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Hepatitis C virus infection among hemodialysis patients in Asia: a meta-analysis

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Abstract. – OBJECTIVE: Current studies reported that patients with hemodialysis duration for three years or more were prone to infection than those with less than three years. This meta-analysis was to assess the prevalence rate and explore the risk factors of hepatitis C virus (HCV) infection among hemodialysis patients in Asia population.

MATERIALS AND METHODS: Embase and PubMed databases were retrieved in 16 September, 2013 for cross-sectional studies, retrospective cohort studies or prospective cohort study about the prevalence of HCV infection of hemodialysis patients in Asian region. The prevalence rate and 95% confidence interval (CI) were used for pooled analysis.

RESULTS: The combined effect of overall HCV prevalence rate in hemodialysis patients of Asian countries was 0.31 (95% CI: 0.24-0.38). Subgroup analysis showed that the prevalence rate among men was 0.28 (95% CI: 0.20-0.35), while the prevalence rate among women was 0.23 (95% CI: 0.17-0.30). Male were more vulnerable to be infected than female population (RR = 1.24, 95% CI: 1.08-1.42). Blood transfusion elevated the risk of HCV infection (RR = 0.82, 95% CI: 0.70-0.95). Short-term hemodialysis population had lower risk of infection than those who receiving the long-term hemodialysis (RR = 0.55, 95% CI: 0.34-0.91).

CONCLUSIONS: The overall HCV prevalence rate of hemodialysis patients in Asian region remained at a high level of 31%, which might be increased by long-term hemodialysis and blood transfusion than people without hemodialysis. More attention and effective preventive measures are necessary.

Key Words:
Asian hemodialysis patients, Hepatitis C virus, Infection, Meta-analysis.

Introduction

Hepatitis C virus (HCV) is a major human bloodborne pathogen transmitted mainly through intravenous infusions[1] and has infected more than 170 million persons alive today[2]. Currently, HCV has become one of the primary causes of acute and chronic hepatitis in end-stage renal disease patients[3]. In Asia, HCV infection has become a serious public health problem because it is difficult to identify carriers of HCV and take effective security measures in the hemodialysis center, so patients undergoing dialysis are often exposed to HCV[4].

Epidemiological studies on the potentially infectious risk factors have found that HCV transmission is mainly by the parenteral exposure to contaminated blood or blood products or by the illegal drug injection[5]. Some scholars reported that patients with hemodialysis duration of three or more years are prone to be infected than those shorter[6,7]. In addition, hemodialysis patients with transfusion have a higher risk of HCV infection than those without[8-10]. However, conclusions on whether long-term hemodialysis and blood transfusion have significant influence are still not consistent.

We, therefore, conducted a meta-analysis of HCV infection among hemodialysis patients in Asia to explore the impacts of hemodialysis duration, blood transfusions and other factors on HCV infection in Asia population.

Materials and Methods

Search Strategy

A computer retrieval of PubMed and Embase databases with ("viral hepatitis C" OR "hepatitis C virus") AND "hemodialysis" as key words was performed for literature search. The last search was performed on 16 September, 2013. In addition, manual search was also conducted for relevant paper documents.

Eligibility Criteria for Study Screening

The inclusion criteria were: (1) the studies must be performed in Asian region; (2) study ob-

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jects should be hemodialysis patients; (3) study design was designed as a cross-sectional study, retrospective or prospective studies; (4) the outcome was HCV infection; (5) the diagnostic criteria of HCV infection was anti-HCV antibody test; (6) the language was limited to English.

The exclusion criteria were: (1) the studies that are not research articles were excluded such as review, letters, comments; (2) the literature with incomplete data or duplication were excluded.

Two investigators independently screened all titles and abstracts from the databases which met our key words and reviewed full texts of the potential eligible studies in accordance with the eligibility criteria.

Data Extraction

Two investigators independently extracted the valuable data from the included studies including the name of the first author, year of publication, region of the study performed, age of the subjects, type of study, size of the sample, and number of the infected cases and so on. Inconsistencies were solved by discussion.

Statistical Analysis

This study investigated the HCV infection of hemodialysis patients in Asian region, so the prevalence rate of 95% CI (confidence interval) was used as the evaluation index. Heterogeneity among the included studies were assessed by Cochrane Q statistic and I^2 test[11]. $p < 0.05$ of Q statistic and $I^2 > 50\%$ indicated an existence of significant heterogeneity among studies; then, a random-effects model was used for combination of effect size; $p \geq 0.05$ and $I^2 \leq 50\%$ indicated a homogeneity among studies, then a fixed-effects model was used for combination of effect size, otherwise, a randomized-effects model was used. Cumulative meta-analysis was conducted to observe the changes of overall prevalence rate over time. In addition, the subgroup analysis was conducted among type of study, area and gender. Impacts of gender, blood transfusion and hemodialysis duration on the risk of HCV prevalence were assessed. The risk of bias were assessed by Egger test[12]. All statistical analysis was performed by Stata 11.0 software.

Results

Literature Search

Literature screening process was shown in Figure 1. A total of 946 documents were obtained by search of Embase database, and 906 documents were obtained from PubMed database. After removing the duplicate literatures, 1509 articles were remained. Then 1405 were ex-

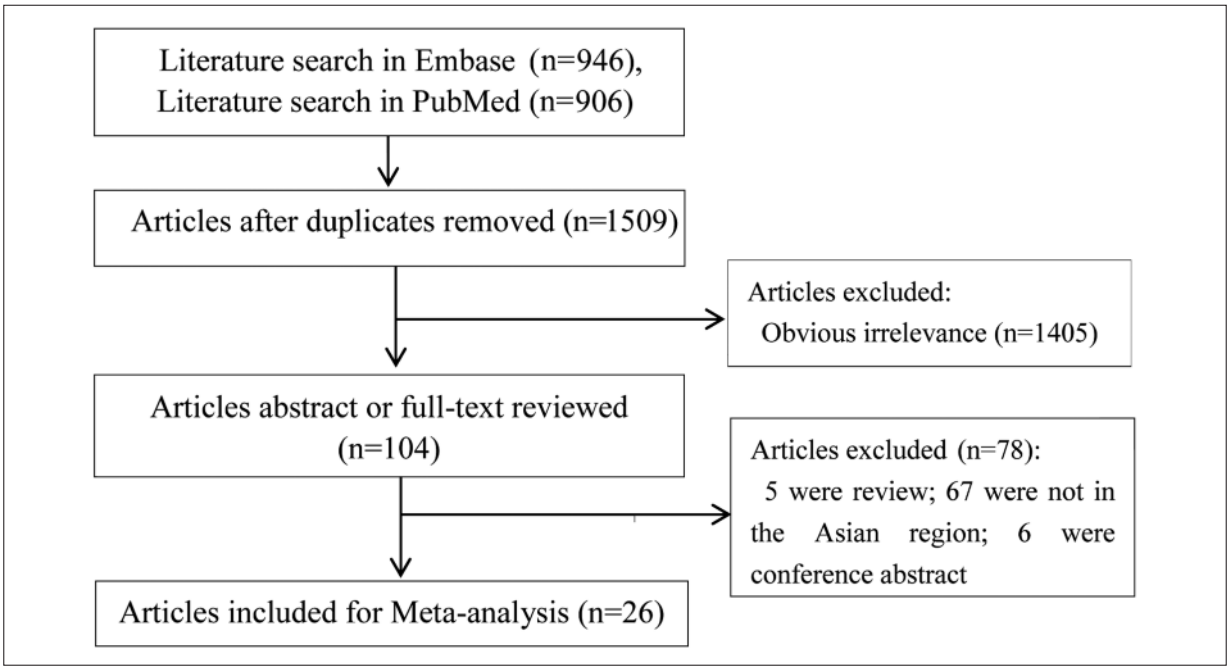

Figure 1. Literature search and study selection.

cluded by browsing the title of the literature. Among the 104 remaining articles, 78 were excluded after reading the abstracts or the full text, including 5 reviews, 67 non-Asian region studies and 6 conference abstracts. No eligible literature for meta-analysis was retrieved by artificial retrieval method. Finally, a total of 26 literatures[4,6-10,13-32] were included in this meta-analysis.

Characteristics of the Included Studies

Among the 26 eligible literatures, Almawi et al[14] and Taziki and Espahbodi[30] both reported two separate studies, so there were a total of 28 studies, including 18 cross-sectional studies, 7 prospective studies and 3 retrospective studies. Total 11 of them were from a single hemodialysis unit and 17 were from multiple (two or more) hemodialysis units. This meta-analysis involved 1856 hepatitis C virus infections and 5239 controls. Basic information extracted from the 26 included documents was summarized in Table I. The articles were published during 1994-2013, and the regions of the studies carried out were distributed in China, Japan, Saudi Arabia, Iran and other nine Asian countries.

The Prevalence of HCV Infection Among Hemodialysis Patients in Asia

In the meta-analysis of prevalence rate of HCV (Figure 2), a significant heterogeneity was observed among studies ($I^2 = 98.3\%$, $p < 0.01$), so a random-effects model was used and a combined prevalence rate of 0.31 (95% CI, 0.24-0.38; $p < 0.01$) was generated. From the

Table I. Characteristics of 26 studies on hepatitis C virus and hemodialysis patients.

id	Author	Year of publication	Year of study	Country	Age (ys) mean	Age (ys) range	Type of study	Case	N	Patients source
1	Kumar	1994	1993-1996	Saudi Arabia	44.1	16-85	Cross-sectional	24	47	Single HD unit
2	Said	1995	1994	Jordan	–	–	Cross-sectional	67	273	3 HD units
3	El-Reshaid	1995	1994	Kuwait	50	2-86	Retrospectively	81	181	2 dialysis units
4	Al-Muhanna	1995	–	Saudi Arabia	–	–	Retrospectively	70	162	6 HD units
5	Shaheen	1995	–	Saudi Arabia	42.9	12-75	Cross-sectional	295	408	4 dialysis centers
6	Bernieh	1995	1991	Saudi Arabia	47.2	–	Cross-sectional	56	94	Single HD unit
7	Shohaib	1995	1992	Saudi Arabia	–	–	Cross-sectional	73	139	3 Different renal units
8	Shahat	1995	1991-1993	United Arab Emirates	41.8	–	Prospective	64	262	Single HD unit
9	Wang	1997	1994	China	51	–	Cross-sectional	32	79	4 dialysis centers
10	Kobayashi	1998	1990-1995	Japan	54.7	28-87	Prospective	169	634	7 HD units
11	Morikawa	1999	–	Japan	55	27-88	Cross-sectional	34	125	Single HD unit
12	Bdour	2002	–	Jordan	–	9-80	Cross-sectional	98	283	6 HD units
13	Kashem	2003	2002	Saudi Arabia	45	18-75	Cross-sectional	42	90	Artificial kidney units of two hospitals
14	Al-Jiffri	2003	–	Saudi Arabia	–	–	Retrospectively	180	248	Single HD unit
15	Almawi	2004	–	Bahraini	–	–	Cross-sectional	6	81	Single HD unit
				Saudi Arabia	–	–	Cross-sectional	5	34	Single HD unit
16	El-Amin	2007	2005	Sudan	43.6	11-76	Cross-sectional	56	236	2 HD units
17	Taziki	2008	2006	Iran	47.3	–	Prospective	61	497	10 HD units
			2001	Iran	47.3	–	Prospective	64	348	
18	Khattab	2008	2003-2005	Iraqi	36	14-67	Prospective	12	169	Single HD unit
19	Assarehzadegan	2009	2005-2006	Iran	37.3	8-60	Cross-sectional	17	214	Single HD unit
20	Al-Jamal	2009	2007-2008	Jordan	52.9	14-84	Cross-sectional	34	120	3 dialysis units
21	Ohsawa	2010	2003-2004	Japan	–	22-95	Prospective	134	1214	25 HD units
22	El-Ottol	2010	2007	Palestine	46.7	6-80	Cross-sectional	54	246	4 HD centers
23	Selm	2010	2007	Yemen	–	–	Cross-sectional	32	51	Single Center
24	Joukar	2011	2009	Iran	54.8	11-66	Cross-sectional	61	514	11 Different HD units
25	Zahedi	2012	–	Iran	51	–	Cross-sectional	16	228	7 Hemodialysis centers
26	Mittal	2013	–	India	50	17-83	Prospective	19	118	Single HD unit

ys: years; HD: hemodialysis.

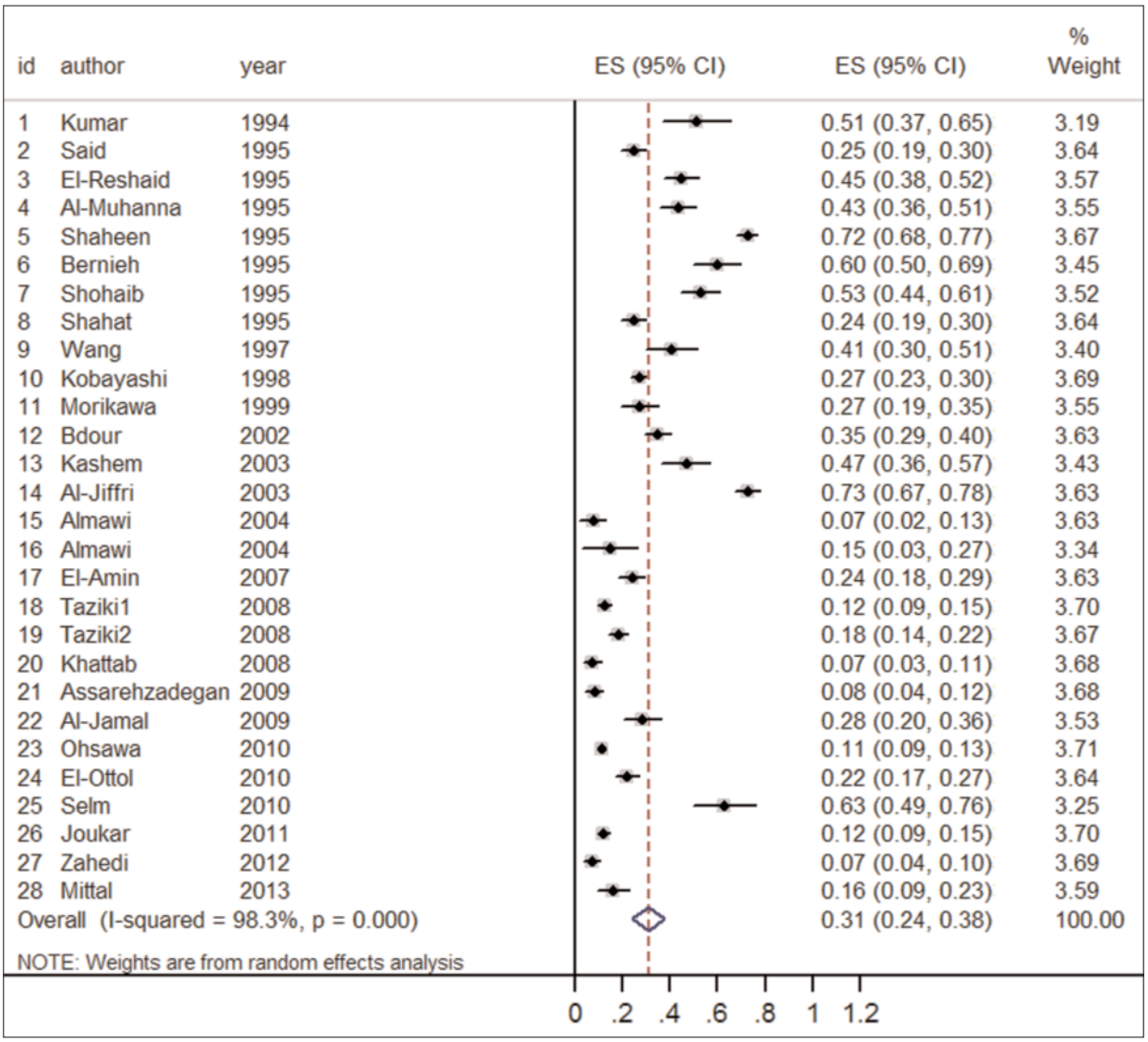

Figure 2. Pooled prevalence rate with 95% confidence interval of hepatitis C virus infection among hemodialysis patients.

cumulative meta-analysis results (Figure 3), since 1997, the overall prevalence rate shown a downward trend until 2010 and maintained in about 32%.

Subgroup Analysis of Type, Region, Subject Gender

The prevalence rate of different types of studies, regions of the studies performed and gender of the subjects were analyzed by subgroup analysis (Table II). The combined prevalence rate of cross-sectional studies was 0.33 (95% CI, 0.23-0.43) with little difference to the overall combined prevalence rate (0.31, 95% CI, 0.24-0.38); and the prevalence rate of prospective studies and retrospective studies was 0.16 (95% CI, 0.11-0.22) and 0.54 (95% CI, 0.33-0.74), respectively. The pooled prevalence rate of Iran, Japan, Jordan and Saudi Arabia was 0.11 (95% CI, 0.08-0.15), 0.21 (95% CI, 0.09-0.34), 0.29 (95% CI, 0.23-0.36) and 0.52 (95% CI, 0.40-0.64). A total of 13 studies reported separated prevalence rate of male and female, and the pooled prevalence rate of male and female was 0.28 (95% CI, 0.20-0.35) and 0.23 (95% CI, 0.17-0.30), respectively. Subgroup analysis showed that the prevalence rate of single hemodialysis unit (0.32; 95% CI, 0.17, 0.46) is similar with multi-center group (0.30; 95% CI, 0.22, 0.38).

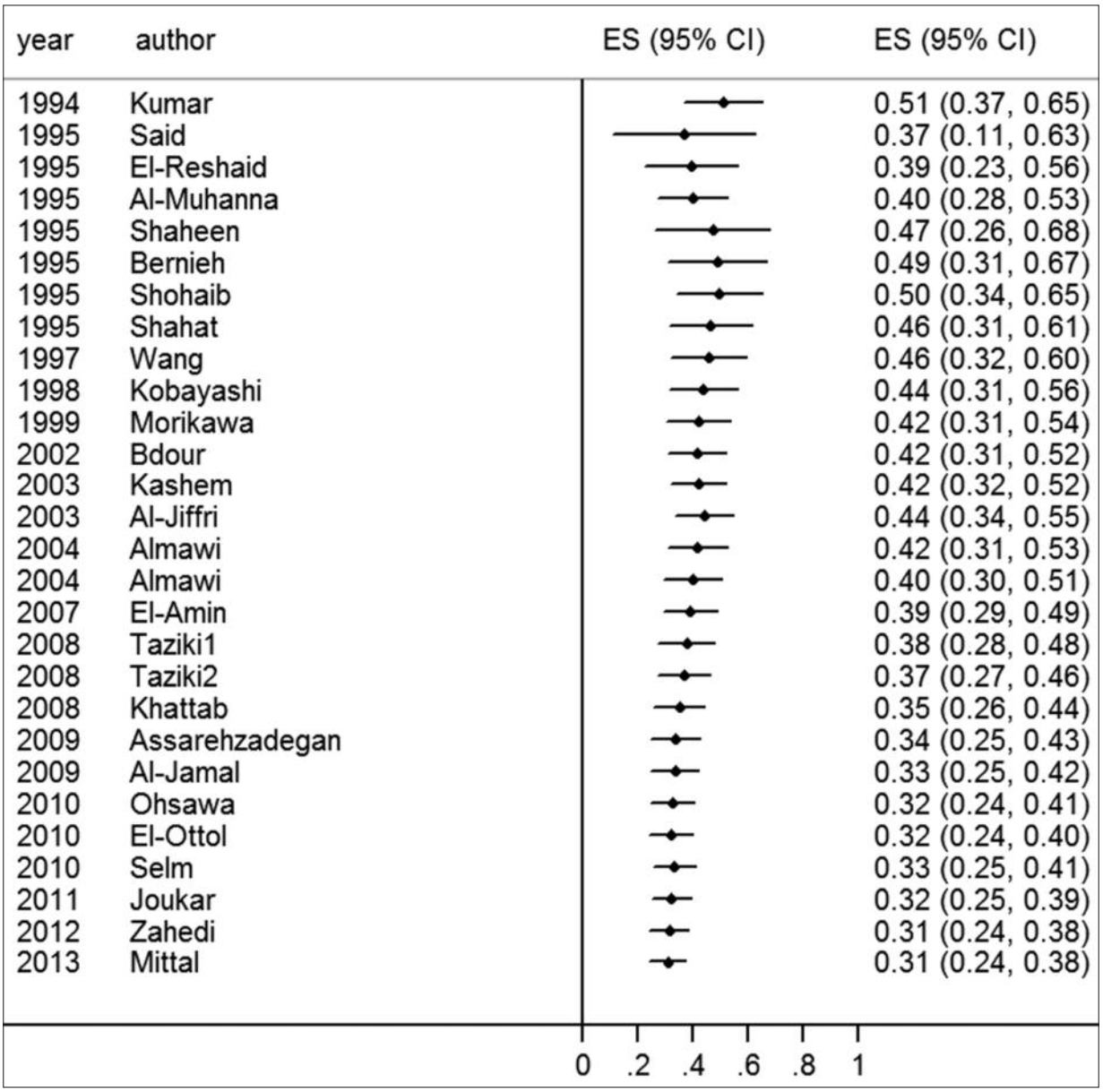

Figure 3. Cumulative meta-analysis of hepatitis C virus infection among hemodialysis patients.

Risk Factors for HCV Infection Among Hemodialysis Patients in Asia

There were thirteen studies referred to the numbers of cases and controls of male and female. The result indicated that infection risk of male hemodialysis patients was significantly higher than women (RR = 1.24; 95% CI, 1.08-1.42; p = 0.003). Six studies reported the HCV infection of hemodialysis patients with or without blood transfusion. Patients without blood transfusion shown a lower prevalence rate than those with it, but the difference was not significant (RR = 0.82; 95% CI, 0.70-0.95; p = 0.008, data not shown). In addition, short-term hemodialysis population had a significantly lower risk of HCV infection than those who receiving long-term hemodialysis (RR = 0.55; 95% CI, 0.34-0.91; p = 0.020).

Risk of Bias Assessment

Egger test result was p = 0.231, indicating that there was no significant publication bias among studies.

Table II. Subgroup analysis of study type, area and gender.

Group	No. of studies	Prevalence rate (95% CI)	Heterogeneity test	
			p	I^2 (%)
All studies	28	0.31 (0.24, 0.38)	< 0.01	98.3
Type of study				
Cross-sectional	18	0.33 (0.23-0.43)	< 0.01	98.2
Prospective	7	0.16 (0.11- 0.22)	< 0.01	93.8
Retrospective	3	0.54 (0.33-0.74)	< 0.01	96.3
Area				
Iran	5	0.11 (0.08-0.15)	< 0.01	81.8
Japan	3	0.21 (0.09-0.34)	< 0.01	97.3
Jordan	3	0.29 (0.23-0.36)	0.031	71.1
Saudi Arabia	8	0.52 (0.40-0.64)	< 0.01	94.8
Gender				
Male	13	0.28 (0.20- 0.35)	< 0.01	95.2
Female	13	0.23 (0.17- 0.30)	< 0.01	92.8
Patients source				
single HD unit	11	0.32 (0.17-0.46)	< 0.01	98.3
Multi-center	17	0.30 (0.22-0.38)	< 0.01	98.4

Discussion

Annually, HCV causes substantial morbidity and mortality worldwide and it is transmitted continuously unabated in many countries[33]. Apart from the illicit injection drug use, iatrogenic exposures (such as hemodialysis) has become the predominant risk factor for HCV transmission, especially in developing countries[34]. Explore of the risk factors of HCV infection among hemodialysis patients were critical for further targeted preventions. The present meta-analysis included 28 studies of 26 documents (involving 1856 HCV infections and 5239 controls) about HCV infection among hemodialysis patients in Asia. The overall HCV prevalence rate among hemodialysis patients in Asia was 31%. Males were more susceptible than females to HCV. Both blood transfusion and long term duration of hemodialysis were risk factors of HCV infection.

WHO have reported that the hepatitis C virus is usually spread when blood from an infected person to the body of a susceptible person[35]. We, therefore, assessed the impacts of blood transfusion and duration of hemodialysis on prevalence rate in the present meta-analysis. Our found suggested that the duration of hemodialysis and whether receiving blood transfusion may affect the prevalence rate of HCV[36,37]. Duration of hemodialysis treatment is clearly correlated with HCV positivity[38], which will increase the chance of exposure to the virus and the inadequate sterilized or contaminated medical equipment[39]. Studies also found that the patients with blood transfusion were more prone to infected by HCV than those without blood transfusion[40,41]. In conclusion, long-term of hemodialysis and blood transfusion may increase the risk of prevalence of HCV.

Gender may affect the sensitivity of people to HCV[42], since the prevalence rate of males hemodialysis patients were much higher than females to HCV. There is also a region-specific distribution of HCV prevalence[43]. The global prevalence of HCV infection is estimated to be 2.35%[44], amounting to approximate 130 million HCV-positive persons, among which, northern Africa and Asia has more HCV infection than Northern Europe (< 1.0%)[45]. Dussol et al[46] found that the HCV prevalence rate in hemodialysis patients is 5 to 25% higher than the general population because that they have significantly higher possibility of exposure to the HCV virus. Besides, the prevalence of HCV infection on long-term dialysis patients in Europe and USA (5%-10% or less) is lower than that in many countries of the developing world, including north Africa, Asia[47]. In this study, the 31% of pooled HCV prevalence rate in recent years were found by cumulative meta-analysis. The prevalence rates of different regions were quite varied, and this might be affected by the disparity of medical conditions in developed countries and developing countries. For example, the prevalence rate in

Iran, Japan, Jordan, and Saudi Arabia were 11%, 21%, 29%, and 52% respectively in this study. Furthermore, the overall prevalence rate showed a downward trend until 2010 and maintained in about 32%, which probably because the medical standards were continuously improved and gradually converged of these countries.

Above all, long-term hemodialysis and blood transfusion were important factors to increase the risk of hemodialysis patients to HCV. Some other factors, such as gender and regions may also contribute to it. Currently, people have realized that and some specific measures are undergoing to reduce the spread of HCV in dialysis units. For example, HCV can be prevented by avoiding of unnecessary and unsafe injections or blood products and treated with antiviral medicines[35]. So the modern antiviral treatments (such as pegylated interferon plus ribavirin) were suggested[47]. Sun et al[48] also thought that the key to reduce the incidence of viral hepatitis in hemodialysis patients is to control contagion and reduce the frequency of blood transfusion and cross-infection. Consequently, combined with our findings, seriously attention should be paid on keeping clean of blood and relative medical equipment to prevent HCV infection during hemodialysis.

However, there are some inevitable limitations in the present meta-analysis. First, the included studies were all observational studies and no confounding factors were corrected, which may result in the significant heterogeneity. Second, the study sample size is relatively small. Third, although there no significant publication bias was found by Egger test and a subgroup analysis was conducted, there is still high heterogeneity among studies.

Conclusions

The present meta-analysis of 26 studies indicates that the overall HCV prevalence rate among Asian hemodialysis patients was 31%, which maintained at a fairly high level. The prevalence rate was possibly influenced by region, blood transfusion and long-term hemodialysis. It's necessary to pay more attention on the HCV infection during hemodialysis and take effective preventive strategies.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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