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SYSTEMATIC REVIEWS

Prevalence of hepatitis C virus infection among hemodialysis patients in the Middle-East: A systematic review and meta-analysis

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Abstract

AIM

To determine hepatitis C virus (HCV) infection prevalence in each country of the Middle-East and the overall prevalence of the region.

METHODS

In this systematic review, we gathered all documents related to HCV infection prevalence among hemodialysis patients in 17 middle-east countries from April 2006 to March 2016. We selected only cross-sectional studies that had proper sampling and measurement methods as well as a valid statistical analysis.

RESULTS

After screening of 7311 documents, 56 studies were selected reporting the prevalence of HCV infection among hemodialysis patients from 10 countries of the region. Seven countries including United Arab Emirates, Afghanistan, Qatar, Bahrain, Kuwait, Oman, Israel, and Cyprus did not have any relevant document; thus, their latest reports were just mentioned. We performed the meta-analysis and determined the prevalence rates for each country as well as the whole region. The overall HCV infection prevalence among hemodialysis patients in the region was reported to be 25.3%; Egypt and Syria had the highest reported rates while Iran and Lebanon had the lowest. Further investigations are still needed to provide more reliable databases, find main risk factors, and to improve diagnosis and treatment plans, particularly in higher prevalent countries.

CONCLUSION
Controlling the prevalence and improving the management methods of HCV infection among hemodialysis patients are of a great concern in the Middle-East region.

Key words: Hepatitis C; Hemodialysis; Prevalence; Middle-East; Meta-Analysis; Review

Core tip: This paper is a systematic review and meta-analysis of the reports published from April 2006 to March 2016 on the prevalence of hepatitis C infection among 17 countries of the Middle-East region including: Iran, Turkey, Iraq, Saudi Arabia, Syria, Yemen, Palestine, United Arab Emirates, Jordan, Lebanon, Oman, Egypt, Cyprus, Qatar, Afghanistan, Bahrain, Israel, and Kuwait.

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INTRODUCTION

Hepatitis C virus (HCV) infection is a major concern for the public health worldwide in both developing and developed countries[1] . Transmission of HCV infection is mainly by exposure to infected devices and tools despite rigid hygienic control, infected blood or blood products, hemodialysis, intravenous (IV) drug abuse, and organ transplantation[2]. The estimation of national prevalence and ways of transmission of HCV should be completed in order to allow the national authorities to prioritize preventive measures and have the best and most appropriate use of available resources. Epidemiological surveys on the roles of potential risk factors, such as injections for medications, vaccinations, medical procedures, tattooing, and injections outside of medical settings, have shown a wide geographical variation with major implications for the populations and potential management, prevention, and control plans[3,4]. Prospective investigations have revealed that about 80% of the acute hepatitis C cases progress to chronic infection; about 10%-20% of these cases will develop chronic liver disease complications, like liver cirrhosis, within two to three decades of onset, and about 1%-5% will end up with liver cancer[4,5].

Among the risk factors of HCV infection which had been evaluated through many studies, the following can be mentioned in brief: Sex (male > female), education (more than 12 years > less than 12 years), ethnicity (whites and Hispanics < others), number of sexual partners, age of starting intercourse, intravenous drug use, addiction, vaccination history, blood transfusion, occupation and employment situation, history of hemodialysis, and organ transplantation, *etc*[6].

Screening for HCV mainly focuses on testing those who have an individual risk factor for exposure, who have evidence of liver disease, and who belong to specific demographic groups that have a high-prevalence of infection[6,7]. Without screening, many infected individuals will be identified late which may lead to longer hospitalization and death[6,7]. In recent guidelines, the CDC (Center for disease control and prevention) recommended that testing for HCV should be performed routinely in patients at increased risk of infection; specifically for those who have ever had illegal drug injections, received blood or organs before July 1992, received clotting factors produced before 1987, were ever on chronic hemodialysis, any evidence of liver diseases, and those infected with HIV[6,7]. The initial screening test for HCV infection is an HCV antibody test. Various antibody tests are available, including laboratory based enzyme-linked Immunosorbent assay (ELISA), HCV RNA by reverse transcription Polymerase chain reaction (RT-PCR), and tests performed on samples that the patient may collect at home[8]. A reactive or indeterminate/equivocal antibody test should be followed by HCV RNA testing to determine occult infections[8,9]. Immunocompromised patients, patients on hemodialysis, transplant recipients, and advanced HIV infected ones might have higher false negative rates of antibody testing than immune-competent patients[8-10].

HCV infection is common and associated with significant morbidity and mortality among dialysis patients and is more common in dialysis patients than in healthy populations. Dialysis Outcomes and Practice Patterns Study, which provides reliable data regarding the prevalence of HCV infection among dialysis patients, is a prospective, observational survey among adult hemodialysis patients who are randomly selected from 308 representative dialysis facilities in many countries such as Japan, France, Germany, Spain, Italy, the United Kingdom, and the United States. In the 2004 report, the overall prevalence was 13.5% (compared to global prevalence in the general population of approximately 3%)[11]. The reported prevalence of anti-HCV antibodies among hemodialysis patients in different countries were from 5.5% to 14% in the United States[12], 13.5% to 31% in Italy[11,13-15], 10% to 42% in France[16], 75% in Moldavia[17], 3.8% in Germany, 14.8% in Japan, 22.9% in Spain, and 2.6% in the United Kingdom[11]. Nonetheless, the relatively high incidence of anti-HCV antibodies in hemodialysis units is a concern for today's health policy makers and care providers. A number of risk factors have

been identified for HCV infection among hemodialysis patients; the number of blood transfusions[18], duration of the hemodialysis treatment[18], and also nosocomial transmissions due to poor infection-control measures are among the most important ones[19,20].

No comprehensive report was presented, particularly during the last decade, in order to give a sight about the prevalence of HCV infection among hemodialysis patients of the Middle-East countries. We found that evaluation and estimation of the prevalence in these countries and performing comparisons among them may help researchers and health policy makers create or modify research projects, preventive programs and management plans for the hemodialysis patients in the region.

In the present study, we have systematically reviewed papers and reports related to HCV infection prevalence among hemodialysis patients in 17 countries in the Middle-East region.

MATERIALS AND METHODS

We studied the prevalence of HCV infection related to hemodialysis in the Middle-East countries and the changes in the trends during the past decade through a comprehensive systematic review of literature followed by integrating the data and analysis of the outcome.

Study question

The populations of interest in this survey was hemodialysis receiving patients among the general population of the Middle-East countries and the interested outcome was presence of positive HCV-antibody in their blood samples based on ELISA test even if other laboratory evaluations are not identified clearly, from April 2006 to March 2016. We intended to find the prevalence of HCV infection related to hemodialysis and the possible alterations in each country regarding this prevalence during the last decade.

Search strategy

For searching in each one of the databases, we used the following terms "Hepatitis C", "HCV," and "Hemodialysis" altogether with the name of each country in the Middle-East region including[21]: Afghanistan, Bahrain, Cyprus, Egypt, Iran, Iraq, Israel, Jordan, Kuwait, Lebanon, Oman, Palestine, Qatar, Saudi Arabia, Syria, Turkey, United Arab Emirates (UAE), and Yemen, as key words for titles and/or abstracts in a MeSH word search. Cross-sectional studies were selected and screened for further evaluations. The searching process was performed in the first week of June 2016.

Electronic databases and Gray literature

We searched 10 international electronic databases of biomedical sciences including Medline (Pubmed), Proquest, Embase, Scopus, Google scholar, CINAHL, CABI, Index Medicus for Eastern Mediterranean Region (IMEMR), Cochrane library, and EMROMedex. Also, three Iranian national databases of medical sciences papers were evaluated including Iranmedex, Scientific Information Database (SID), IranDoc, and Magiran for the papers which were not added to the international electronic databases. Since the language of many countries of the region is Arabic, the keywords were also searched in Arabic to find any data in this regard.

The Gray literature evaluation included 82 international and regional congresses and seminars that were held in the study time period around the world and specifically in the region, and we selected and hand searched the abstract books that were obtainable as well as possible by two independent reviewers. We also searched national reports from CDC centers of the countries, those which were accessible, and the websites of the university, thesis, and reports which were related to the subject during the study time period. Moreover, forward and backward citations of the searched items were performed.

Critical appraisal and selection of studies

Documents were catalogued using Endnote X4. Two independent reviewers who were trained in this field reviewed all citations thoroughly for eligibility criteria to be included in the analysis. The inclusion criteria were all descriptive and/or analytical cross-sectional surveys which had specified temporal and geographic characteristics of the study, sufficient populations, correct and proper sampling methods with identical and valid measurement tools for all study subjects, and proper analytical methods considering the sampling design and the demographic data. A previously obtained method which was a revision of the criteria developed by Sharifi *et al*[22] was occupied for this purpose.

Data extraction and analysis

The extracted data were first author, year of the study, location, sample population, sampling method and sample size, HCV detection method, age, male to female ratio, and HCV point prevalence in the subjects. Cochrane Q-test was used with a significance level of less than 0.1 for statistical heterogeneity of the results. I^2, presented a range of 0% (no heterogeneity) to 100% (significant heterogeneity), was employed to assessing level of heterogeneity; values of 25%, 50% and 75% were considered as representing low, medium, and high heterogeneity, respectively[23]. Wherever Cochrane Q-test and I^2 confirmed the studies heterogeneity, random effect meta-analysis based on DerSimonian and Laird method was used to combine the outcomes; otherwise, fixed effect meta-analysis was used. Statistical analyses were carried out with "metan" command in Stata, version 11.0 (Stata

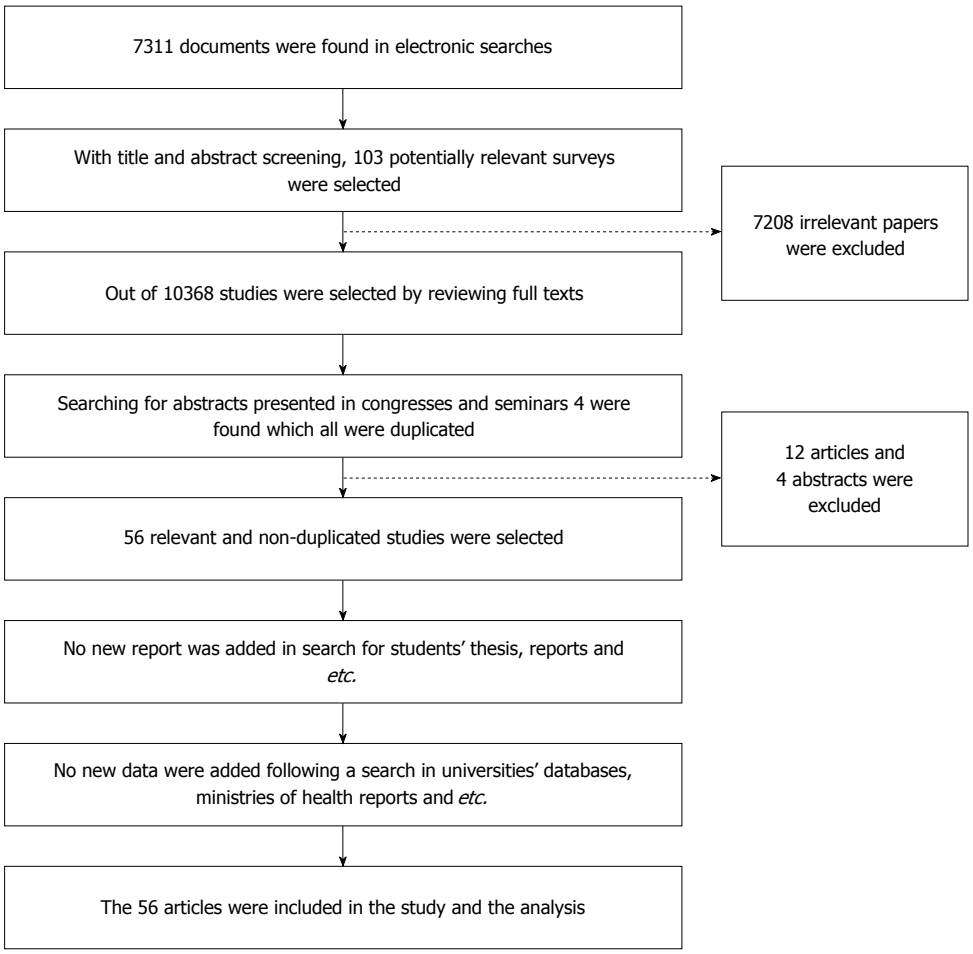


Figure 1 Follow diagram of systematic review and searches for hepatitis C virus infection prevalence among hemodialysis patients in the Middle-East countries.

Corp, College Station, TX, United States)[24].

RESULTS

In our primary search in databases with the aforementioned search strategy 7311 documents were found. After assessment of the documents according to their titles and also their abstracts, 7208 unrelated documents were omitted. We found 103 relevant citations out of all searched documents among which 68 studies were not overlapping (duplicate studies found by many search routes); of these 68 papers 56 were included in this investigation according to their publication year which are mentioned in the result part; studies which were not cross-sectional, had inappropriate methods of sampling, or inappropriate data analysis and invalid data reporting were excluded after full-text screening. In some countries such as Afghanistan, Cyprus, Qatar, Kuwait, UAE, Oman, and Bahrain, no related document was found that was published after; thus, no study could be included in the meta-analysis for these countries[4,25-45]. In gray literature evaluations 4 studies were found of which all had overlapping with the published articles. The detailed search process is exhibited in Figure 1.

The research method in all included studies was cross-sectional conducted within the hemodialysis patients from April 2006 to March 2016. Since the investigations in this field were limited, we did not set any exclusion criteria for the population of the study, hence, the sample size varied from 31 to 22070 patients in different centers in the Middle-East countries. The age of the studies subjects was between 8.3± 2.4 and 80.9 ± 4.9 years old. In the majority of the surveys (49 of 56), 50.6 to 69.9 percent of the subjects were males, while in the other 7 documents 50 to 58.1 percent of the participants were females. ELISA methods were the most dominant methods used for HCV antibody detection; some studies had also used other more specific methods like RT-PCR beside ELISA which had led to lower rates of false negative results. The reported prevalences in this study are based on ELISA test results. All papers that used ELISA for HCV detection had implemented second or third generations of the test.

The overall prevalence of HCV infection among hemodialysis patients in the Middle-East countries was 25.3% (95%CI: 20.2%-30.5%). As it is shown in Table

Table 1 The prevalence of Hepatitis C infection in Middle-East countries. Summary of studies by countries[1], age and hemodialysis duration are presented

Subgroup	Number of studies	Prevalence (95%CI)	Between studies		Between subgroups	
			I^2	$P_{Heterogeneity}$	Q	$P_{Heterogeneity}$
Country						
Iran	21	12% (10%-15%)	90.0%	0.001	30052.52	0.001
Iraq	9	20% (12%-28%)	97.3%	0.001		
Egypt	7	50% (46%-55%)	94.7%	0.001		
Jordan	4	35% (17%-54%)	97.4%	0.001		
Yemen	4	42% (28%-56%)	93.4%	0.001		
Turkey	4	23% (18%-28%)	66.3%	0.031		
Palestine	3	18% (5%-30%)	94.8%	0.001		
Lebanon	2	9% (1%-17%)	98.4%	0.001		
Syria	1	54% (50%-59%)	-	-		
Saudi	1	19% (13%-25%)	-	-		
Age(yr)						
< 40	4	24% (11%-38%)	95.4%	0.001	334.82	0.001
40-50	16	35% (26%-45%)	97.8%	0.001		
⩾ 50	26	20% (10%-29%)	99.7%	0.001		
Hemodialysis duration (yr)						
< 3	13	22% (15%-29%)	96.4%	0.001	3085.57	0.001
3-5	8	22% (4%-40%)	99.7%	0.001		
⩾ 5	9	30% (16%-45%)	99.0%	0.001		

[1]United Arab Emirates, Afghanistan, Qatar, Bahrain, Kuwait, Oman, Israel, and Cyprus, were not added due to insufficient data. The prevalences are reported as ratio (95%CI).

1, the reported percentages were heterogeneous and showed statistical significance (test for heterogeneity: Q = 30052.5, df = 9, P < 0.001).

Iran

An overall anti-HCV antibody prevalence of less than 1% was reported in the general population of Iran[46-48]. The most dominant genotype of HCV in Iran was subtype 1a (44.9%) followed by 3a (39.6%), and 1b (11.3%) among the general population[49]. The reported prevalences of hepatitis C infection among hemodialysis patient in different areas are as follows: In 2006, 38% (19/50) and 4.9% (10/204) in Urmia city and Markazi province, respectively[50,51]; in 2007, 10.3% (9/89) in Ghazvin[52], 20.4% (66/324) in Tabriz[53], and 8.5% (11/130) in Tehran[54]; In 2008 6.5% (44/674) in Eastern-Azerbaijan[55], 24.7% in Golestan[56], 6.8% in Markazi[57], 21% (39/186) in Sari and Ghaemshahr[58], and another 12.3% in Sari[59]; In 2009, 18.4% (30/163), 7.9% (34/214), and 5.3% (6/112), in Gilan, Khuzestan, and Tehran, respectively[60-62]; in 2010, 20.1% (67/334) in Amol, Tonekabon, Rasht, and Ramsar[63]; in 2011, 11.9% in Gilan[64], and 31.5% (64/203) in Kerman province[65]; in 2012, 6% (9/160) and 7% (16/228) in Yazd and Kerman provinces, respectively[66,67]; in 2013, 7.2% (13/181) in Shiraz[68]; in 2014, 8.1% (37/455) in Tabriz[69], and 5.2% (26/499) in Isfahan[69]; in 2015, 5.9% (11/185) in Alborz Province[70].

As it is exhibited in Figure 2, the overall prevalence of HCV infection among hemodialysis patients in Iran according to the last decade's publications was estimated as 12% (95%CI: 9%-15%).

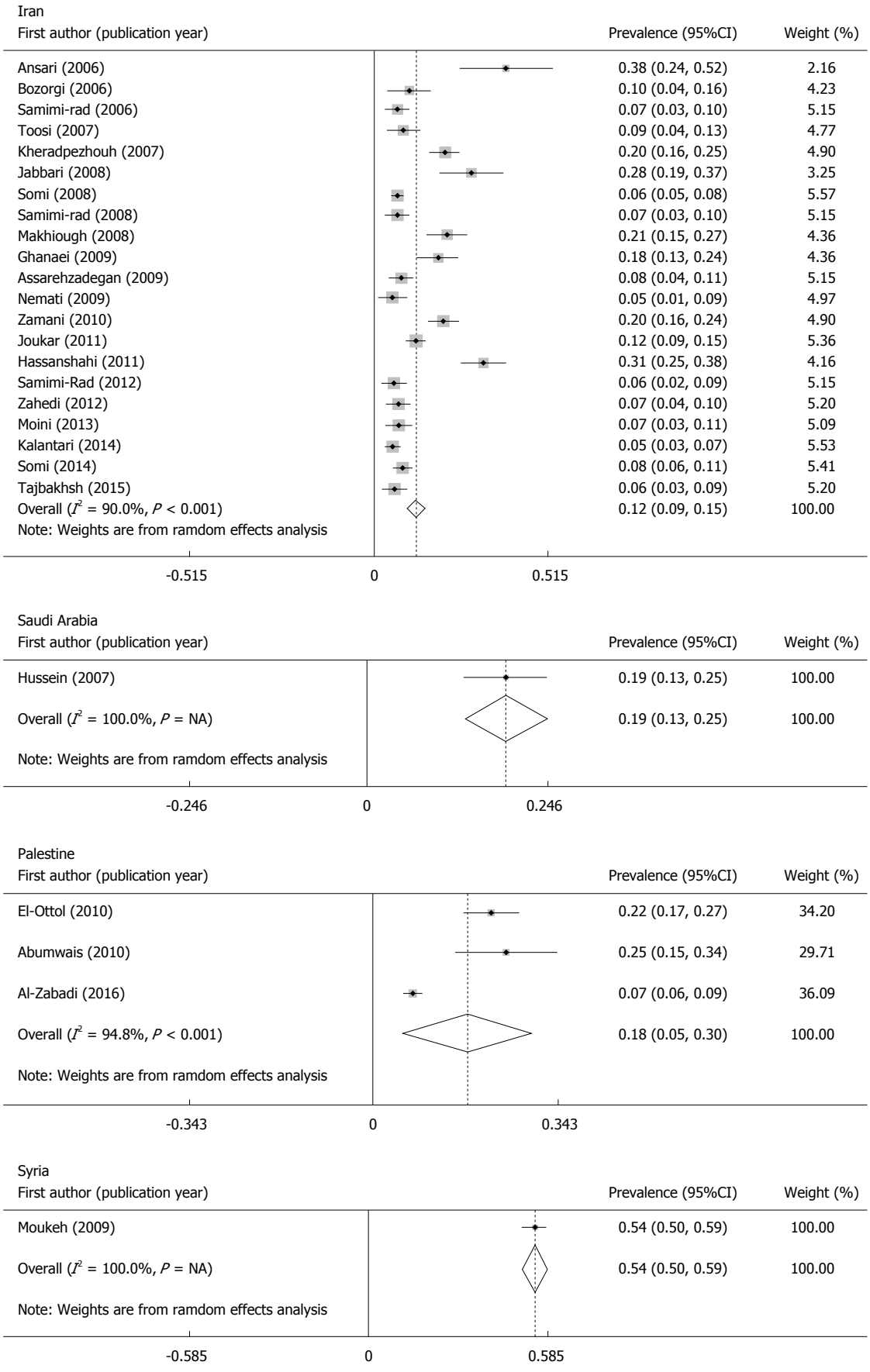
Turkey

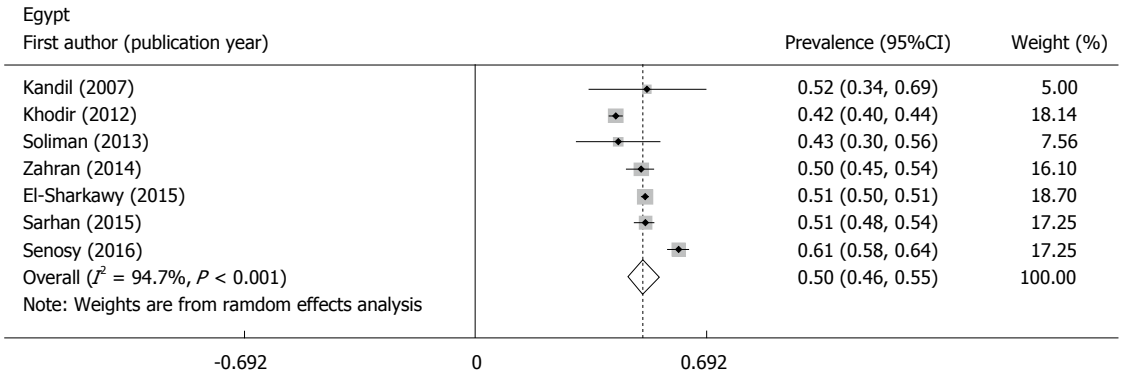
The prevalence of HCV infection among the general population of turkey was reported as 1.6%[71]. Genotype 1b was found to be the most common genotype of HCV (67.7%) followed by genotype 1 (7.7%), 4 (7.3%) and genotype 3 (6.7%) among the general population[72,73]. Investigations on the prevalence of HCV infection among hemodialysis patients are limited in this country and are as follows: in 2004, 19% (19/83) in Izmir[74], in 2006, 26% (245/934)[75], and 28.7% (54/188)[76], in the whole country, and 35.6% (26/73) in Ankara[77]; in 2009, 19% (83/437) in the Ege region[78]; in 2014, 19.9% (40/201) in Antalya[79]. As it is demonstrated in Figure 2, the prevalence of HCV infection among hemodialysis patients in Turkey according to the publications of the last 10 years was estimated as 23% (95%CI: 13%-28%).

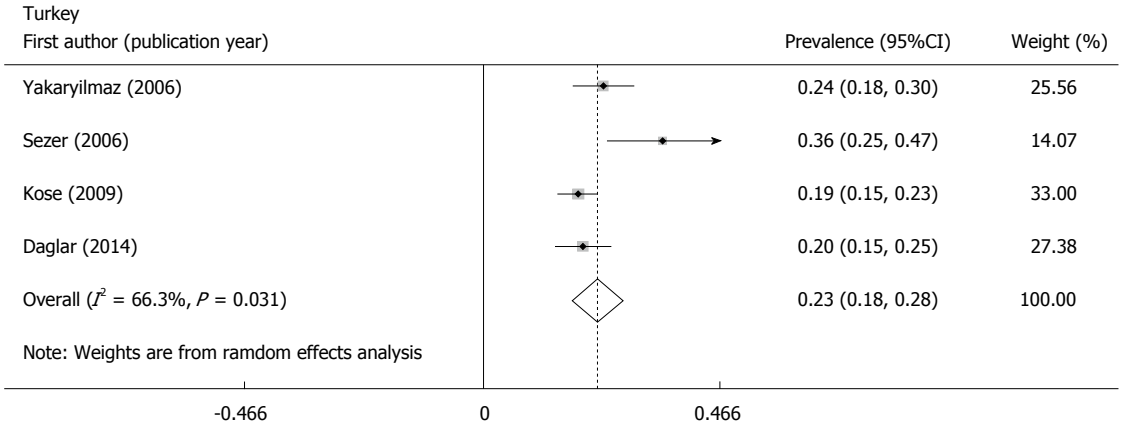
Saudi Arabia

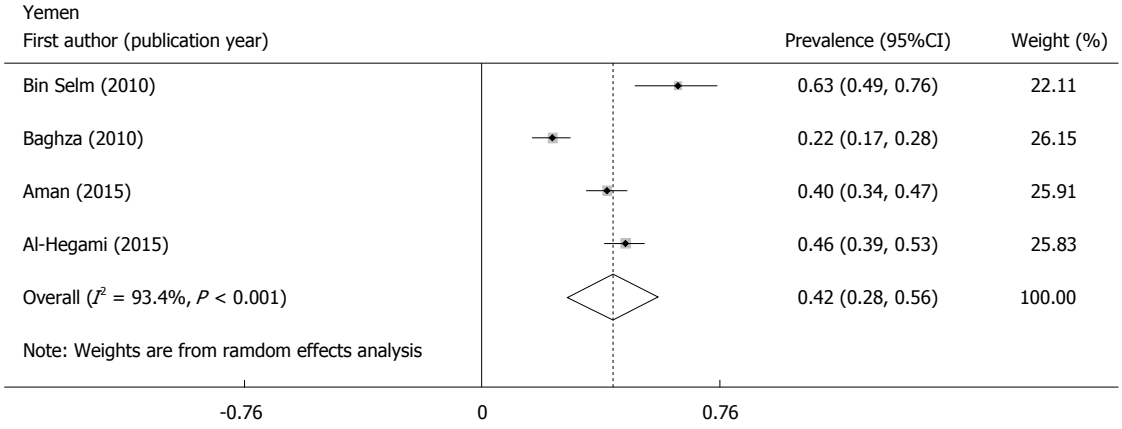
A report compiled by the WHO mentions 437,292 official reports of HCV infections among the general population of Saudi Arabia, revealing an estimated prevalence of nearly 1.8%[80]. The most prevalent genotype of the virus in Saudi Arabia was genotype 4 followed by 1a and 1b, whereas genotypes 2a/2b, 3, 5, and 6 were rarely detected among the general population[42,81,82].In one study in 2007, a prevalence of 18.9% (34/180 patients) was reported[83].

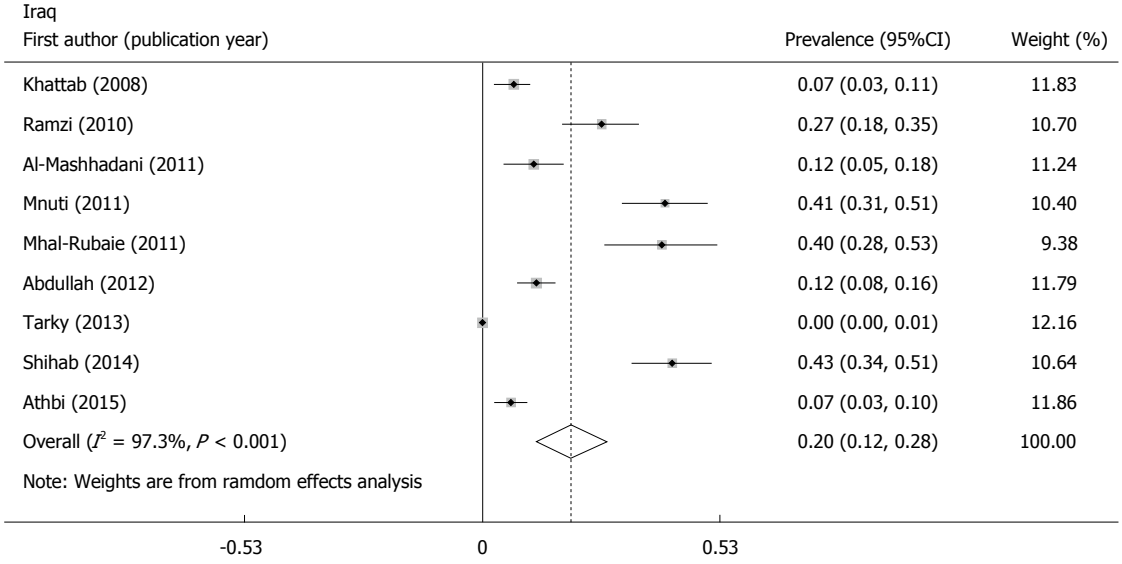
As shown in Figure 2, the overall prevalence in the


Iran
First author (publication year)
Prevalence (95%CI)
Weight (%)
Ansari (2006) 0.38 (0.24, 0.52) 2.16
Bozorgi (2006) 0.10 (0.04, 0.16) 4.23
Samimi-rad (2006) 0.07 (0.03, 0.10) 5.15
Toosi (2007) 0.09 (0.04, 0.13) 4.77
Kheradpezhouh (2007) 0.20 (0.16, 0.25) 4.90
Jabbari (2008) 0.28 (0.19, 0.37) 3.25
Somi (2008) 0.06 (0.05, 0.08) 5.57
Samimi-rad (2008) 0.07 (0.03, 0.10) 5.15
Makhiough (2008) 0.21 (0.15, 0.27) 4.36
Ghanaei (2009) 0.18 (0.13, 0.24) 4.36
Assarehzadegan (2009) 0.08 (0.04, 0.11) 5.15
Nemati (2009) 0.05 (0.01, 0.09) 4.97
Zamani (2010) 0.20 (0.16, 0.24) 4.90
Joukar (2011) 0.12 (0.09, 0.15) 5.36
Hassanshahi (2011) 0.31 (0.25, 0.38) 4.16
Samimi-Rad (2012) 0.06 (0.02, 0.09) 5.15
Zahedi (2012) 0.07 (0.04, 0.10) 5.20
Moini (2013) 0.07 (0.03, 0.11) 5.09
Kalantari (2014) 0.05 (0.03, 0.07) 5.53
Somi (2014) 0.08 (0.06, 0.11) 5.41
Tajbakhsh (2015) 0.06 (0.03, 0.09) 5.20
Overall (I^2 = 90.0%, P < 0.001) 0.12 (0.09, 0.15) 100.00
Note: Weights are from ramdom effects analysis
-0.515
0
0.515
Saudi Arabia
First author (publication year)
Prevalence (95%CI)
Weight (%)
Hussein (2007) 0.19 (0.13, 0.25) 100.00
Overall (I^2 = 100.0%, P = NA) 0.19 (0.13, 0.25) 100.00
Note: Weights are from ramdom effects analysis
-0.246
0
0.246
Palestine
First author (publication year)
Prevalence (95%CI)
Weight (%)
El-Ottol (2010) 0.22 (0.17, 0.27) 34.20
Abumwais (2010) 0.25 (0.15, 0.34) 29.71
Al-Zabadi (2016) 0.07 (0.06, 0.09) 36.09
Overall (I^2 = 94.8%, P < 0.001) 0.18 (0.05, 0.30) 100.00
Note: Weights are from ramdom effects analysis
-0.343
0
0.343
Syria
First author (publication year)
Prevalence (95%CI)
Weight (%)
Moukeh (2009) 0.54 (0.50, 0.59) 100.00
Overall (I^2 = 100.0%, P = NA) 0.54 (0.50, 0.59) 100.00
Note: Weights are from ramdom effects analysis
-0.585
0
0.585


Egypt
First author (publication year)
Prevalence (95%CI)
Weight (%)
Kandil (2007) 0.52 (0.34, 0.69) 5.00
Khodir (2012) 0.42 (0.40, 0.44) 18.14
Soliman (2013) 0.43 (0.30, 0.56) 7.56
Zahran (2014) 0.50 (0.45, 0.54) 16.10
El-Sharkawy (2015) 0.51 (0.50, 0.51) 18.70
Sarhan (2015) 0.51 (0.48, 0.54) 17.25
Senosy (2016) 0.61 (0.58, 0.64) 17.25
Overall (I^2 = 94.7%, P < 0.001) 0.50 (0.46, 0.55) 100.00
Note: Weights are from ramdom effects analysis
-0.692
0
0.692


Turkey
First author (publication year)
Prevalence (95%CI)
Weight (%)
Yakaryilmaz (2006) 0.24 (0.18, 0.30) 25.56
Sezer (2006) 0.36 (0.25, 0.47) 14.07
Kose (2009) 0.19 (0.15, 0.23) 33.00
Daglar (2014) 0.20 (0.15, 0.25) 27.38
Overall (I^2 = 66.3%, P = 0.031) 0.23 (0.18, 0.28) 100.00
Note: Weights are from ramdom effects analysis
-0.466
0
0.466


Yemen
First author (publication year)
Prevalence (95%CI)
Weight (%)
Bin Selm (2010) 0.63 (0.49, 0.76) 22.11
Baghza (2010) 0.22 (0.17, 0.28) 26.15
Aman (2015) 0.40 (0.34, 0.47) 25.91
Al-Hegami (2015) 0.46 (0.39, 0.53) 25.83
Overall (I^2 = 93.4%, P < 0.001) 0.42 (0.28, 0.56) 100.00
Note: Weights are from ramdom effects analysis
-0.76
0
0.76


Iraq
First author (publication year)
Prevalence (95%CI)
Weight (%)
Khattab (2008) 0.07 (0.03, 0.11) 11.83
Ramzi (2010) 0.27 (0.18, 0.35) 10.70
Al-Mashhadani (2011) 0.12 (0.05, 0.18) 11.24
Mnuti (2011) 0.41 (0.31, 0.51) 10.40
Mhal-Rubaie (2011) 0.40 (0.28, 0.53) 9.38
Abdullah (2012) 0.12 (0.08, 0.16) 11.79
Tarky (2013) 0.00 (0.00, 0.01) 12.16
Shihab (2014) 0.43 (0.34, 0.51) 10.64
Athbi (2015) 0.07 (0.03, 0.10) 11.86
Overall (I^2 = 97.3%, P < 0.001) 0.20 (0.12, 0.28) 100.00
Note: Weights are from ramdom effects analysis
-0.53
0
0.53

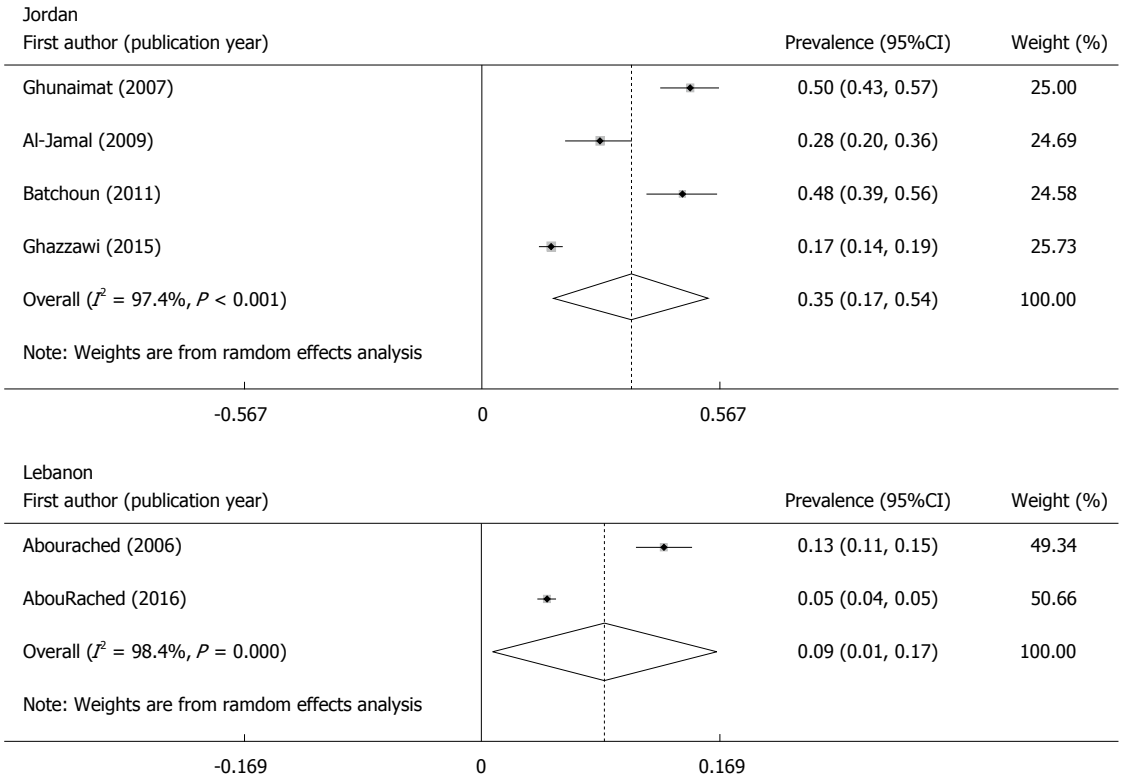


Figure 2 Prevalence of hepatitis C virus infection among hemodialysis patients in the Middle-East region during the last decade according to the results of enzyme-linked Immunosorbent assay. The reported prevalence of each country separated by First author name and sorted by publication year. The overall prevalence and 95%CI is also reported for each country. Prevalence data are reported as ratio (95%CI). United Arab Emirates, Afghanistan, Qatar, Bahrain, Kuwait, Oman, Israel, and Cyprus, were not added due to insufficient data.

last decade's only one publication was estimated as 19% (95%CI: 13%-25%).

Kuwait

The latest reports of WHO showed a prevalence of 1.8% of HCV infection in general population of Kuwait[26]. The most common genotypes of HCV in Kuwait was genotype 4 with a rate of 43% (95%CI: 33%-52%) followed by genotype 1 with a rate of 28% (95% CI: 21%-34%)[29]. There was no published study during the last decade regarding the prevalence of HCV infection in Kuwait.

UAE

Regarding the latest reports, the prevalence of HCV infection in UAE was about 1% in general population[31]. In 1995, a prevalence of 24% (64/262) of HCV infection among hemodialysis patients was reported[32]. The predominant genotypes were 4, 3, and 1[33]. No study was found reporting the prevalence of HCV infection among hemodialysis patients during the last decade in UAE.

Qatar

According to the literature, HCV prevalence in the general population of Qatar was 0.5% among Qataris people, and 1% (95%CI: 0.43%-1.82%) overall. Genotype 4 is the most common HCV genotype reported in Qatar which accounts for almost 100% of all infections[36,38]. No report was found for Qatar on the prevalence of HCV infection during the last decade.

Yemen

HCV prevalence in the general population was estimated to be 1.8%[84]. In 2010, the anti-HCV antibody prevalence rate among the hemodialysis patients was reported as 62.7%[85]; In 2014, 22.5% (45/200)[86]; In 2015, it was reported as 40.2% (88/219; 95%CI: 33.6%-46.73%)[87], and 46% (98/213)[88]. The most prevalent genotype of HCV was 4 with a prevalence of 63.7% followed by genotype 1a + 1b with a rate of 26.9% among the general population[89].

As it is presented in Figure 2, the overall prevalence of HCV infection among hemodialysis patients in Yemen according to the publications of the last decade was estimated as 42% (95%CI: 28%-56%).

Iraq

A meta-analysis in 2015 estimated the prevalence of HCV infection to be 0.2% among the general population of Iraq (range: 0%-7.2%; 95%CI: 0.1%-0.3%)[90]; HCV genotype 4 is the most common genotype[38]. Regarding the prevalence of hepatitis C among hemodialysis patients during the past decade, the reported rates ranged from 0 to 42.6%[91-98]: In 2007, 11.7% (10/87)[94]; in 2008, 7.1% (12/169)[98];

in 2009, 40.3% (23/57)[99]; in 2010, 26.7% (27/101)[96]; in 2012, 12.3% (29/236)[92]; in 2014, 42.6% (52/122)[97]; in 2015, 6.6% (11/165)[100].

As Figure 2 shows, the overall prevalence of HCV infection among hemodialysis patients in Iraq according to the last decade's publications was estimated as 20% (95%CI: 12%-28%).

Afghanistan

HCV prevalence in the population at large in Afghanistan appears to be around 1%; however, there are no reliable data on the prevalence of HCV infection and hepatitis C among hemodialysis patients as a high risk group[39]. Regarding the common genotypes in this country, only one study reported HCV genotype data among 71 HCV positive from Mazar-i-Sharif, Herat, and Jalalabad between 2006 and 2008[40]. In this report, about two-thirds of participants were infected with genotype 3a while the rest of them were infected with genotype 1[40].

Palestine

The prevalence of HCV infection in Palestine was reported as 0.2% rate (range: 0%-9.0%; 95%CI: 0.2%-0.3%). The most dominant genotype was found to be genotype 4 followed by 1 and 3a among the general population[101,102]. Studies on the prevalence of hepatitis C among hemodialysis patients were limited in this country. The reported prevalence rates were as follows: 24.7% (19/77) and 22% (54/246) in 2010[102,103]; 7.4% (64/868) in 2016[104]. As it is demonstrated in Figure 2, the overall prevalence of HCV infection among hemodialysis patients in Palestine according to the last decade's publications was calculated as 18% (95%CI: 5%-30%).

Oman

HCV infection prevalence among the general population in Oman, nationals and expatriates, was reported to be below 1%, ranging from 0.4% to 0.9% in blood donors[30]. To our knowledge, there are no reports on the prevalence of HCV among hemodialysis patients in the past decade in this country.

Bahrain

Regarding the prevalence of HCV infection in Bahrain's general population, two recent studies were found which reported a low prevalence of 0.3%[42,43]. The predominant genotype among Bahraini patients was type 1 (36.7%), followed by genotypes 3 and 4 (15.6% each)[44]. We searched all of the databases and no more recent studies were found on the prevalence of HCV among hemodialysis patients to estimate the possible changes in its rate and the trend of the disease.

Syria

The prevalence of HCV infection among the general population of Syria was estimated as 0.4% (range: 0.3%-0.9%; 95%CI: 0.4%-0.5%)[90]. The dominant genotype in this country were genotype 4 and then genotype 1 among the general population[90]. Regarding the prevalence of HCV among hemodialysis patients in 1995 a prevalence of 75% (90/120) and 48.9% (68/139) in 1996 were reported which were not included in our meta-analysis[105,106]. The latest and the only found survey in 2006 revealed a rate of 54.4% (299/550)[107].

The prevalence of HCV infection among hemodialysis patients in Syria regarding the last decade's publications was estimated as 54% (95%CI: 50%-59%; Figure 2).

Jordan

According to the recent reports, the prevalence of HCV infection in Jordan's general population was estimated to be ranging from 0.3% to 2.1%[4,90]. The most dominant genotypes of HCV was genotypes 4 and 1 according to their research among the general population[108]. Regarding the prevalence of hepatitis C among hemodialysis patients, in 1994 and 2001, 24.5% and 34.6% were reported, respectively[108,109]. During the last decade the rates of 49.8% (104/209)[110], 28% (34/120)[111], 47.7% (64/134)[112], and 16.5% (117/712)[113], in 2007, 2009, 2011, and 2015, respectively. The overall prevalence of HCV infection among hemodialysis patients in Jordan considering the last decade's publications was measured as 35% (95%CI: 17%-54%; Figure 2).

Lebanon

The prevalence of HCV in Lebanon is reported to be 0.2% according to a recent report[114]. HCV genotype 4 is reported to be the most dominant genotype among the general population as well as among hemodialysis patients[30,115]. The prevalences of HCV infection among hemodialysis patients were 13% (134/1030) in 2007[116] and 4.7% (177/3769) in 2016[117]. Prior to that, in 1995 a prevalence of 27% (range: 10%-39%) was reported which could not be included in our study[118]. As it is exhibited in Figure 2, the overall prevalence of HCV infection among hemodialysis patients in Lebanon according to the last ten years' publications was estimated as 9% (95%CI: 1%-17%).

Egypt

Egypt is one of the countries which are heavily affected by HCV having a prevalence of 14.7%; HCV genotype 4 is by far the most common genotype in Egypt[30]. During the past two decades literature reported prevalences ranging from 48.2% to 87.5% for HCV infection among hemodialysis patients which were not taken into account in our analysis[119-125]. The reports of the prevalence of hepatitis C infection among hemodialysis patients during the last decade are as follows: In 2007, 51.6% (16/31)[126]; in 2012,

43% (36/83)[127], and 42.2% (992/2351)[128]; in 2014, 49.6% (255/514)[129]; in 2015, 51% (503/987)[130], and 50.7% (11189/22070)[131]; in 2016, 60.9% (591/971)[132].

Considering the chart in Figure 2, the overall prevalence of HCV infection among hemodialysis patients in Egypt was calculated as 50% (95%CI: 46%-55%).

Israel

The latest reports on the prevalence of HCV infection among general Israeli population reveal a rate of 1.96%[133]. HCV genotype 1 (70%) and 3 (20%) were the most inspected ones among the individuals[133]. No recent study was found for Israel regarding the HCV infection among hemodialysis patients.

Cyprus

The general prevalence of HCV infection in Cyprus is reported as 0.5% and the most dominant genotype in Cyprus was reported to be genotype 1[4,45]. To our knowledge, there is no publication on the prevalence of HCV infection among hemodialysis patients in this country.

DISCUSSION

In hemodialysis centers, hepatitis C virus infection remains a major concern. Blood transfusion as well as nosocomial infection continue to play important roles in the transmission of HCV[134]. An overall prevalence of 25.3% of HCV infection was reported among hemodialysis patients in the Middle-East region according to the present study. Regarding the result of the present investigation, the prevalence was higher in ages 40 to 50 years old; this might be due to higher rate of renal diseases in older ages. Also, among patients who were under hemodialysis for more than 5 years the prevalence of hepatitis C was higher than those who were treated for a shorter time period. Other than some countries such as Afghanistan, Israel, Cyprus, Qatar, Kuwait, UAE, Oman, and Bahrain, which had no recent data on the prevalence of HCV infection among hemodialysis patients, among the other countries a rate of 9% in Lebanon to 54% in Syria were observed. Despite insufficient data on Syria, according to the only presented paper from this country, it had a higher prevalence even than Egypt, a country with the highest reported HCV infection among the Middle-East countries[90]. Lebanon (9%), Iran (12%), Saudi Arabia (19%), Iraq (20%), Turkey (23%), and Palestine (18%), depicted lower prevalences although the number of studies seems to be not sufficient in Lebanon, Saudi Arabia, and Palestine. More investigations are expected and suggested to give out more accurate conclusion in these countries. Moreover, providing updated surveys in UAE, Oman, Afghanistan, Israel, Cyprus, Qatar, Kuwait, and Bahrain, are greatly recommended.

In Saudi Arabia before 2000, prevalence reports ranged from 15% to 90% among different hemodialysis centers[81]. Afterwards, studies showed a range of 14.7% to 43.9%[42,82]. Many of these studies suggested that the duration of the dialysis session was more related to the chance of infection than the repeated blood transfusions[42,82]. Despite the further increase in dialysis services, the prevalence did not have a significant change during the recent years in Saudi Arabia which may be due to better implementation of infection-control policies and also the screening methods in certain hemodialysis units[81]. However, the studies on the epidemiology of HCV infection related to hemodialysis are noticeably insufficient. Our estimated prevalence in Iran is also lower than the previously reported 13.57% in 2010 by Alavian *et al*[135]. In their systematic review that was performed from April 2001 to March 2008 and even before, 12 studies were evaluated, of a total sample size of 5280, a prevalence of 12.91 (95%CI: 10.25-15.56) was reported; however, most of the studies are conducted in a limited number of provinces which applies some limitations to the outcome. In Iraq, Adherence to infection precautions, screening of transfusions, the use of separate machines for the infected patients, and using erythropoietin instead of blood transfusions may be the cause of the overall lower prevalence rates[92,94,96-100].

In Yemen, sensitivity analyses suggest that there may be an underestimation for HCV prevalence since measured HCV prevalence in this country increased from 1.9% in baseline analysis to 2.8% and 2.4% in the two sensitivity analyses, respectively[84]; HCV prevalence among hemodialysis patients increased from 40.0% in 1999 to 62.7% in 2007[85,136], and 42% in our estimation. Insufficient data on the prevalence of HCV infection, particularly among the patients on maintenance hemodialysis is a barrier for determining the alterations in the trend and risk factors of transmission; thus, present literature show an increase in the overall prevalence in Yemen. Moreover, in Syria, the higher rates of infection, ranged from 48.9% to 75%[105,106], seems to be continued during the past two decades as well as our present evaluation (54.4%). This might be due less than optimal screening of blood and blood products and poor sterilization of equipment in these patients[105-107]. Studies in Jordan showed a decline in the rates of HCV infection among hemodialysis patients (from 49.8% to 16.5%) though the overall rate was high (35%)[108-112]; standardized infection control protocols including the use of disposable gloves, kits, needles, dialyzers, and single use vials as well as disinfection of surfaces and dialysis machines between hemodialysis sessions with appropriate solutions were the reasons for the decline in the prevalence rates[113].

In Kuwait, Qatar, and UAE, non-nationals comprise more than three-fourths of the population[35].

Documents depict a high prevalence of HCV infection before 2006 among hemodialysis patients in Kuwait, ranging between 27% and 71%[27,28,30]. Obviously, studies on the prevalence of HCV infection and the possible changes in its trend are not well investigated in Kuwait country during the last decade, even the reports of the health ministry revealed no data in this case. In UAE, it seems that the medical care providers still do not take HCV infection as a major concern, especially among patients undergoing dialysis treatment, and studies are lacking and the changes in the trend are not measurable. In Qatar, HCV prevalence was as high as 44.6% in hemodialysis patients according to a recent systematic review[36]. Qadi *et al*[42] reported the prevalence of HCV infection among the Bahraini hemodialysis patients, a rate of 7.4% among 81 patients recruited from tertiary health centers of the country in 2004. The prevalence of HCV infection among Israeli hemodialysis patients in 1997 and 2001 reports showed rates of 12.3%[137] and 18%[138]. The latest reports published for Oman in 1992 and 1993 by Al-Dhahry *et al*[41] revealed a 26.5% prevalence for HCV infection in these patients. Although the prevalence of HCV infection is not high in these countries considering the latest reports, it is assumed that conducting new epidemiological surveys is needed for a better estimation.

Latest reports depicted the prevalence of HCV infection in the United States hemodialysis centers to be in a range of 8% to 16.8%[12,139], which was about 5 times greater than the prevalence within the country's general population (1.6%)[140]. The time spent on dialysis therapy has been suggested as an independent risk factor for the infection[141]. In Europe, a prevalence of 11.5% was reported in 2003, while Japan's HCV infection prevalence among hemodialysis patients was 13.4%[142]. In some other reports from European developed countries such as Belgium, Germany, Spain, France, Sweden, Poland, Hungary, United kingdom, and Italy, prevalence rates of 6.8%, 6%, 12%, 30%, 9%, 44%, 15%, 3%, and 16% were reported, respectively[143]. As it is demonstrated, in contrast with the developed countries, some Middle-East countries such as Iran, Iraq, Turkey, Lebanon, Palestine, and Saudi Arabia may have had better hygienic condition; however, the lower rates of infection can be due to lower number of patients and the sample population and also number of dialysis units in the country, for example in areas like Iraq and Palestine, specifically Gaza strip[102-104].

The mechanisms responsible for HCV infection transmission in hemodialysis services in the Middle-East countries has not been recognized properly yet. However, some investigations have reported that cross infection through hemodialysis machines may be in charge for the transmission which necessitates more attention on sterilization and control of infection in dialysis units[144]. Diagnosis and treatment of all hemodialysis patients who are infected with the virus, education of nurses and all health care providers involved with these cases, and organizing prevention programs regarding the natural characteristics of each country and its population are suggested as prevention programs which can be initiated in Middle-East countries for better evaluation and reduction of HCV infection[144,145]. Nevertheless, successful control of the infection needs further investigations to assess the effectiveness of different preventive and diagnostic policies. Preventive programs varies in different regions and various societies. Several studies are focused on isolating hemodialysis patients while some others attempted to use specified equipment and services for these patients and disinfection of the devices and the environment[135,146,147].

As a limitation of this study, the limited number of studies in some countries can be noticed. The low sample populations in a number of studies in some centers can be mentioned as another limiting factor for which the outcome could not be generalized. However, since the prevalence of HCV infection and also the number of the studies in this field were not significant, we could not omit these surveys.

Overall, in this paper we reported the prevalence of HCV infection among the countries of the Middle-East region considering the documents published during the past decade. Health policy makers and health care system should focus on the possible risk factors of each country individually in order to plan for effectively reduce the transmission rates and improve treatment methods for the infected ones. Also, experiences of the countries which were succeeded in reducing the incidence rate and the infection prevalence might be helpful if being shared.

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COMMENTS

Background

Hemodialysis is a major risk factor for hepatitis C virus (HCV) infection among the patients suffering from renal disease. Knowing the prevalence of this infection may help the health policy makers and care providers plan for better screening, management, and treatment of the infection.

Research frontiers

In this systematic review and meta-analysis the authors determine the prevalence of hepatitis C infection among 17 countries of the Middle-East region according to the related documents published during the last decade.

Innovations and breakthroughs

This research provides data for the health care system to have a sight on the

rates of the infection, complete and update their information, and plan for the future. Countries which lack data in this field should do their efforts toward providing them and those with high rates of infection should plan for better management of the case.

Applications

The results of the present study can be applied in health policy making and programming for better management of the dialysis centers as well as the infected individuals who may need for dialysis treatment in the future. Knowing the infection rate, the possible ways of transmission and complications of the infection are beneficial for future's planning.

Peer-review

This is a very interesting review article on the prevalence of hepatitis C among hemodialysis patients among the Middle-East countries. The author is investigating the infection state of HCV of the Middle-East region in the precise. Description of an Middle-Eastern medical state and the discussion about a route of infection think a requirement.

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