lower survival rate in hemodialysis patients in general might have also contributed to this low prevalence.

The seroprevalence of HBc Ab in this study was found to be 34% (56 patients) indicating previous exposure to the virus. Again it is interesting to note that all of them except one were born before implementation of vaccination, pointing to the efficacy of vaccination in preventing the infection.

Vaccination is reported to be less effective in hemodialysis patients.[19] This is not going with our

findings, as 100% (95patients) of our patients who tested negative for other HBV serological markers; showed positivity to HBs Ab probably indicating excellent response to vaccination.

For different reasons HBV-DNA may persist in the absence of HBs Ag. With the relatively recent advances of detection of HBV in the body and specifically the advanced, sensitive and specific PCR tests, a new category of viral infection appeared; that is occult HBV infection which denotes those patients who have negative HBs Ag (with or without other HBV antibody markers) and positive PCR as the only indicator of infection.[20,21]

Different prevalence rates of occult HBV in hemodialysis population were seen in different countries and even in the same country. Generally, it was reported to range between 0% and 58%.[22] Prevalence rates of 0-9% came from Western countries.[23] Low rates were reported from Turkey (2.7%), Egypt (4.1%) and Moracco (6%). Higher rates of 12.5% and 15% were reported earlier in Palestine and elsewhere.[24-26]

These high figures of occult HBV infection are very alarming, as these patients are potentially infectious and they are amenable to develop all the complications of chronic HBV infection.

Around 80% of patients with occult HBV have serological evidence of previous infection.[27] It had been reported that 40% of high risk patients including hemodialysis ones showed HBc Ab as the only marker of HBV infection, and their sera may contain HBV-DNA.[28]

None of our patients who had HBV PCR testing has occult HBV infection, however, 70% of our patients had no PCR testing. As a significant number (56 patients) of our patients has evidence of previous infection (HBc Ab positive) -and 52 of them had no PCR testing- *we can strongly recommend PCR testing at least for this highly vulnerable and potentially infectious population*.

Similar to HBV the prevalence of HCV differs from one country to the other and in the same country at different regions. Very low prevalence (≤0.5%) was reported in northern countries of Europe, while higher rates (≥3%) were reported from Romania and Russia.[29] In the Arab world very high prevalence (18%) was reported from Egypt, while it was low (1-2%) in Saudi Arabia and Syria.[30, 31]

The prevalence of HCV infection in hemodialysis patients also differs depending on the region and the population studied. Low rates of 1.9% and 4% were reported in Solvania and Britain respectively.[32, 33] Very high rates (40%-84.6%) were reported from other countries including Kuwait, Saudi Arabia, Syria, Tunisia, Iran, Pakistan.[33-38] These very high rates were probably related to old less specific ELISA tests used for detection of the virus and denotes high false results as was reported elsewhere.[39-41] The low prevalence rate of 5.1% seen in this study goes more with the reports from Europe, indicating better, more specific diagnostic tests and meticulous dialysis precautions in our institute.

Relatively recent reports showed prevalence rates of 0%-12% in patient who were HCV RNA-positive (PCR) and anti-HCV-negative indicating significant difference between the two tests.[42] Nevertheless, even more recent data reveled very minor or even no discrepancies between the more specific ELISA and PCR testing for HCV.[43] All our patients who were HCV RNA-positive were also positive for anti HCV showing no discrepancy between these tests, and *indicating that ELISA assay may be enough as a screening test for HCV in hemodialysis patients.* This study is limited by the fact that few patients might have done some virological testing outside the hospital and their results were documented only on their paper files and so that will not appear in the electronic files from which we have collected the data.

CONCLUSION

The prevalence of Hbs Ag positivity in this study is very low (3%) compared to previous studies probably due to the effect of wide implementation of vaccination and indicating good preventive measures in our dialysis unit. None of our patients who had HBV PCR had occult HBV infection, however, many patients who were vulnerable especially those who had evidence of previous exposure, had no PCR testing for the virus. The prevalence of HCV was also low (5.1%) in our population pointing to the meticulous dialysis precautions and probably better preventive measures in the community. HBV PCR testing for vulnerable patients and vaccination of those with negative screening tests were recommended.

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