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Seroprevalence of Hepatitis C Virus among Blood Donors in Middle Eastern Countries: A Systematic Review and Meta-Analysis

Hossein Ghaderi-Zefrehi,[1,2] Heidar Sharafi,[1,3] Farzin Sadeghi,[4] Mohammad Gholami-Fesharaki,[5] Alireza Farasat,[6] Fatemeh Jahanpeyma,[7] and Seyed Moayed Alavian[1,3,*]

[1]Baqiyatallah Research Center for Gastroenterology and Liver Diseases, Baqiyatallah University of Medical Sciences, Tehran, IR Iran
[2]Department of Clinical Biochemistry, Faculty of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, IR Iran
[3]Middle East Liver Diseases (MELD) Center, Tehran, IR Iran
[4]Cellular and Molecular Biology Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, IR Iran
[5]Department of Biostatistics, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, IR Iran
[6]Young Researchers and Elite Club, Pharmaceutical Sciences Branch, Islamic Azad University, Tehran, IR Iran
[7]Department of Medical Biotechnology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, IR Iran

[*]*Corresponding author*: Seyed Moayed Alavian, Baqiyatallah Research Center for Gastroenterology and Liver Diseases, Baqiyatallah University of Medical Sciences, Mollasadra Ave, Vanak Sq, P.O. Box 14155-3651, Tehran, IR Iran. E-mail: alavian@thc.ir

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Abstract

Context: Hepatitis C virus (HCV) has been the main cause of post transfusion hepatitis. Long-term hepatitis can ultimately result in cirrhosis and hepatocellular carcinoma. Viral hepatitis, especially HCV infection, is a major health concern in the Middle East. The current study carried out a systematic search concerning HCV seroprevalence among blood donors in Middle Eastern countries.
Evidence Acquisition: Articles were identified through searching databases including PubMed, Scopus, and Web of Science. We reviewed systematically all studies reporting HCV seroprevalence among blood donors in Middle Eastern countries.
Results: A total of 5662 relevant records were identified by the electronic search, of which a total of 47 studies were identified as eligible papers that were meta-analyzed for the pooled seroprevalence of HCV among blood donors. Overall, HCV seroprevalence among blood donors in Middle Eastern countries was estimated 0.88% (95%CI = 0.79% - 0.97%). The highest pooled HCV seroprevalence rate was related to Egypt (5.76% [95%CI = 3.30% - 8.22%]), Libya (1.56% [95%CI = 0.99% - 2.13%]), and Yemen (1.09% [95%CI = 0.69% - 1.50%]) while the lowest pooled seroprevalence rate was in Iran and Israel with the rates of 0.14% (95%CI = 0.12% - 0.17%) and 0.16% (95%CI = 0.06% - 0.25%), respectively. Results of annual HCV seroprevalence suggest that there is a decrease in seroprevalence rate of HCV over time among blood donors in Egypt, Iran, Oman, Lebanon, Libya, and Saudi Arabia.
Conclusions: Our results showed that the trend of HCV seroprevalence over time among Middle Eastern blood donors was decreasing. It suggests that recent safety measures implemented in Middle Eastern countries have been effective.

Keywords: Blood safety, Epidemiology, Hepatitis C, Middle East, Systematic review

1. Context

First found in 1989, hepatitis C is caused by hepatitis C virus (HCV) (1) from the Flaviviridae family and it is the main reason of post transfusion hepatitis (2). HCV is most commonly transmitted through direct contact with blood as in blood transfusion (3). Screening of donated bloods for hepatitis C has been implemented in blood transfusion services since 1990s in most Middle Eastern countries (4). The post-transfusion hepatitis C has been a main cause of mortality and morbidity in poly-transfused patients such as patients with thalassemia and hemophilia in Middle Eastern countries (5). Viral hepatitis, especially HCV, is a major health concern in the Middle East, which is a geographical region with diverse ethnic groups including Arabs, Turks, Persians, etc. With an over 3.5% prevalence of HCV infection, Middle East is considered a hotspot for this disease (6, 7). There has been inadequate research on HCV prevalence and prevention methods in the Middle East (8). Moreover, prevalence of HCV infection among blood donors has not been discussed in some countries of this region. Therefore, this paper reviews the conducted studies in order to provide the current estimate of HCV seroprevalence among blood donors in Middle Eastern countries.

2. Evidence Acquisition

2.1. Data Resources and Search Strategies

Literatures on HCV prevalence among blood donors in Middle Eastern countries, such as Bahrain, Cyprus, Egypt, Iran, Iraq, Israel, Jordan, Kuwait, Lebanon, Libya, Oman, Palestine, Qatar, Saudi Arabia, Syria, Turkey, UAE, and Yemen, were acquired through searching PubMed, Scopus, and Web of Science in the time span of 1996 to 2016. Our last search was conducted on October 05, 2016. In order to search and include related studies as many as possible,

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we used the following terms: "Hepatitis C virus", "HCV", "prevalence", "blood donor", and name of the Middle Eastern countries.

2.2. Eligibility Criteria

Published studies were regarded qualified for analysis if they met the following criteria: 1- Studies with full text of the paper available in English language; 2- Studies with a sample size more than 100; and 3- Studies that reported anti-HCV antibody (HCV Ab) prevalence among blood donors in the Middle Eastern countries. Conversely, the followings were exclusion criteria: 1- Non-English reports on the seroprevalence of HCV; 2- Studies that reported seroprevalence of HCV among paid blood donors; 3-Studies which all of the participants were first-time blood donors; 4- Studies with overlapped time or place of donation; 5- Studies that used first-generation or second-generation HCV enzyme-linked immunoassay (ELISA) without supplemental or confirmatory assay, and 6- Studies failing to present evident data.

2.3. Study Selection and Data Extraction

All articles categorized as potentially relevant were reviewed separately by two of the authors (H. G-Z. and H. S.) In addition, blinding and task separation were applied in selection of articles and data extraction. For each eligible study, the following information was extracted: first author's name, year of publication, study period, study location, the method for the screening of HCV Ab, the method used for confirmation of HCV Ab, sample size, number of positive cases for HCV Ab, and the type of donors. Analysis was conducted according to the preferred reporting items for systematic reviews and meta-analysis (PRISMA) (9).

2.4. Data Analysis

In the current meta-analysis, the seroprevalence rate of HCV among blood donors from each country was computed by metan command. Statistical tests of heterogeneity among the studies were carried out using the Q test ($P < 0.10$ indicates statistically significant heterogeneity) and I-squared statistics. According to the results of heterogeneity test, we used fixed- or random-effect models for determining the prevalence of HCV Ab among blood donors. We also used funnel plot to investigate publication bias. All data analyses were performed using STATA 10.

3. Results

3.1. Study Screening and Characteristics of the Included Studies

The study selection process is depicted in Figure 1. A total of 5662 studies potentially associated with the seroprevalence of HCV infection among blood donors in the Middle Eastern countries were identified through web search, of which 2,291 duplicates were excluded. After reviewing the abstracts and titles, 3,181 studies were eliminated based on the stated inclusion and exclusion criteria. After full-text screening, a total of 47 records were deemed as eligible papers published between 1995 and 2016. These 47 records were composed of 13 studies from Iran (4, 10-21), 8 studies from Turkey (22-29), 8 studies from Saudi Arabia (30-37), and 6 studies from Egypt (38-43). Two studies were available from each of the following countries: Syria (44, 45), Libya (46, 47), Yemen (48, 49), and Israel (50, 51). Only one study was available from each of the following countries: Lebanon (52), Oman (53), Cyprus (54), and UAE (55). The characteristics of included studies are summarized in Table 1.

3.2. Seroprevalence of HCV among Blood Donors in Middle Eastern Countries

Data on HCV seroprevalence as well as other indicators were abstracted from the 47 records as presented in Table 1. Information on HCV seroprevalence among blood donors was available from twelve countries.

As shown in Table 1, using random-effect model, the pooled seroprevalence of HCV among blood donors in the Middle Eastern countries from 1989 to 2014 was estimated 0.88% (95%CI = 0.79% - 0.97%). In addition, we used random-effect model to estimate pooled HCV seroprevalence rate for each of the Middle Eastern countries. The highest pooled HCV seroprevalence rate was related to Egypt (5.76% [95%CI = 3.30% - 8.22%]), Libya (1.56% [95%CI = 0.99% - 2.13%]), and Yemen (1.09% [95%CI = 0.69% - 1.50%]) while the lowest pooled seroprevalence rate was in Iran and Israel with the rates of 0.14% (95%CI = 0.12% - 0.17%) and 0.16% (95%CI = 0.06% - 0.25%), respectively. HCV seroprevalence among blood donors in countries with one study including Lebanon, Oman, Cyprus, and UAE was 0.40% (95%CI = 0.31% - 0.51%), 0.75% (95%CI = 0.64% - 0.88%), 0.45% (95%CI = 0.30% - 0.68%), and 0.11% (95%CI = 0.10% - 0.13%), respectively. Seroprevalence of HCV among blood donors by different countries is depicted in Figure 2.

For evaluating annual HCV seroprevalence rates and their trends, we only considered studies that reported HCV seroprevalence rate among blood donors annually. By exploring the trends of HCV seroprevalence rate in 6 countries, including Egypt (2007 - 2012), Iran (2003 - 2014), Lebanon (1997 - 2003), Libya (2008 - 2013), Oman (1995 - 2001), and Saudi Arabia (1998 - 2014), a decline in HCV seroprevalence rate among blood donors over time was observed (Figure 3). Detailed information on trends is shown in Figure 3.

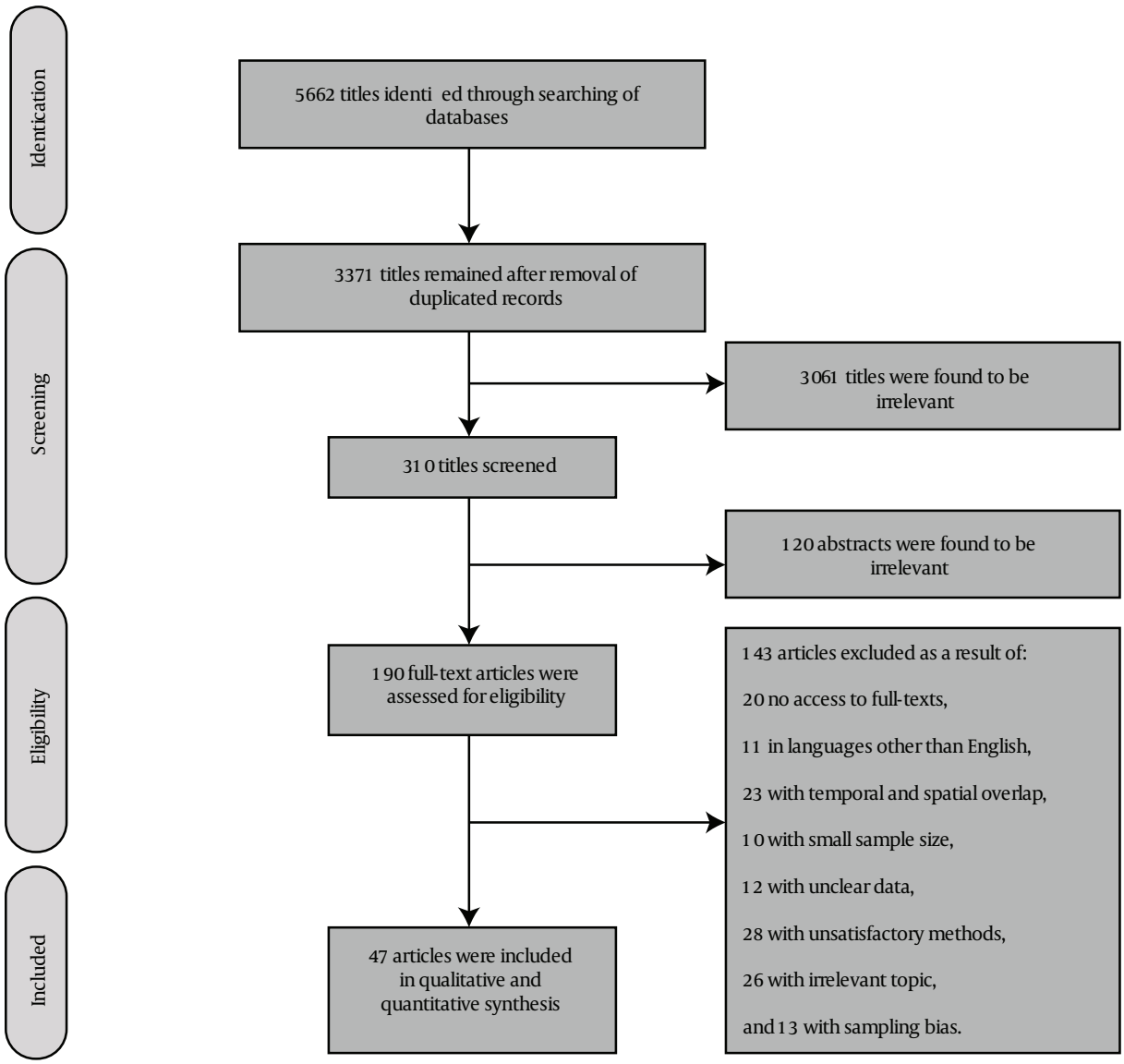


Figure 1. Flowchart of Article Selection Based on PRISMA Statement

4. Discussion

Blood transfusion and blood donation continue to play significant roles in the transmission of HCV in Middle Eastern countries (56). Several recent studies have provided good evidence on genotype distribution and epidemiology of HCV in the Middle East region (57-59). However, determination of HCV seroprevalence rates among blood donors in the Middle East region could be helpful to develop prevention and control strategies more effectively. The current systematic review was conducted to shed more light on the seroprevalence of HCV among blood donors in the Middle East region; a transcontinental region with diverse ethnic groups including Arabs, Turks, Persians, Azeris, Kurds, etc. To determine HCV seroprevalence rate among blood donors, the estimated pooled seroprevalence rate was calculated for each of the Middle Eastern countries. The results of our study indicated that HCV seroprevalence rates among blood donors in the Middle East region is 0.88% that is higher than the seroprevalence rates in North-European blood donors (0.01% - 0.02%) (60). In addition, a recently published meta-analysis reported 0.65% HCV seroprevalence rate among blood donors in

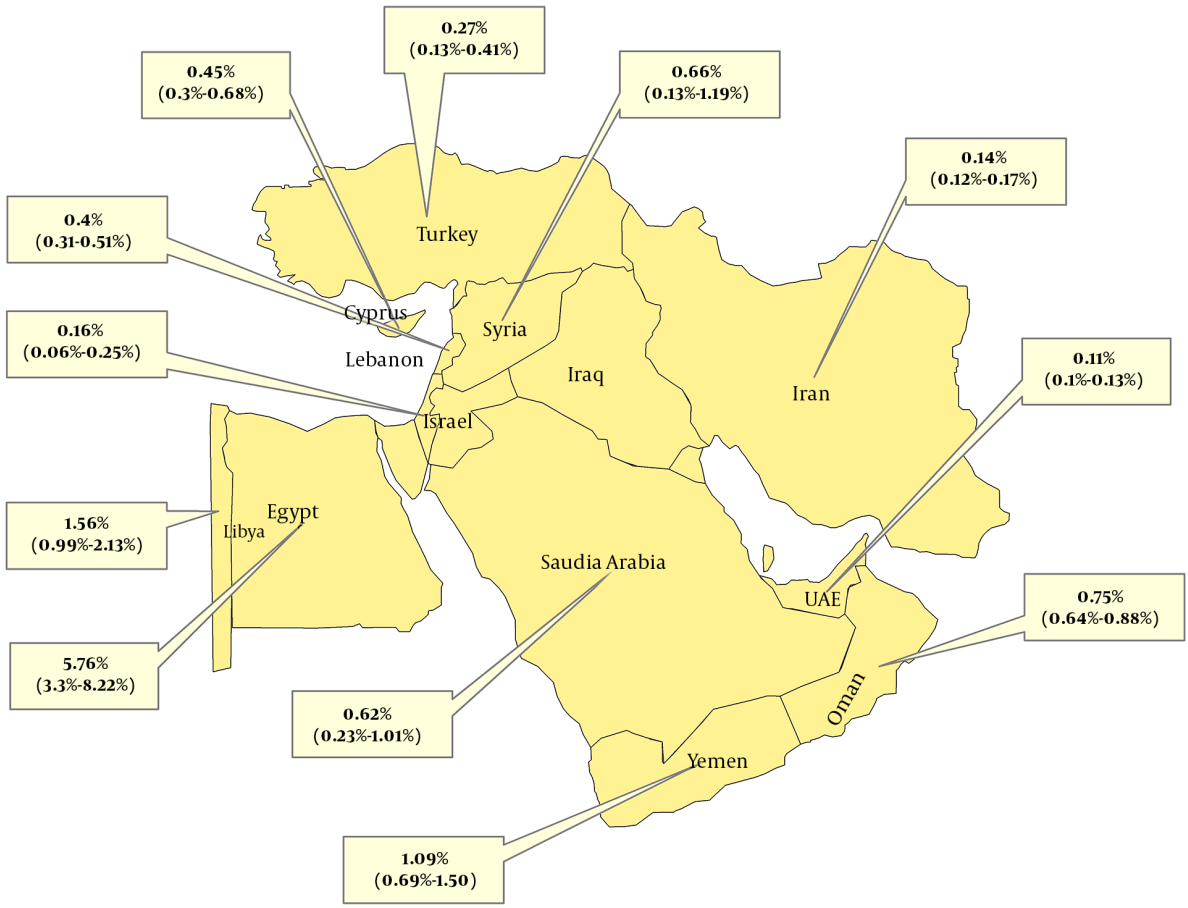
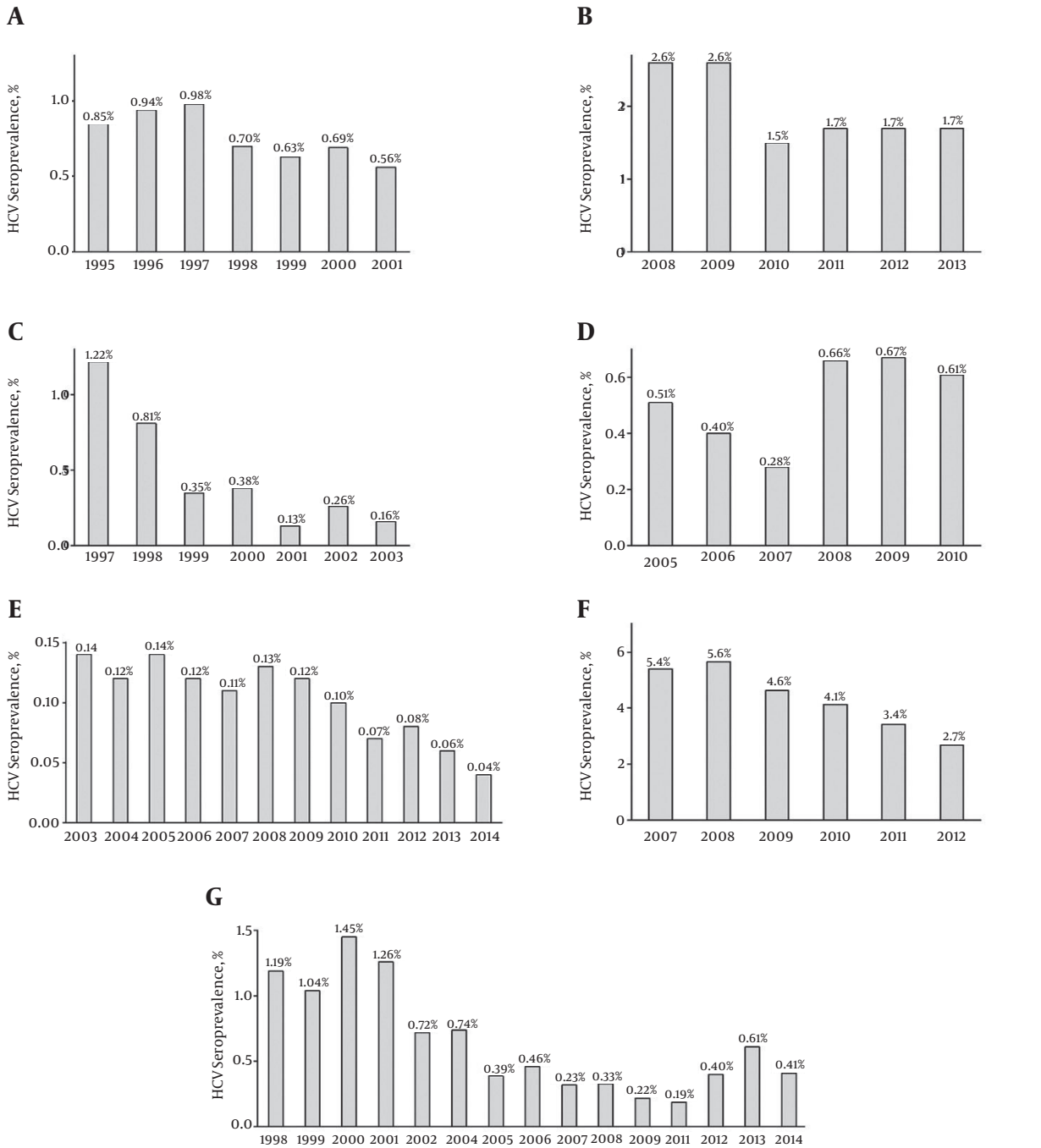


Figure 2. Seroprevalence of HCV among Blood Donors in Middle Eastern Countries

African countries, which is also lower than the rate found in our study (61). Based on our statistical analysis, there is a dramatic geographical difference between Middle Eastern countries in terms of HCV seroprevalence rate in blood donors. The highest seroprevalence was found in Egypt with the rate of 5.7% and the lowest seroprevalence was found in UAE and Iran with the rates of 0.11% and 0.14%, respectively. Our results are in good agreement with some studies from Egypt, including two investigations with large sample sizes among Egyptian blood donors conducted by Eita et al. (62) and Rushdy et al. (63). In addition, based on a newly published systematic review from Egypt, HCV seroprevalence rates among blood donors ranged 5% - 25% (64). It should be noted that data from the aforementioned systematic review has to be treated with caution due to employing ELISA as a detection index and lack of confirmatory RIBA test. Moreover, the low sample size in some of the studies included in the aforementioned systematic review may affect the obtained results. The results of the present study are consistent with a number of reports from Iranian blood donors (16, 65). Interestingly, a comprehensive study by Kafi abad et al. among Iranian blood donors revealed 0.13% HCV seroprevalence rate that is in good agreement with our results (16). According to our results, Libya and Yemen have the second and third highest HCV seroprevalence rates in blood donors in the Middle East region. These findings are broadly consistent with other comprehensive epidemiologic studies on general populations in Libya and Yemen (66, 67). Seroprevalence of HCV in Libya and Yemen may increase in the next few years due to ongoing military conflicts and destruction of health-care infrastructures. The results of the present study demonstrated almost similar HCV seroprevalence rates in Saudi and Syrian blood donors. These findings are also consistent with the findings of more recent studies among blood donors in Saudi Arabia and Syria

Figure 3. Annual HCV Seroprevalence Rates and Their Trends among Blood Donors



A. Oman; B. Libya; C. Lebanon; D. Turkey; E. Iran; F. Egypt; G. Saudi Arabia.

(68). However, our results are not supported by Shobokshi et al. who found 1.1% HCV seroprevalence rate among Saudi blood donor (31). Moreover, military conflicts and refugee crisis in Syria may increase HCV seroprevalence rate in the next few years. In the present study, seroprevalence of HCV in blood donors from Turkey and Israel was low (0.27% and 0.16%, respectively) that might be explained by good infection control practices and organized system of blood

screening and transfusion. Our results showed a fluctuating trend in annual HCV seroprevalence rate in the Middle East region. With the exception of Turkey, other countries included in this investigation had a decreasing HCV seroprevalence trend.

Recently, with introduction of HCV direct-acting antiviral agents, the treatment of hepatitis C has transformed greatly (69, 70). These new therapies resulting in more than 95% treatment success have made hepatitis C a curable infectious disease (71-73). With availability of efficient treatments for hepatitis C, there is great hope to eliminate this disease by 2030; however, prevention of hepatitis C transmission through blood and blood products has a key role in elimination programs, as well (69).

A number of limitations exist in the present investigation that should be noted. First, the sample size in some of the Middle Eastern countries was not adequate and the quantity of data varied between countries. Second, different types of kits were utilized for detection of HCV Ab, which would have affected the obtained results of the current systematic review. Third, HCV seroprevalence rates in blood donor populations of some countries might be underestimated due to selection bias. In addition, data deficiencies existed in some studies did not allow us to include them in the final analysis.

Taken together, the present systematic review provides detailed and reliable data on the HCV seroprevalence rates among blood donors in Middle Eastern countries. The available data showed a dramatic geographical difference in the seroprevalence of HCV among Middle Eastern blood donors. The lowest seroprevalence rates were seen in Iranian and UAE blood donors, while the highest rate was observed in Egyptian blood donors. The trend of HCV infection among Middle Eastern blood donors was decreasing in recent years. It is suggesting recent safety measures implemented in Middle Eastern countries have been effective.

Footnote

Authors' Contribution: Concept and design: Seyed Moayed Alavian, Heidar Sharafi; data acquisition: Heidar Sharafi, Hossein Ghaderi-Zefrehi, Alireza Farasat, Fatemeh Jahanpeyma; data analysis: Mohammad Gholami-Fesharaki; drafting the manuscript: Hossein Ghaderi-Zefrehi, Heidar Sharafi, Farzin Sadeghi, Alireza Farasat, Fatemeh Jahanpeyma; critical revising of the manuscript: Heidar Sharafi; final approval of the manuscript: Seyed Moayed Alavian.

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Table 1. Characteristics of Included Studies from Middle Eastern Countries

Country	City, Province or Region	Reference Number	Screening Test	Confirmatory Test	Year of Publish	Year of Study	Sample Size, n	HCV Ab Rate, %	Donor Type
Cyprus	Nicosa and Kyrenia	(54)	EIA ≥ 3	NA	2006	2000	5057	0.45	NA
Total[a]					0.45% (0.30% - 0.68%)				
Egypt	Cairo	(38)	EIA ≥ 3	EIA ≥ 3	2007	1999 - 2000	2146	8.90	Replacement donor
	Cairo	(39)	EIA ≥ 3	EIA ≥ 3	2008	2005	760	5.00	Voluntary donor
	Minya governorate	(40)	EIA ≥ 3	NA	2010	2000 - 2008	211772	9.03	Voluntary donor
	Alexandria	(41)	EIA ≥ 3	EIA ≥ 3	2011	2007 - 2008	3420	3.48	Voluntary donor
	Cairo	(42)	EIA ≥ 3	NA	2014	2006 - 2012	308762	4.34	Voluntary or replacement donor
	Cairo	(43)	EIA ≥ 3	NA	2014	2010 - 2011	17118	3.84	Voluntary or replacement donor
Total[a]					5.76% (3.30% - 8.22%)				
Iran	Shiraz	(10)	EIA < 3	RIBA	2000	1998	7879	0.60	Voluntary donor
	Tehran	(11)	EIA ≥ 3	RIBA	2002	1996 - 1998	319375	0.09	Voluntary donor
	Kashan	(12)	EIA ≥ 3	NA	2004	2001 - 2002	600	0.50	Voluntary donor
	Tehran	(13)	EIA < 3	RIBA	2005	2001 - 2002	1959	0.46	Voluntary donor
	Guilan	(14)	EIA ≥ 3	RIBA	2007	1998 - 2003	221508	0.32	Voluntary donor
	Tehran	(15)	EIA ≥ 3	RIBA	2009	2003 - 2005 (2003)[b]	329516	0.14	Voluntary donor
	Iran	(16)	EIA ≥ 3	RIBA	2009	2004 - 2007	6499851	0.13	Voluntary donor
	Shiraz	(17)	EIA ≥ 3	RIBA	2010	2003	1933	0.52	Voluntary donor
	Arak	(18)	EIA ≥ 3	NA	2010	2008	531	0.19	Voluntary donor
	Qazvin	(19)	EIA ≥ 3	RIBA	2012	2009	20591	0.17	NA
	Tehran	(4)	EIA ≥ 3	RIBA	2015	2008 - 2013	1796090	0.10	Voluntary donor
	Bushehr, Borazjan and other cities	(20)	EIA ≥ 3	RIBA	2016	2004 - 2014 (2008 - 2014)[b]	219552	0.06	Voluntary donor
	Shiraz	(21)	EIA ≥ 3	RIBA	2016	2012 - 2013	101245	0.05	NA
Total[a]					0.14% (0.12% - 0.17%)				
Israel	Tel HaShomer	(50)	EIA < 3	RIBA	1998	1994 - 1996	193806	0.20	Voluntary donor
	Tel HaShomer	(51)	EIA ≥ 3	RIBA	2007	2003	225452	0.11	Voluntary donor
Total[a]					0.16% (0.06% - 0.25%)				
Lebanon	Beirut	(52)	EIA ≥ 3	EIA ≥ 3	2006	1997 - 2003	16084	0.40	NA
Total[a]					0.4% (0.31% - 0.51%)				
Libya	Tripoli	(46)	EIA ≥ 3	NA	2002	1999 - 2001	1200	1.17	NA
	Tripoli	(47)	EIA ≥ 3	NA	2016	2008 - 2013	1008214	1.78	Voluntary donor
Total[a]					1.56% (0.99% - 2.13%)				
Oman	Muscat	(53)	EIA2&3	RIBA	2003	1991 - 2001 (1995 - 2001)[b]	21131	0.75	NA
Total[a]					0.75% (0.64% - 0.88%)				
Saudi	Riyadh	(37)	EIA ≥ 3	NA	1991	1991	10646	1.01	NA
	Riyadh	(30)	EIA < 3	RIBA	1994	1992 - 1993	18540	0.44	NA
	Bisha, El-Baha, Najran, Jizan, Aseer, Hafer El-Baten, Al-Hessa and El-Sharkia, Al-Qassim, Riyadh, Jeddah, Makkah, Medinah, Taif, El-Qunfuda, Tabuk, Al-Goofe, El-Quriate, Hail, El-Shamalia	(31)	EIA ≥ 3	RIBA	2003	1998 - 2002	557813	1.13	NA
	Eastern Saudi Arabia	(32)	EIA ≥ 3	NA	2004	1998 - 2001	13443	1.44	Voluntary, replacement or employ-ment/licensing donor
	Jazan	(33)	EIA ≥ 3	EIA ≥ 3	2013	2004 - 2009	29949	0.42	Voluntary or replacement donor
	Aseer Region	(34)	EIA ≥ 3	EIA ≥ 3	2015	2012 - 2013	7267	0.07	Voluntary donor
	Makkah	(35)	EIA ≥ 3	NA	2015	2011 - 2014	22963	0.44	Voluntary or replacement donor
	Al-Baha	(36)	EIA ≥ 3	RIBA	2016	2009 - 2011	2807	0.04	NA
Total[a]					0.62% (0.23% - 1.01%)				
Syria	Damascus	(44)	EIA ≥ 3	EIA ≥ 3	2002	2002	2100	0.95	NA
	Damascus	(45)	EIA ≥ 3	NA	2013	2011	1939	0.41	NA
Total[a]					0.66% (0.13% - 1.19%)				
	Aydin	(22)	EIA	RIBA	2004	1993 - 2002	37866	0.19	Voluntary donor