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Prevalence of Hepatitis E virus among Iranian hemodialysis patients: A systematic review and meta-analysis

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Abstract

Introduction: Although hepatitis E is a mild disease, it can become severe and has a high mortality rate. There have been recent reports of chronic hepatitis caused by this virus especially in transplant recipients. Because hemodialysis patients are volunteers for transplant, it is more important in these patients. The aim of this study was evaluated the Prevalence of Hepatitis E virus among Iranian hemodialysis patients.

Methods: The searches were conducted by two independent researchers and the objective was to find studies published from 1/1/2000 to 30/5/2019. Hoy et. al.'s developed scale was used to assess the quality of the method and the risk of bias of observational studies.

Results: According to the random effects model, the overall prevalence of hepatitis E in 1275 hemodialysis patients was 12.2% (0.10-0.13% at 95% confidence interval and $I^2 = 98.8\%$, 26.1-26.6%).

Conclusion: Studies conducted on the relationship between chronic hemodialysis disease and hepatitis E virus indicate the different prevalence of this virus in dialysis patients than in healthy individuals, suggesting that contaminated blood donors could be one of the causes of virus transmission and endemic in a single region, and represents another possible way of virus transmission.

Keywords: Hepatitis E; Hemodialysis, infection, Iran

Introduction

Hepatitis E is a viral disease transmitted through the mouth. The virus leading to Hepatitis E was discovered in 1988 (1). This virus belongs to the calcivirus family with single-stranded RNA genomes of positive integrated polarity (2). Its genome size is 7.4 to 8.3 kb. It has no cover and is somewhat robust to environmental factors (3). The incubation period of hepatitis E is 15 to 60 days and in most cases it is asymptomatic, and jaundice symptoms in these patients are like other cases of classic hepatitis, but fever, arthralgia, and

cholestasis are more common in hepatitis E (4). Although hepatitis E is a mild disease, it can become severe and has a high mortality rate (5). There have been recent reports of chronic hepatitis caused by this virus especially in transplant recipients. Because hemodialysis patients are volunteers for transplant, it is more important in these patients (6). Compared to other viral hepatitis, hepatitis E in pregnant women and especially in the third trimester of pregnancy causes maternal deaths in 20- 25% of cases (7). Hepatitis E virus is recently found worldwide but is more prevalent in Central Asia and South-West

Asia than other parts of the world (8). This disease is sporadic in industrial countries (0-3%) and is epidemic in developing countries (7.2-24.5%). The virus is reported to be epidemic in India, Pakistan, Nepal, Burma, North Africa, and Mexico, with the largest epidemic in northwest China that has affected nearly 100,000 people.

Methods

Inclusion Criteria (eligibility criteria)

The methods used in this systematic review are developed based on the Checklist Guidelines (PRISMA). Cross-sectional studies, case control study, and cohort study are included in this study and case reviews, letters to editors, case reports, clinical trials, study protocols, systematic reviews, and review studies are excluded.

Participants: All studies about the prevalence of hepatitis were conducted on hemodialysis patients. The main objective of the study was the prevalence of hepatitis E in hemodialysis patients.

Sampling Methods and Sample Size: All observational studies were included in the systematic review regardless of their design. The minimum sample size was 25 patients or more.

Search Strategy

The searches were conducted by two independent researchers and the objective was to find studies published from 1/1/2000 to 30/5/2019. Studies were searched in Cochrane Library and the English database, and studies published in MEDLINE were searched through PubMed, and those published in EMBASE™ were searched through Ovid. We searched the national database of Magiran and SID to find studies published in Iran. To ensure the adequacy of the studies, a list of references or related reviews found through searches was studied. Systematic review studies were searched through MESH and open-ended terms in accordance with publication standards. After finalizing the MEDLINE strategy, the results were compared to search other databases, and PROSPERO was searched for recent or ongoing systematic reviews. The key words used

in the search strategy include: Hepatitis E; Hemodialysis, infection, Iran.

Study Selection and Data Extraction

Two researchers independently analyzed the titles and abstracts of the studies according to eligibility criteria. After excluding additional studies, the full texts of the studies were analyzed based on eligibility criteria and information about authors were collected if necessary. General information (relevant author, province, and publication year), study information (sampling technique, diagnostic criteria, data collection method, research conditions, sample size and risk of bias) and exclusion criteria were collected.

Quality Assessment

Hoy et. al.'s developed scale was used to assess the quality of the method and the risk of bias of observational studies.

Data Collection

All eligible studies were included in the data collection after systematic review and data were integrated using the forest plot. The random effects model was evaluated based on the overall prevalence of the disease among the participants. The heterogeneity of the initial studies was assessed using I^2 test. In addition, subgroups were analyzed based on the participants' age, publication year, and country to determine heterogeneity. Finally, a meta-analysis was performed in STATA14 statistical software.

Study Selection

A total of 182 studies were extracted through initial searches in various databases. Among 182 studies identified by analyzing titles and abstracts, 139 studies were removed due to irrelevant titles. Of the remaining 43 studies, 7 met the study criteria. (Figure 1).

Research Properties

A total of 1275 patients undergoing dialysis were evaluated. Of the 7 studies, all studies were

retrospective, and the study design was not mentioned in the other study. A total of 7 studies from 6 provinces that met the inclusion criteria were evaluated. studies conducted in Tabriz, Ahvaz, Zanjan, Gorgan, Boushehr, Kerman were included in the study. Simple sampling method was used to select the sample (n = 7). In most studies the risk of bias was low. The main method of data collection was medical records. The main study sites were the hospitals (Table 1).

Meta-analysis of Hepatitis E Frequency in Hemodialysis Patients:

According to the random effects model, the overall prevalence of hepatitis E in 1275 hemodialysis patients was 12.2% (0.10-0.13% at

95% confidence interval and $I^2 = 98.8%$, 26.1-26.6%) (Figure 2, Table 2).

Subgroup Analysis:

Meta-Regression Results:

Results of Meta-Regression Between Participants' Age and prevalence of Hepatitis E in Dialysis Patients:

Regression of the study was analyzed based on the relationship between prevalence of hepatitis E in hemodialysis patients and participants' age. There was no significant linear trend in univariate meta-regression to explain the change in effect size of participants' age (Figure 3).

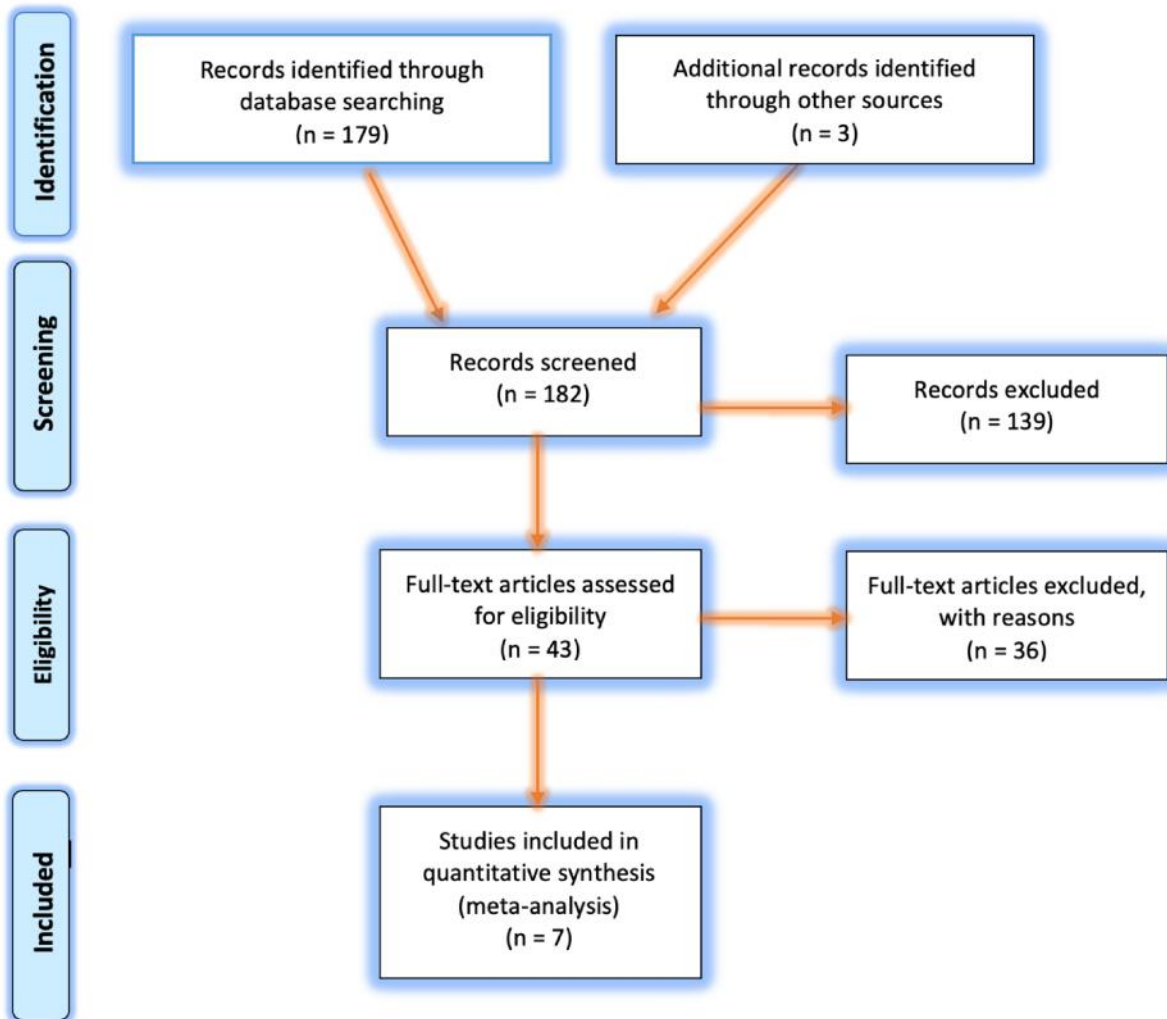


Figure 1. PRISMA flow diagram

Table 1. characteristics of the included studies

| ID | Author | Province | Publications year | Number of patients | Male to female | Mean of age |
|----|-----------------------|----------|-------------------|--------------------|----------------|-------------|
| 1 | Manochehrkhoshbin | Tabriz | 2004 | 324 | 190/134 | 53.5 |
| 2 | Alireza tahmatan | Gorgan | 2013 | 150 | ----- | -- |
| 3 | Fateme Azari | Boushehr | 2014 | 104 | 74/76 | - |
| 4 | AhmadrezaMobayen | Zanjan | 2013 | 93 | 61/43 | - |
| 5 | Mohammad javad Zahedi | Kerman | 2012 | 228 | 49/44 | 51 |
| 6 | MaahnazTaemi | Tabriz | 2005 | 329 | 136/92 | 58 |
| 7 | SeyedSefollahmousavi | Ahvaz | 2013 | 47 | 175/125 | 55.2 |

Table 2. Meta-analysis of the Prevalence of Hepatitis E virus among Iranian hemodialysis patients

| First author | 95% confi. interval | | | | Publications year | Number of patients |
|----------------------------|---------------------|--------------|--------------|------------|-------------------|--------------------|
| | Low | Up | ES | Weight | | |
| Manochehrkhoshbin (16) | 0.042 | 0.098 | 0.070 | 30.41 | 2004 | 324 |
| Alireza tahmatan (17) | 0.009 | 0.071 | 0.040 | 23.85 | 2013 | 150 |
| Fateme Azari (18) | 0.38 | 0.57 | 0.48 | 2.55 | 2014 | 104 |
| AhmadrezaMobayen (19) | 0.18 | 0.36 | 0.27 | 2.89 | 2013 | 93 |
| Mohammad javad Zahedi (20) | 0.64 | 0.75 | 0.70 | 6.65 | 2012 | 228 |
| MaahnazTaemi (21) | 0.042 | 0.098 | 0.70 | 30.71 | 2005 | 329 |
| SeyedSefollahmousavi (22) | 0.021 | 0.199 | 0.110 | 2.94 | 2013 | 47 |
| Pooled ES | 0.107 | 0.137 | 0.122 | 100 | ----- | ----- |

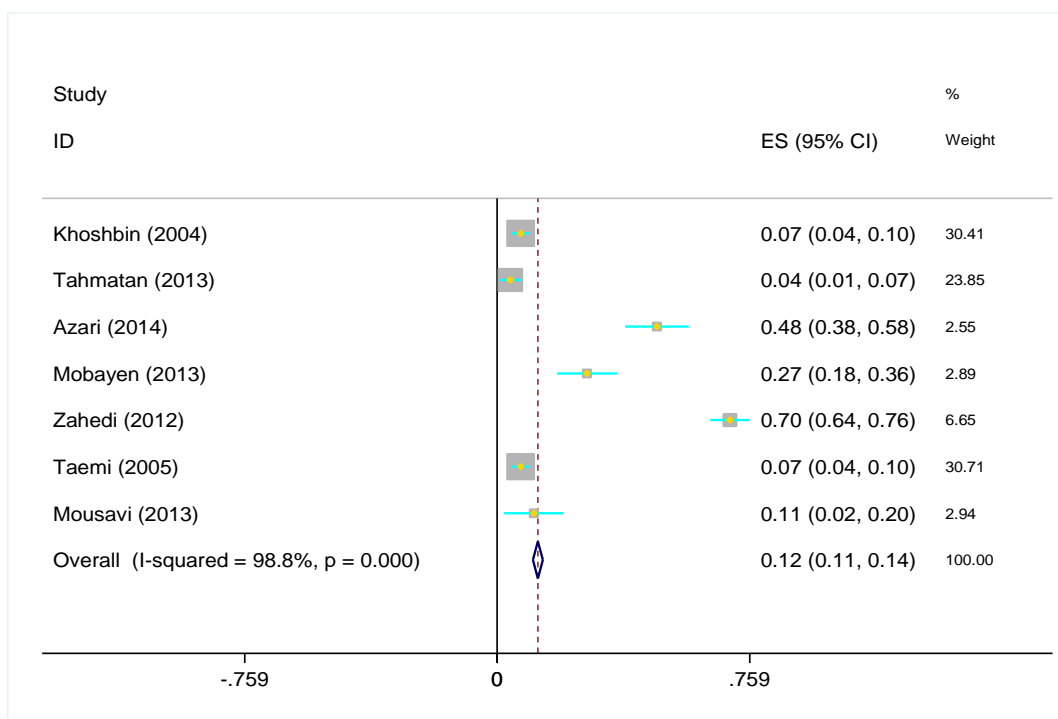


Figure 2. Meta-analysis of the Prevalence of Hepatitis E virus among Iranian hemodialysis patients

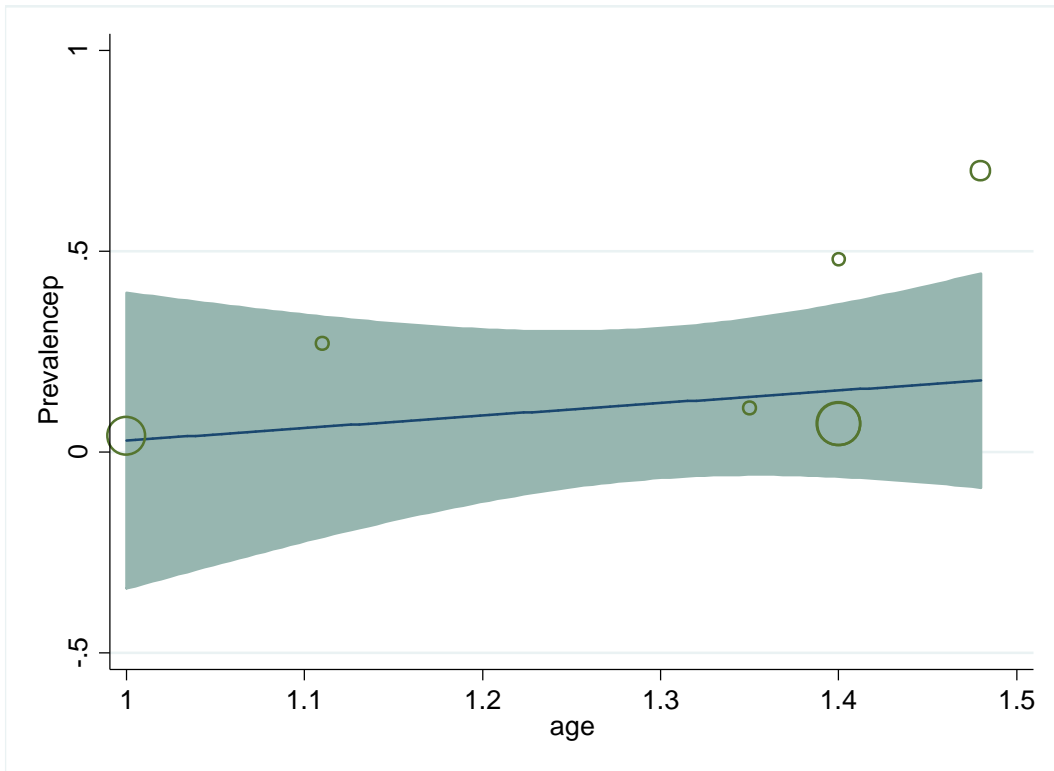


Figure 3. Meta-regression between mean age and Prevalence of Hepatitis E virus among Iranian hemodialysis patients

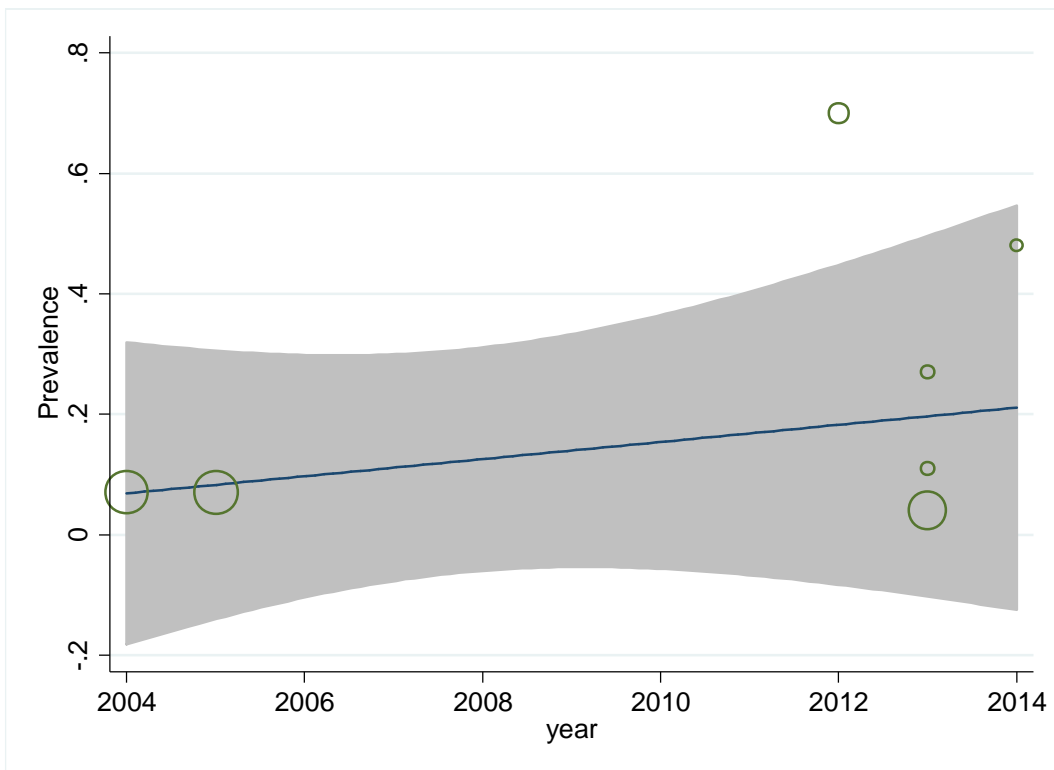


Figure 4. Meta-regression between publication year of study and Prevalence of Hepatitis E virus among Iranian hemodialysis patients

Discussion

According to the random effects model, the overall prevalence of hepatitis E in 1275 hemodialysis patients was 12.2% (0.10-0.13% at 95% confidence interval and $I^2 = 98.8\%$, 26.1-26.6%). The first epidemic in Iran was reported in Kermanshah in 1989 and the second epidemic in ChaharmahalvaBakhtiari in 1992. The prevalence of hepatitis E in Iran has been reported to be between 2.3-10% and also in Gorgan, the prevalence of hepatitis E among pregnant women is 7.3% and among women of childbearing age is 6.3% (9). The prevalence of this virus in hemodialysis patients in Iran is 7.4%. Transmission of HEV virus is mostly spread by the fecal-oral route, but it can be transmitted to humans from animals and to infants and from infected mothers (10-13). Studies conducted on the relationship between chronic hemodialysis disease and hepatitis E virus indicate the different prevalence of this virus in dialysis patients than in healthy individuals, suggesting that contaminated blood donors could be one of the causes of virus transmission and endemic in a single region, and represents another possible way of virus transmission (14-15). Studies have also indicated that duration of dialysis, increased dialysis frequency, and a history of blood transfusions are associated with the infection of dialysis patients to hepatitis E virus. Anti-HEV IgM and anti-HEV IgG performed using ELISA and Western blot methods are used to detect hepatitis E (23). Other methods such as immunofluorescence and RT-PCR are also used to detect this infection. The ELISA method seems to be more convenient and practical than other methods for screening (24). Hepatitis E is the major cause of acute hepatitis in developing countries with poor health conditions in terms of epidemiology and is one of the diseases whose epidemiological pattern differs in developed and developing countries. The prevalence of this virus in different parts of the world (Greece, Spain, Taiwan, Saudi Arabia, Belgium, Japan, Brazil, and Sweden) accounts for 0.3-9% in public and 0-31% in the dialysis patients that is more frequent during infections. Although the mortality rate in public is about 1%, it is up to 30% in hemodialysis patients especially in pregnant women. Different studies in different

parts of Iran have reported the same rate for the prevalence of hepatitis E and its infection epidemics and mortality are reported especially in the west of the country. The epidemiology of hepatitis E in hemodialysis patients is a function of its prevalence in the healthy population of this community. In this study, which is the first report of the relative prevalence of anti-body against hepatitis E virus in hemodialysis patients in Gorgan, 4% of patients showed antibody against this virus, although no comprehensive studies were conducted on the general population of the area, but the relative frequency in this study was higher than the reported frequency in pregnant women (7.3%) and women at childbearing age (6.3%) (25). In addition, the frequency of this study is lower than the only report from Iran, which had a relative frequency of 47.4% in the dialysis patients, while the results of the present review are approximately equivalent to the data obtained from the study conducted in Saudi Arabia and is close to the relative frequency reported from many European countries.

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