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ORIGINAL ARTICLE

Prevalence of hepatitis B and C virus infections in hemodialysis patients in Vietnam: A systematic review and meta-analysis

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Abstract

Background and Aim: Chronic hemodialysis patients are at high risk of contracting hepatitis B (HBV) and C (HCV) virus infections. In Vietnam, the seroprevalence of HBV and HCV infections is approximately 10 and 4%, respectively. Although the chronic hemodialysis population is increasing, relatively little epidemiology is available for HBV and HCV infections in this population. To address this, we reviewed the current literature on the magnitude of these infections in the hemodialysis population in Vietnam.

Methods: Four databases were used to search for publications containing the prevalence of HBV and/or HCV infections in hemodialysis patients in Vietnam. Grey literature search was utilized to identify local publications. Prevalence and 95% confidence interval were used or calculated, and a meta-analysis was conducted on HBV and HCV prevalence for comparison.

Results: Sixteen studies were included in the review. The search identified knowledge gaps in the current literature. Available data show that HBV and HCV infections remain prevalent in the hemodialysis population. HBV prevalence is not different between the north and the south of Vietnam. The pattern of HCV prevalence is different, with recent reports of lower prevalence in the south than in the north, while HCV prevalence varies between hemodialysis units in the same regions.

Conclusions: A national prevalence survey of hemodialysis patients would improve the reliability and generalizability of the findings. However, the review confirmed that both HBV and HCV were prevalent in hemodialysis patients. The findings support a reinforcement of infection prevention to minimize the risk of HBV and HCV transmission in hemodialysis facilities.

Introduction

Renal replacement therapies, including hemodialysis, peritoneal dialysis, and kidney transplantation, are the main treatment modality for end-stage renal disease (ESRD).[1] In low- to middle-income countries, such as Vietnam, kidney transplantation is rare, and the majority of patients require life-long dialysis[1,2] in which hemodialysis is more common than peritoneal dialysis.[3] However, due to the invasive techniques associated with hemodialysis, patients are at high risk of acquiring hepatitis B virus (HBV) and hepatitis C virus (HCV) infections.[4–6] In Vietnam, the seroprevalences of HBV and HCV infections in the general community are approximately 10 and 4%, respectively.[7,8] Although these figures may be underestimated due to the limited data currently available, they are high compared to other countries in the region.[7,8] In Vietnam, the first hemodialysis for ESRD patients was conducted at tertiary hospitals in 1983.[9] According to the most recent report in 2015, the estimated number of patients with chronic kidney disease was 6 million or 6.73% of the general population.[10] This number will increase by 8000 new patients annually.[10] Of these estimated 6 million patients, 80 000 (1.3%) have ESRD.[10] Although an estimate of the number of hemodialysis units in Vietnam is not available, it is documented that hemodialysis services are being increasingly expanded to address its growing demand.[5] A systematic review was performed on the available literature on the pattern of HBV and HCV infections in the hemodialysis population in Vietnam. The findings are expected to provide some insights on the burden of HBV and HCV infections in the hemodialysis population that may be related to infection prevention and control practices in Vietnam.

Methods

Information sources, selection criteria, and study selection

Information sources. Four formal databases (Medline, EMBASE, Scopus, and Global Health) were used for searches in January 2018. Search terms included "(hepatitis B virus OR hepatitis C virus OR hepatitis virus OR HBV OR HCV) AND (prevalence OR seroprevalence OR seropositive OR serological OR serosurvey) AND (hemodialysis OR haemodialysis OR dialysis) AND Vietnam." A citation search was subsequently performed using the Scopus database. All articles were published in English.

A grey literature search was performed, including Google search and a manual search, at the University of Medicine and Pharmacy at Ho Chi Minh City (UMPH) archives for local published papers and dissertations. The UMPH was established in 1947 and is considered one of the leading universities in Vietnam, with several significant sources of material and special collections in its archives.[11] To improve the local grey literature search, we utilized our professional networks in the Vietnam Ministry of Health (MOH) and the National Institute of Hematology and Blood Transfusion (NIHBT). All documents were in either English or Vietnamese and were in one of the following formats: hospital surveillance report, published paper, or dissertation. After the manual search, a citation search was also performed using the Scopus database and the UMPH archives. The rationale for the inclusion of the grey literature searches was based on our experience that Vietnamese medical journals are not listed on PubMed, and few local journals have online access.

Eligibility criteria. Inclusion criteria for the study were as follows:

1. Study population included ESRD patients receiving chronic hemodialysis treatment
2. Study population included ESRD patients receiving chronic hemodialysis treatment as a subgroup
3. Reported on hemodialysis treatment in Vietnam
4. Reported on the prevalence of HBV and/or HCV infection
5. Reported on the prevalence of HBV and HCV coinfection.

Exclusion criteria were as follows:

1. The studies were modeling studies
2. Duplicate studies of the same hemodialysis population in a wider patient population base for the same study periods that addressed the prevalence of hepatitis infections
3. Papers published before 1983 because official hemodialysis treatment for ESRD patients in Vietnam commenced in 1983.[9]

Study selection. One bilingual researcher (author Minh C Duong) read the abstracts of all papers and dissertations in Vietnamese. After removing ineligible or duplicated papers, all potential eligible abstracts of papers and dissertations were reviewed (authors Minh C Duong and Mary-Louise McLaws). Full-text papers and dissertations were retrieved for review, and extraction of information included authors, year of publication, year of HBV and/or HCV testing, types of HBV and HCV diagnostic tests, study location, number of subjects tested, and point estimate of the prevalence of viral hepatitis infection. Where data were missing, the authors of the paper were contacted personally to obtain that data.

Statistical analysis. Excel was used to manage records and data. Where a study failed to report 95% confidence interval (95% CI) for the prevalence rate, we performed a calculation of 95% CI based on the number of subjects and the point estimate of the prevalence of viral hepatitis infection reported in the paper so that a comparison and assessment of random errors of each rate could be carried out. A meta-analysis was performed on all included studies using Comprehensive Meta-Analysis software (Version 3.0, Biostat, Englewood, NJ, USA).[12] Individual study prevalence rates were assessed at the pooled effect. A test for heterogeneity of the prevalence rates over the studies was calculated based on Cohran's Q and degree of inconsistency (I^2).[13] In all the summaries or pooled analyses, a random-effects model was used when heterogeneity was present due to variations of effects from individual studies. A fixed-effects model was used when heterogeneity was absent. When the results of the test for heterogeneity and I^2 contradicted each other, the random-effects model was used provided that studies were gathered from the published literature.[14] The statistical significance was set at $P < 0.05$. Subanalyses were conducted for the periods within which HCV studies were published (e.g. 1994–1999 and 2008–2016) and for all included studies among the two main geographical locations (e.g. south and north) of Vietnam.

Maintenance of study standard. This systematic review was reported in line with preferred reporting items for systematic reviews and meta-analyses (PRISMA statement) and a PRISMA checklist.[15]

Results

Fourteen results were obtained from the grey literature search, and none included surveillance reports. Searches of the formal databases produced 21 results (Fig. 1). Of the 35 results from grey and database searches, 13 duplicates were removed. Of the remaining 22 results, 2 were excluded based on the abstract or where the authors could not be reached to obtain missing data. Full-text articles were retrieved for the remaining 20 results. Four papers were further excluded because their study populations were duplicated in other papers for the same study period. Citation search of the remaining 16 results found no further result. Finally, 16 papers were included in the review (search strategy details given in full in Appendix S1).

Study base location. Of the 16 studies included for review, 13 studies were conducted in the two largest cities, Hanoi in the north and Ho Chi Minh City in the south; one study was conducted in Thai Binh City in the north;[16] and two studies were conducted in five major cities across Vietnam, including Hanoi and Hai Phong in the north, Da Nang in the central region, and Khanh Hoa and Can Tho in the south.[17,18] Fifteen studies were conducted at well-equipped tertiary hospitals, and one study was conducted at a satellite hemodialysis unit.[19]

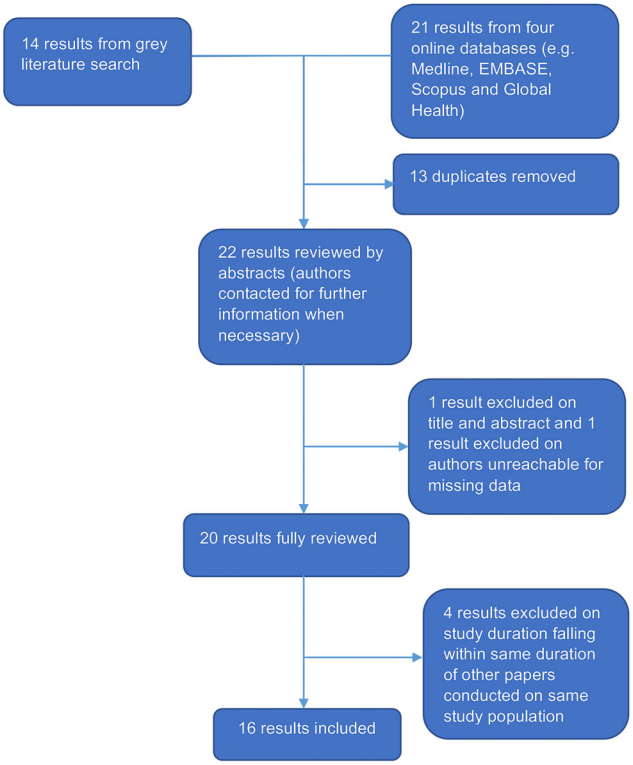

Figure 1 Flow chart of study analysis.

Of the 16 studies, only 9 studies exclusively focused on chronic hemodialysis patients, and the remaining 7 studies included hemodialysis patients in combination with other high-risk groups, including injecting drug users, commercial sex workers, thalassemia patients, multitransfused patients,[17,18,20–23] and hemodialysis patients who underwent kidney transplantation.[24]

Screening for HBV and HCV in hemodialysis patients. Of the 16 studies, 2 studies reported the prevalence of both HBV and HCV, 4 studies also included HBV and HCV coinfection, 8 studies reported HCV alone, and 2 studies reported HBV alone (Table 1). All used the HBsAg serology assay to screen for HBV infection. HCV core antigen (HCV-coreAg) testing was used to screen for HCV infection in one study,[19] while the remaining 13 studies reporting HCV utilized different generations of anti-HCV serology assay, with just 3[26,30,31] of these 13 studies using the HCV-RNA technique for the genotype identification of positive samples.

Prevalence rates. There were eight studies that reported the prevalence of HBV infection. All studies were published after 2009, with the exception of one study published in 1994 (Table 1). Of these eight studies, the reported prevalence rates ranged from 4.9% (95% CI 2.4–9.7%)[27] to 14.3% (95% CI 11.6–17.4%).[17] The width of 95% CI in seven of eight studies was in excess of 50% of the point estimate. The pooled prevalence of HBV in the north and the south of Vietnam was 10.6% (95% CI 8.8–12.4%) and 7.4% (95% CI 4.9–9.8%), respectively, demonstrating that it was not different between the two regions (Fig. 2). The national pooled prevalence of HBV in Vietnam was 9.7% (95% CI 7.5–12%) with considerable heterogeneity (I^2 = 74.68%; Q = 31.6, df = 8, P < 0.001).

There was no evidence of publication bias among the eight studies reporting HBV prevalence with Egger's test, with a P = 0.582, whereas Begg and Mazumdar's rank correlation test had a P = 0.466. This was depicted graphically by a funnel plot, which showed a symmetrical display of prevalence reported by all eight studies (Fig. 3a).

Fourteen studies reporting HCV prevalence were either published between 1994 and 1999 or later between 2008 and 2016. The width of the 95% CI in 6 of the 14 studies was in excess of 50% of the point estimate. Examining estimates for the south of Vietnam before 1999 found no difference between three studies, with ranges from 44% (95% CI 26.7–62.9%)[21] to 57.3% (95% CI 49.3–65%)[22] (Table 1). HCV prevalence reported since 2008 in the south of Vietnam were similar across two studies, with ranges from 12% (95% CI 8–18%)[19] to 19.6% (95% CI 13.9–26.8%).[27] The pooled prevalence after 2008 (15.5%, 95% CI 8.1–22.9%, P < 0.001) was lower than the pooled prevalence from 1994 to 1999 (54.8%, 95% CI 48–61.5%) (Fig. 4). In contrast, in northern Vietnam before 1999, HCV prevalence rates were not different between two studies, and the pooled prevalence (2.3%, 95% CI 0.7–3.9%) was lower than after 2008 (37.8%, 95% CI 31.8–43.7%). In addition, the prevalence rates after 2008 were different between seven studies, starting at 28.6% (95% CI 20.3–38.6%)[16] in chronic hemodialysis patients and peaking at 52.7% (95% CI 47.3–58%)[24] in chronic hemodialysis patients undergoing transplantation. The national pooled prevalence of HCV in Vietnam was 32.6% (22.9–42.3%) with considerable heterogeneity (I^2 = 98.7%; Q = 1078.45, df = 14, P < 0.001).

There was evidence of publication bias among 14 studies reporting HCV prevalence with Egger's test, with a P = 0.006, whereas Begg and Mazumdar's rank correlation test had a P = 1.0. This was depicted graphically by a funnel plot which showed a non-symmetrical display of prevalence reported by all 14 studies (Fig. 3b).

The prevalence of HBV and HCV coinfection ranged from 2.1% (95% CI 0.7–6.0%)[27] to 5.5% (95% CI 3.5–8.4%)[24] (Table 1). The width of 95% CI in all four studies was in excess of 50% of the point estimate. The pooled rate in northern Vietnam was 4.3% (95% CI 1.9–6.7%) and was not different from the south (2.1%, 95% CI 0.7–6.0%) (Fig. 5). The national pooled prevalence of HCV and HBV coinfection in Vietnam was 3.7% (95% CI 1.9–5.4%) with considerable heterogeneity (I^2 = 80.34%; Q = 15.26, df = 3, P = 0.002).

There was evidence of publication bias among four studies reporting HBV and HCV coinfection with Egger's test, with a P = 0.044, whereas Begg and Mazumdar's rank correlation test had a P = 0.308. This was depicted graphically by a funnel plot, which showed a near-symmetrical display of prevalence reported by all four studies (Fig. 3c).

Discussion

Our systematic review identified 12 contemporary studies between 2008 and 2016 and an additional 4 studies published in or prior to 1999 that reported HBV and/or HCV prevalence in

Table 1 Estimated prevalence of HBV, HCV, and HBV and HCV coinfection in chronic hemodialysis patients in Vietnam

Author	Year of publication (year of testing)	Study city (geographical location)	Study population	Prevalence % (95% CI)		
				Hepatitis B	Hepatitis C	HBV and HCV coinfection
Duong *et al.*[19]	2016 (2012–14)	Ho Chi Minh City (South)	Chronic hemodialysis patients	8 (5–12)	12 (8–18)	—
Bui *et al.*[24]	2013 (unknown)	Hanoi (North)	Chronic hemodialysis patients undergoing kidney transplantation	12.1 (9.0–16.1)	52.7 (47.3–58.0)	5.5 (3.5–8.4)
Nguyen and Pham[16]	2013 (2013)	Thai Binh (North)	Chronic hemodialysis patients	8.8 (4.5–16.4)	28.6 (20.3–38.6)	2.2 (1.0–7.7)
Nguyen *et al.*[25]	2013 (2007–12)	Hanoi (North)	Chronic hemodialysis patients	—	32.5 (29.4–35.8)	—
Ha *et al.*[26]	2013 (2007–11)	Hanoi (North)	Chronic hemodialysis	—	33.5 (30.0–37.3)	—
Dunford *et al.*[17]	2012 (2008–09)	multicenter in 5 major cities	Several high-risk groups including hemodialysis	14.3 (11.6–17.4)		
Dunford *et al.*[18]	2012 (2009–2009)	multicenter in 5 major cities	Several high-risk groups including hemodialysis	—	26.6 (23.2–30.4)	—
Nguyen *et al.*[27]	2012 (2006–11)	Ho Chi Minh City (South)	Chronic hemodialysis patients	4.9 (2.4–9.7)	19.6 (13.9–26.8)	2.1 (0.7–6.0)
Vu[31]	2011 (2006–08)	Hanoi (North)	Chronic hemodialysis patients	—	31.8 (27.7–36.1)	—
Hoang *et al.*[28]	2009 (unknown)	Hanoi (North)	Chronic hemodialysis patients	10.3 (7.5–14.0)	49.4 (44.0–54.8)	5.4 (3.5–8.4)
Tran[29]	2008 (2006–07)	Ho Chi Minh City (South)	Chronic hemodialysis patients	7.9 (5.0–12.1)	—	—
Nguyen[30]	2008 (2001–06)	Hanoi (North)	Chronic hemodialysis patients	—	35.7 (31.2–40.4)	—
Bui *et al.*[22]	1999 (1997)	Ho Chi Minh City (South)	Several high-risk groups including hemodialysis	—	57.3 (49.3–65)	—
Nguyen *et al.*[20]	1995 (unknown)	Hanoi (North)	Several high-risk groups including hemodialysis	—	15.4 (4.3–42.2)	—
Phan *et al.*[21]	1995 (1993)	Ho Chi Minh City (South)	Several high-risk groups including hemodialysis	—	44 (26.7–62.9)	—
Nakata *et al.*[23]	1994 (1993)	Ho Chi Minh City (South)	Several high-risk groups including hemodialysis	14.3 (5.7–31.5)	53.6 (35.9–70.5)	—
		Hanoi (North)		9.8 (4.3–21)	2.0 (0.4–10.3)	—

CI, confidence interval; HBV, hepatitis B virus; HCV, hepatitis C virus.

hemodialysis patients in seven major cities in Vietnam. Half (56%, 9/16) of the studies reported exclusively on hemodialysis patients, and the majority (15/16) of publications were based in well-equipped tertiary hospitals. Hemodialysis is being decentralized across Vietnam into district and provincial centers where adherence to infection prevention and control policy and guidelines associated with HBV and HCV may be sub-optimal.[4,32,33] Among 14 studies reporting HCV infection, only 1 study utilized the HCV-coreAg, while 13 studies utilized different generations of anti-HCV serology assay for screening that may have underestimated the burden of HCV because anti-HCV assay has a reduced sensitivity and specificity compared to HCV-coreAg.[34–37] The move away from anti-HCV toward HCV-coreAg screening is based on the need for accuracy, with experts suggesting that, while the nucleic acid testing (NAT) technique is superior to anti-HCV, it should be replaced with HCV-coreAg for routine monitoring of chronic hemodialysis patients because HCV-coreAg is more cost-effective, less labor-intensive, and comparable for accuracy.[36,38]

Based on our systematic review, HBV and HCV infections are endemic in the hemodialysis population in Vietnam. The prevalence reported by two multicenter studies[17,18] included in our review were significantly higher than the other groups these studies reported, such as voluntary blood donors, military recruits, and pregnant women in Vietnam. The national pooled prevalence rates of HBV and HBV and HCV coinfections peaked at 9.7 and 3.7%, respectively. These prevalence rates did not differ by region within Vietnam or between hemodialysis units. Our national pooled HBV prevalence was not different from other Asian countries such as Indonesia (12%, 95% CI 7–17%).[39] Yet, our national pooled HBV and HBV and HCV coinfection rates were higher than rates in low-resource regions outside Asia, such as Libya where the rates were lower for HBV (2.6%, 95% CI 2–3.3%) and HBV and HCV coinfection (1.2%, 95% CI 0.9–1.7%).[40]

Geographical differences within Vietnam were identified for HCV prevalence, with higher pooled HCV prevalence in the south than the north prior to 1999 (54.8%, 95% CI 48–61.5% *vs*

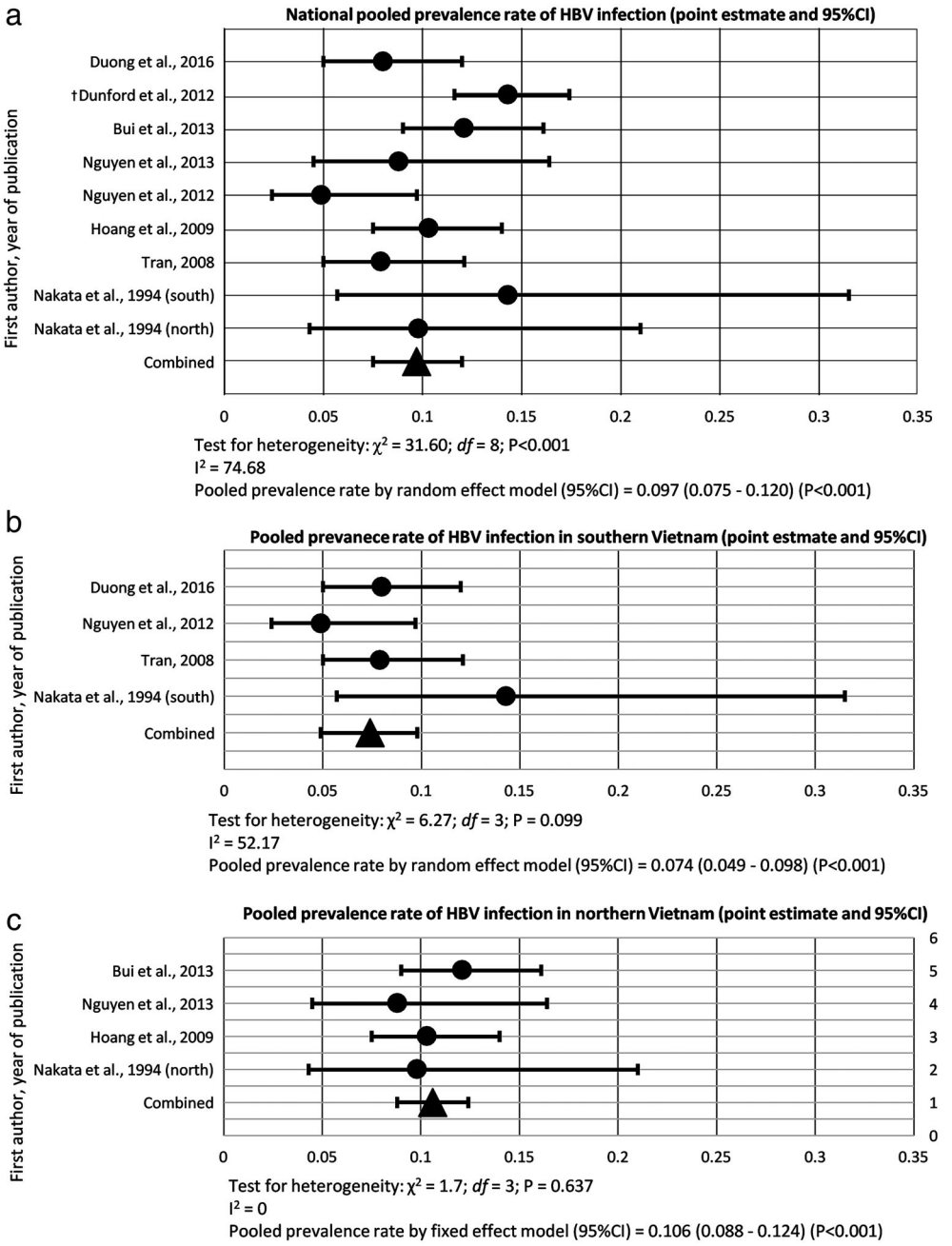

Figure 2 Forest plot of the prevalence of HBV infection in hemodialysis population across Vietnam (a) and in the south (b) and north (c). †Paper written by Dunford et al., 2012 (multicenter study), was only included to estimate the national pooled prevalence of HBV infection. HBV, hepatitis B virus.

2.3%, 95% CI 0.7–3.9%). However, the pooled HCV rate was lower in the south compared with the north after 2008 (15.5%, 95% CI 8.1–22.9% *vs* 37.8%, 95% CI 31.8–43.7%). Our national pooled HCV prevalence rate (32.6%, 95% CI 22.9–42.3%) in hemodialysis patients was 2.5 times lower than Indonesia (80.7%, 95% CI 74–86.1%)[39] but was similar to Libya (31.1%, 95% CI 29.3–33%).[40] It should be remembered that an anti-HCV test was utilized for screening in both these locations.

Screening blood products for blood-borne viruses commenced in 2001,[41] and this should have impacted the magnitude in hemodialysis patients who receive blood products during treatment. However, the high national pooled rate and the increased pooled rate of HCV infection in northern Vietnam suggest that infection prevention and control practices are to be improved to meet global standards.[42–44] Due to financial constraints, dialyzer and bloodline are commonly reused in Vietnam.[33] From our observations of hemodialysis units in northern Vietnam, there have been delays in utilizing the modified priming protocol. This protocol is a technique for reprocessing dialyzer membrane that reduces the risk of acquiring HCV infection,[25] and this may have

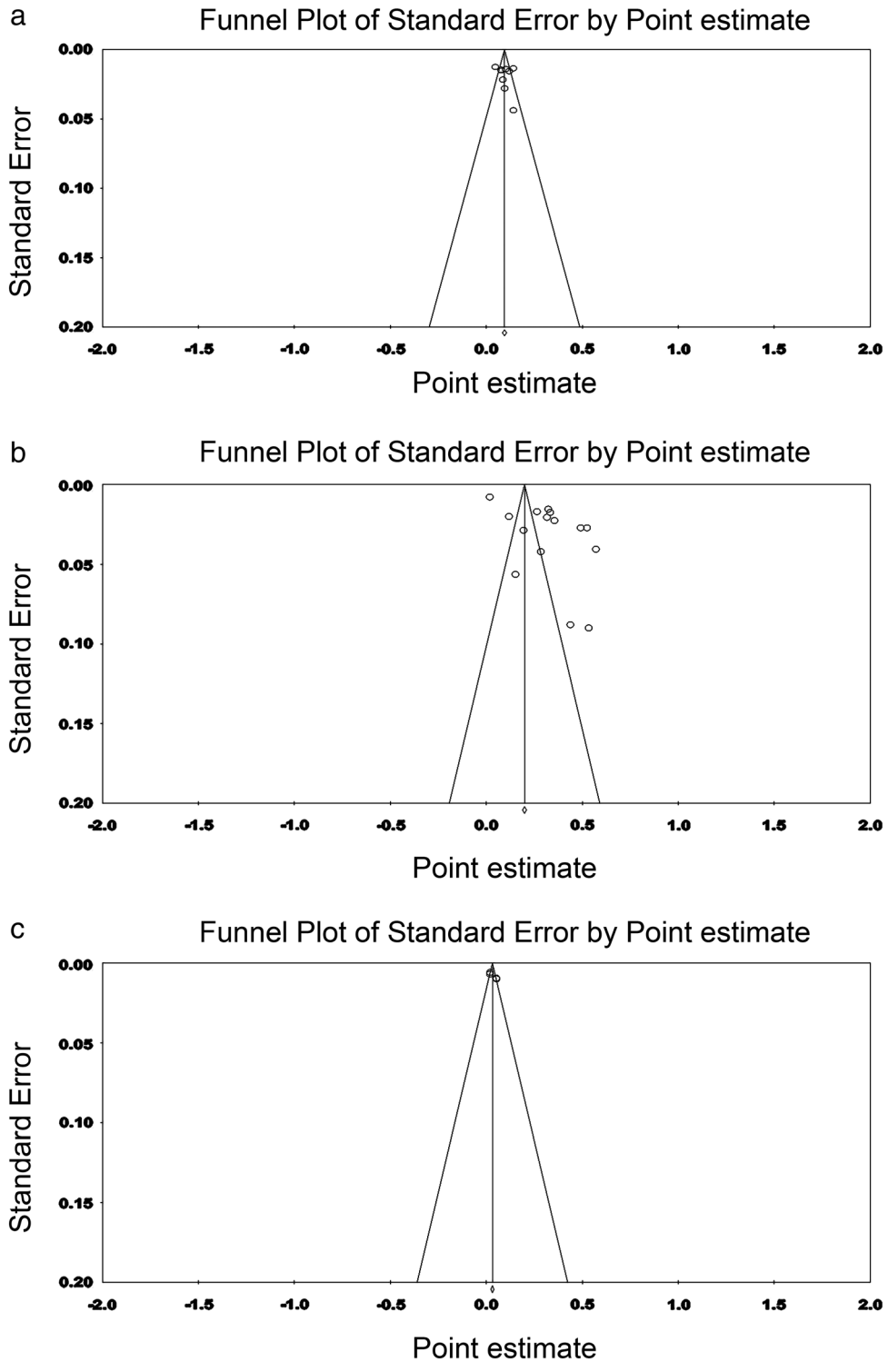

Figure 3 Bias assessment plot of eight studies reporting HBV prevalence (a), 14 studies reporting HCV infection (b), and 4 studies reporting HBV and HCV coinfection (c) in the hemodialysis population in Vietnam. HBV, hepatitis B virus; HCV, hepatitis C virus.

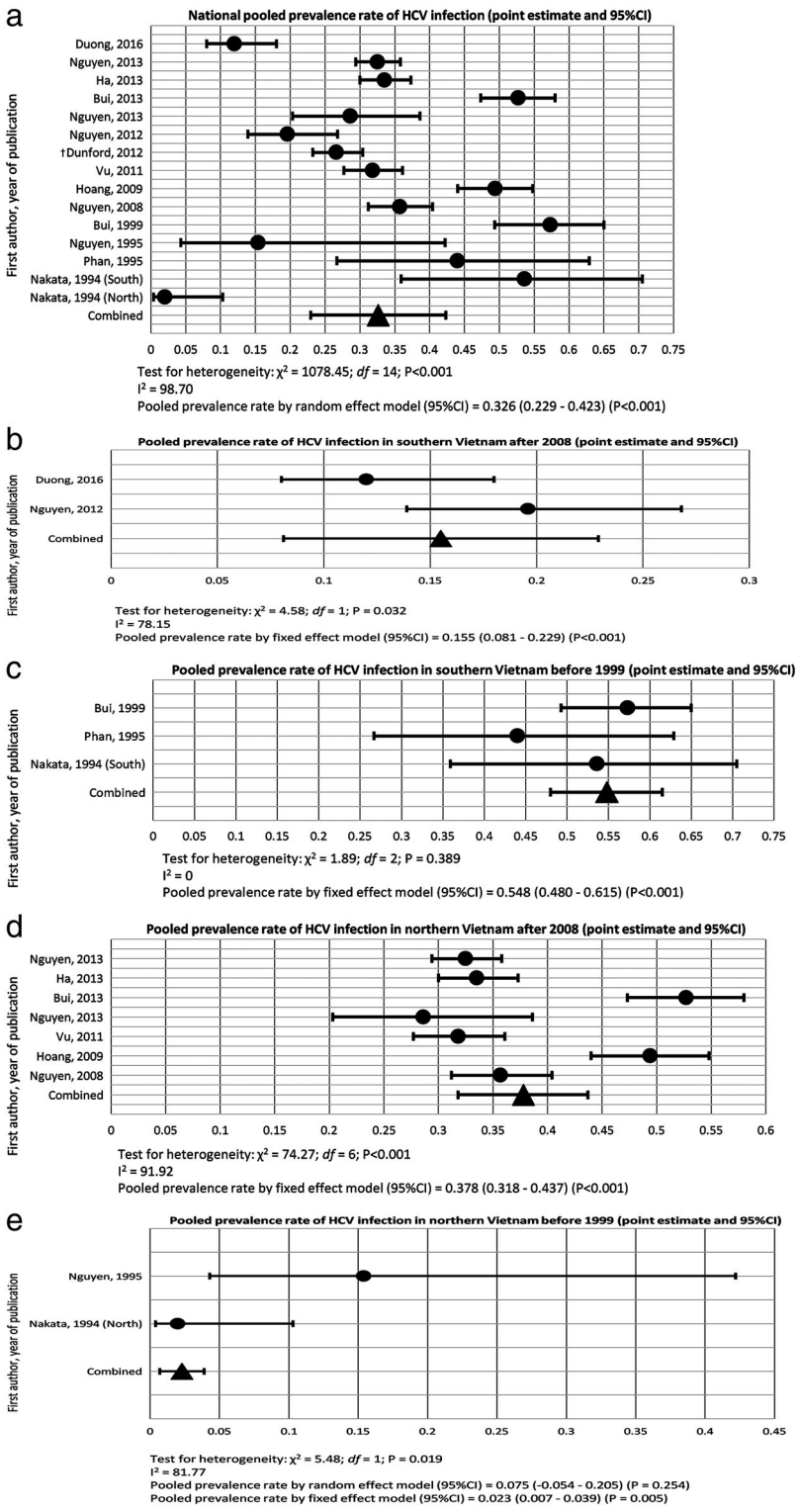

Figure 4 Forest plot of the prevalence of HCV infection in the hemodialysis population across Vietnam (a) and in the south after 2008 (b), the south before 1999 (c), the north after 2008 (d), and the north before 1999 (e). †Paper written by Dunford et al., 2012 (e.g. multicenter study), was only included to estimate the national pooled prevalence of HCV infection. HCV, hepatitis C virus.

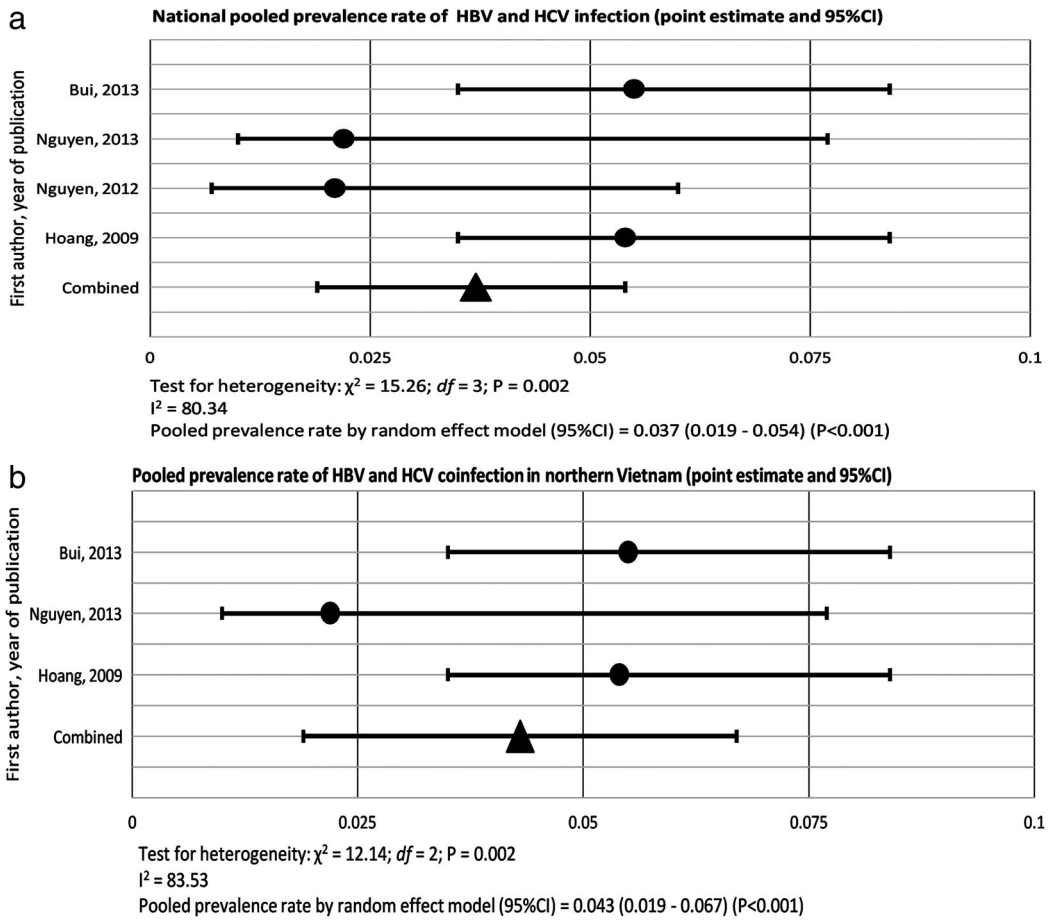

Figure 5 Forest plot of the prevalence of HBV and HCV coinfection in the hemodialysis population across Vietnam (a) and in the north (b). HBV, hepatitis B virus; HCV, hepatitis C virus.

attributed to the higher HCV prevalence in the north. The Vietnamese MOH requires dialyzers and bloodline to be reused for up to six times for many patients.[45] According to the unpublished World Health Organization's stakeholder consultation meeting report on HBV and HCV transmission risks and infection prevention and control practices at hemodialysis units in Vietnam conducted on 23 August 2018, hemodialysis units in the south do not reuse bloodline, although it is still a common practice in some units in the north, and may have been causal in the dissemination of HCV infection. Although there is a protocol for reprocessing bloodline and dialyzer,[25,30] patients remain at high risk of acquiring HCV when hemodialysis-related equipment is reused in a hemodialysis setting where the prevalence of HCV is high and infection control practices are suboptimal.[46] Difference in the prevalence of HCV between hemodialysis units located within the same region may be explained by the variation in implementing and adhering to infection control practices between units. Studies of infection control in tertiary hospitals found that the dominant hand of health-care staff even without direct patient contact may act as a reservoir of pathogens.[47,48] In addition, hand hygiene compliance by health-care workers at tertiary hospitals in Vietnam has been suboptimal, ranging from 17.6 to 62%.[42–44,49] A recent study on an HCV outbreak in a hemodialysis unit in Vietnam identified that health-care workers providing clinical care activities to multiple consecutive patients without changing gloves between patients and with low hand hygiene compliance were likely to have facilitated the outbreak.[4] These findings of high prevalence rates for HCV across Vietnam suggest that there is a variety of adherence to infection prevention and control practices between hospitals in Vietnam.

Study limitations. Our study is the first to attempt to review all current literature for the magnitude of HBV and HCV infections in the hemodialysis population in Vietnam. The heterogeneity between the studies and size of the studies, as demonstrated by wide 95% CIs for the prevalence of HBV and HCV infections, may have increased the risk of random error. Study populations were homogenous in that all reported hemodialysis patients were from major cities. However, the lack of studies on the prevalence in decentralized hemodialysis units remains a challenge to estimate. Results from our grey literature search may have potential unknown biases and errors as these local documents did not undergo an internationally standardized peer review process. However, all local documents included in our review were local journal publications and dissertations that had undergone local peer review. We may not have identified all grey

literature in Vietnam as online databases for local publication did not exist, but we increased our yield by identifying local publications through the supports of MOH and NIHBT.

In conclusion, estimates of the prevalence of HBV and HCV indicate high levels of endemicity in the hemodialysis population tested in Vietnam. The prevalence rates of HBV in a limited number of hemodialysis units were similar, while HCV prevalence rates differed by location. In Vietnam, the number of patients requiring hemodialysis is trending upward. This review has highlighted that the accuracy of the estimated risk of HBV and HCV for hemodialysis patients was limited by the number of treatment centers and geographic locations. Therefore, a more comprehensive national prevalence of HBV and HCV in the hemodialysis population in Vietnam is required to design appropriate infection control strategies and education programs.

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Supporting information

Additional supporting information may be found in the online version of this article at the publisher's website:

Appendix S1. The detail of search strategy.