PREVALENCE AND INCIDENCE OF HEPATITIS B AND C INFECTION AMONG HEMODIALYSIS PATIENTS IN THE PHILIPPINES FROM 2016-2019: A RETROSPECTIVE COHORT STUDY

Significance. Patients on hemodialysis are at increased risk for hepatitis B and hepatitis C infection. This paper aims to determine the prevalence and incidence of HbsAg and anti-HCV among hemodialysis patients in the Philippines from 2016-2019.

Methodology. This retrospective cohort study included all patients undergoing hemodialysis in eight B Braun Avitum Dialysis Centers in Luzon, Philippines from 2016-2019. All patients with HbsAg and anti-HCV testing were included in the study. HbsAg and anti-HCV were tested every 6 months.

Results. Of the 567 patients included in the study, 344 (60.7%) were male while 223 (39.3%) were female. Median age was 52 years. Prevalence rate of HbsAg positivity was 11% (10/91) in 2016, 6.5% (18/279) in 2017, 7.3% (35/481)) in 2018 and 8.1% (30/369) in 2019. Incidence rate of HbsAg was 0.2% (1/524). Prevalence rate of anti-HCV positivity was 5.5% (5/91) in 2016, 1.8% (5/279) in 2017, 2.1% (10/481) in 2018 and 1.9% (7/369) in 2019. There was no reported incidence of anti-HCV transmission.

Conclusion. The overall prevalence of HbsAg and anti-HCV positivity in patients undergoing hemodialysis in Luzon, Philippines from 2016-2019 is 7.6% and 1.2%, respectively. Incidence rate for HbsAg transmission is 0.2% while there was no reported incidence of anti-HCV transmission.

Keywords: retrospective, cohort, hepatitis B, hepatitis C, hemodialysis, prevalence, incidence.

Introduction

Hepatitis B and Hepatitis C infection remain to be a global burden of disease and is a major cause of liver failure in the world(1). In the Philippines, approximately 7.3 million adult Filipinos are chronically infected with Hepatitis B(2). A study done by Wong et al. in 2013 concluded that HbsAg seroprevalence in the Philippines is 16.7%, which is estimated to be about 7.3 million Filipinos and is more prevalent in the 20-39 age group(3). On the other hand, at least 1% of Filipinos are estimated to be infected with Hepatitis C (4).

End stage renal disease is currently the 7th leading cause of death in the Philippines and as of 2016, more than 36,000 Filipinos are on hemodialysis(5). According to the data presented by the Philippine Renal Disease Registry as of 2016, there has been a 14% increase in the incidence of new dialysis patients from 2010-2016(5). Patients undergoing hemodialysis are at increased risk of exposure to hepatitis infection. This may be due to use of common equipment, frequent hospitalizations and surgeries, multiple blood transfusions and exposure to infected individuals(6). A retrospective study among hemodialysis patients done by Santos et al in 1998 showed a prevalence rate of 12.8% for HbsAg-positive patients and 39.8% for anti-HCV positive patients undergoing hemodialysis in a private institute(7). Results showed no significant difference in the duration of hemodialysis among patients with and without hepatitis B, however, they noted that anti-HCV positive patients had significantly higher duration of hemodialysis compared to anti-HCV negative patients. Moreover, there did not seem to be a correlation between blood transfusion and HbsAg/anti-HCV positivity.

Due to the high risk of hepatitis B transmission among hemodialysis patients, the Department of Health issued Administrative Order No. 2012-0001, which states that at least 1 designated hemodialysis machine should be assigned to hepatitis B infected patients(8). Moreover, part of the PhilHealth accreditation requirements for dialysis clinics include dedicated machines for both hepatitis B and hepatitis C

patients as well as a separate reprocessing machine for this population[9]. Standard control measures to prevent transmission of hepatitis B and hepatitis C include the following: designated machines for HbsAg(+) and anti-HCV(+) patients, separate dialyzer and reprocessor, separate room, staff and equipment for hepatitis B and hepatitis C patients[10]. At present, there are no local data available measuring the effectiveness of these control measures as evidenced by the incidence of hepatitis B and hepatitis C transmission among hemodialysis patients.

Objectives

This paper aims to determine the prevalence and incidence of HbsAg positivity and anti-HCV positivity among hemodialysis patients in the Philippines from 2016-2019.

Significance of the study

To date, there is lack of comprehensive data on the increasing burden of viral hepatitis in the Philippines among vulnerable groups. Part of the sustainable development goals of the World Health Organization is to eliminate hepatitis B and hepatitis C infection by 2030. As such, outcomes from this study will help us identify key areas where we can potentially lessen the burden of this disease among the vulnerable population, particularly hemodialysis patients. Data collected may also help us raise awareness regarding the incidence of this disease among hemodialysis patients and contribute to additional policy-making and program control among this subset of patients.

Methodology

This is a retrospective cohort study on hemodialysis patients from January 2016 to October 2019 of institution-based and free-standing dialysis units of a single privately owned hemodialysis service provider (B. Braun Avitum) in Luzon, Philippines.

Inclusion Criteria:
Dialysis patients of both gender and all ages from January 2016 to October 2019 of select B Braun Avitum dialysis units in Luzon were included in the study.

Exclusion Criteria:
Patients without HbsAg and anti-HCV testing were excluded from the study.

Data Collection
Data (age, gender, HbsAg status, anti-HCV status) were collected from institution-based and freestanding hemodialysis units owned by a single private hemodialysis service provider in the Philippines. Above data was requested from the different hemodialysis units and the primary investigator did not have access to the individual patient charts as part of the company's data privacy policy. HbsAg and anti-HCV were tested every 6 months in all subjects.

Ethical considerations
During data gathering and analysis, patient confidentiality and anonymity were observed at all times. Patients' names and other personal information were not disclosed to the primary investigator. During the collection and tabulation of data, specific codes were assigned to each patient and these codes were linked to the patient identifier found on a separate file that is accessible only to the head nurse of each participating dialysis unit so as to maintain confidentiality. Consent to access patients' data from the different centers was secured through the company's country manager prior to the start of the study.

Sample Size Justification

A **minimum** of **172** eligible hemodialysis patients was required to have a 95% reliability and 5% precision for determining prevalence of hepatitis B and C infection among hemodialysis patients. Sample size was calculated using the estimation of population proportion with the formula: $n = Z^2 (PQ)/ d^2$

Statistical Methods

Summary statistics were reported as median (interquartile range) for quantitative variables with skewed distribution and as count (percent) for qualitative measures. Minimum and maximum values of quantitative data were also reported. Shapiro-Wilks test was used to check for normality assumption of continuous data. Prevalence, incidence proportion and incidence rate were estimated. Two-tailed 95% confidence intervals were also generated. STATA v14 was used in data processing and analysis.

Results

There were 567 patients who underwent hemodialysis in eight units of a single privately owned hemodialysis service provider from 2016 to 2019 (see Table 1). Three units were from the National Capital Region, 4 units from Region IV-A (Rizal, Cavite, Laguna), and 1 unit from Region III (Nueva Ecija). Median age was 52 years, age range from 14 to 86. Patients belonged to the 50 to 59 demographics (29.3%). Three hundred fourty-four (60.7%) were male compared to 223 (39.3) female.

Table 1: Demographic characteristics of hemodialysis patients, 2016-2019

Characteristic	2016-2019 n = 567	2016 n = 91	2017 n = 279	2018 n = 481	2019 n = 369
Hemodialysis center	8	6	7	8	7
Age in years	52 (19)	50 (20)	51 (22)	52 (19)	51 (17)
≤19	8 (1.4%)	1 (1.1%)	7 (2.5%)	8 (1.7%)	2 (0.5%)
20-29	27 (4.8%)	9 (9.9%)	19 (6.8%)	21 (4.4%)	22 (6.0%)
30-29	83 (14.6%)	12 (13.2%)	44 (15.8%)	72 (15.0%)	49 (13.3%)
40-49	124 (21.9%)	22 (24.2%)	58 (20.8%)	104 (21.6%)	89 (24.1%)
50-59	166 (29.3%)	23 (25.3%)	76 (27.2%)	143 (29.7%)	112 (30.4%)

Characteristic	2016-2019 n = 567	2016 n = 91	2017 n = 279	2018 n = 481	2019 n = 369
60-69	132 (23.3%)	20 (22.0%)	60 (21.5%)	110 (22.9%)	81 (22.2%)
≥70	27 (4.8%)	4 (4.4%)	15 (5.4%)	23 (4.8%)	14 (3.8%)
Gender					
Male	344 (60.7%)	46 (50.5%)	161 (57.7%)	291 (60.5%)	225 (61.0%)
Female	223 (39.3%)	45 (49.5%)	118 (42.3%)	190 (39.5%)	144 (39.0%)
Hepatitis B status	85 (15.0%)	9 (9.9%)	18 (6.5%)	30 (6.2%)	28 (7.6%)
Hepatitis C status	26 (4.6%)	5 (5.5%)	5 (1.8%)	9 (1.9%)	7 (1.9%)

Data presented as median (interquartile range) or count (percent).

The cohort of patients was observed for a total of 1,266 person-years. The incidence rate of Hepatitis B infection was estimated at 7.9 cases per 10,000 person-years.

In 2016, 11 per 100 population (11%) (95% CI: 5.4 to 19.3) of the patients had reactive HBsAg test results, but this decreased substantially to 6.5 (95% CI: 3.9 to 10) in 2017 and increased to 7.3 (95% CI: 5.1 to 10) in 2018 and 8.1 per 100 population (95% CI: 5.6 to 11.4) in 2019 (see Figure 1 and Table 2). The prevalence of HbsAg positivity from 2016 to 2019 was 7.6 per 100 population (95% CI: 5.5 to 10.1).

Figure 1: Prevalence of HBsAg positivity among hemodialysis patients

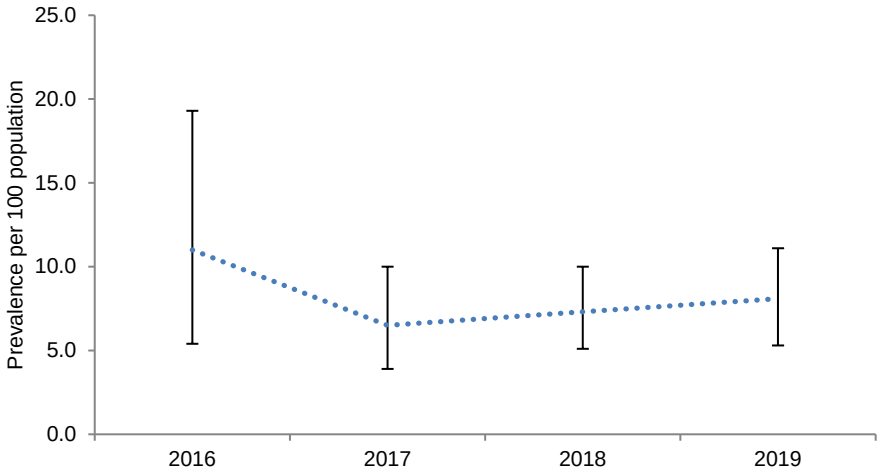

Table 2: Prevalence of HbsAg positivity among hemodialysis patients

Year	Positive/Total	Prevalence per 100 population	95% CI
2016	10/91	11.0	5.4 to 19.3
2017	18/279	6.5	3.9 to 10.0
2018	35/481	7.3	5.1 to 10.0
2019	30/369	8.1	5.6 to 11.4

HBsAg: Hepatitis B surface antigen, CI: confidence interval

There were 524 susceptible patients followed-up in the course of the study. There was only one (0.2%) reported case of new HbsAg positivity during hemodialysis.

In 2016, 5.5 per 100 population (95% CI: 1.8 to 12.4) of the patients had reactive anti-HCV test result but this decreased substantially to 1.8 (95% CI: 0.6 to 4.1) in 2017 and steadily fluctuated to 2.1 (95% CI: 1.0 to 3.8) in 2018 and 1.9 per 100 population (95% CI: 0.8 to 3.9) in 2019 (see Figure 2 and Table 3). The overall prevalence of anti-HCV positivity was 1.2 per 100 population (95% CI: 0.8 to 3.2).

Figure 2 Prevalence of anti-HCV positivity among hemodialysis patients

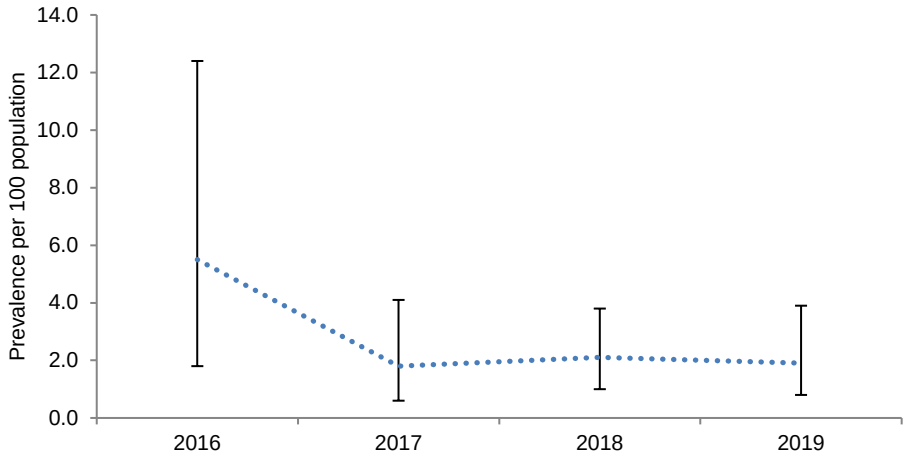

Table 3: Prevalence of anti-HCV positivity among hemodialysis patients

Year	Positive/Total	Prevalence Per 100 Population	95% CI
2016	5/91	5.5	1.8 to 12.4
2017	5/279	1.8	0.6 to 4.1
2018	10/481	2.1	1.0 to 3.8
2019	7/369	1.9	0.8 to 3.9

Anti-HCV: Hepatitis C antibody test, CI: confidence interval

There were 560 susceptible patients followed-up in the course of the study. There were no reported cases of new anti-HCV positive patients.

Mortality rates were 25% (95% CI: 13.2% to 40.3%) and 10% (95% CI: 0.3% to 44.5%) for those with Hepatitis B and C infection, respectively. Overall mortality was 14.8% (95% CI: 12% to 18%).

Discussion

Patients on hemodialysis are at an increased risk for HBV and HCV infections. This study showed that the prevalence rate of HbsAg and anti-HCV seropositivity among hemodialysis patients in the Philippines from 2016-2019 is 7.6% and 1.2%, respectively. The incidence rate of HbsAg positivity among hemodialysis patients from 2016-2019 is 0.2% while there were no reported new cases of anti-HCV. The geographic distribution of hepatitis B and C infection among hemodialysis patients varies throughout the world. Hepatitis B infection in patients undergoing hemodialysis is estimated to range from 2-20% among developing countries (13)(14)(15) and 1% among industrialized nations (16). On the other hand, hepatitis C infection in hemodialysis patients is estimated to be as high as 70% among developing countries and ranges from 2-22% in developed nations(17).

In the Philippines, HbsAg seroprevalence is estimated to be 16.7% in the general population(3) and 12.8% among hemodialysis patients (7). Our study showed that

there is a decrease in the prevalence of HbsAg positivity among hemodialysis patients from 12.8% in 1998 to 7.3% in 2018. Incidence was also noted to be low at 0.2% (1/567). The decreased prevalence of hepatitis B in the hemodialysis units generally reflects the HbsAg prevalence in the general population while the low incidence of HbsAg conversion in hemodialysis units may imply better adherence to universal precautions and hepatitis-specific infection control measures such as use of separate room, machines, and staff for patients infected with hepatitis B.

Prevalence of anti-HCV positivity among Filipino hemodialysis patients was reported to be 39.8% in 1998(7) with a dramatic decrease to 4.5% in 2007(18) and 1.9% in 2019 as seen in our study. In the former study, anti-HCV positive patients were treated as regular patients with non-separation of room, machines, and staff but with adherence to the universal infection control precautions; while the two subsequent studies implemented separation of machines for anti-HCV positive patients and in some centers, even separation of room and staff depending on available resources. The study done by Santos et al in 1998(7) was a pilot study on HCV positivity in hemodialysis units and this initiated the recommendation of separation of dialysis machines and room for anti-HCV positive patients. This recommendation has led to a marked decrease in the prevalence and incidence of anti-HCV in hemodialysis units in the succeeding years as reflected by the prevalence of 4.5% in 2007(18).

At present, CDC does not recommend isolation of anti-HCV positive HD patients since studies show that HCV is not efficiently transmitted through hemodialysis(19). They recommend strict adherence to universal infection control measures as prevention of HCV transmission in hemodialysis. However, results from previous studies evaluating the benefit of isolating anti-HCV positive dialysis patients are conflicting. Some studies showed no additional benefit of dedicated machines for anti-HCV positive patients while some studies showed significantly lower incidence of HCV transmission in those with dedicated machines (20)(21). A

prospective cohort study done by Agarwal et al in India concluded that isolating anti-HCV positive hemodialysis patients may significantly decrease HCV transmission especially among centers with high conversion rates (22). This benefit is consistent with the results of our study. In 2005, PhilHealth mandated all accredited dialysis units to have a dedicated machine for both hepatitis B and C patients(9). As such, the previously reported anti-HCV prevalence rate of 39.8% in 1998 significantly decreased to 4.5% in 2007 in the same dialysis center. This underscores the probable benefit of isolating anti-HCV positive hemodialysis patients and policies to this effect should be considered in vulnerable groups.

Conclusion

Our study showed a decreased prevalence of HbsAg (7.6%) and anti-HCV (1.2%) positivity among hemodialysis patients in the Philippines from 2016-2019. Moreover, the 4-year incidence of HbsAg transmission among HD patients is 0.2% and 0% for HCV transmission. This implies that current policies on infection control measures among hemodialysis patients and isolation of HbsAg and anti-HCV positive patients are effective in decreasing transmission in this subset of patients.

Limitation

Our study only included dialysis centers from Luzon from a single privately owned hemodialysis service provider. Poorer regions that have less access to vaccination, sanitation, and adequate infection control may have a higher prevalence and incidence rate of hepatitis B and C infection. Likewise, other hemodialysis service providers may have a different prevalence and incidence rate due to differences in implementation and adherence to hepatitis infection control measures.

Recommendation

Further studies including other service providers and regions (Visayas and Mindanao) in the Philippines are recommended.

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Conflicts of interest

The author has no conflicts of interests related to this publication.

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