Hepatitis C infection seroprevalence in pregnant women worldwide: a systematic review and meta-analysis

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Summarv

Background Monitoring progress towards the WHO global target to eliminate hepatitis C virus (HCV) infection by 2030, entails reliable prevalence estimates for HCV infection in different populations. Little is known about the global burden of HCV infection in pregnant women. Here, for the first time to our knowledge, we estimated the global and regional seroprevalence of HCV antibody (Ab) and determinants in pregnant women.

Methods In this systematic review and meta-analysis study, we searched PubMed/MEDLINE, Web of Science, Embase, Scopus, and SciELO databases for peer-reviewed observational studies between January 1, 2000 and April 1, 2023, without language or geographical restrictions. Pooled global seroprevalence (and 95% confidence interval, CI) were estimated using random-effects meta-analysis and seroprevalences were categorised according to World Health Organization regions and subregions, publishing year, countries' income and human development index (HDI) levels. We used sensitivity analysis to assess the effect of four large sample size studies on pooled global prevalence through the "leave-one-out" method. We also investigated the association of potential risk factors with HCV seropositivity in pregnant women by subgroup and meta-regression analyses. The Protocol was registered in PROSPERO CRD42023423259.

Findings We included 192 eligible studies (208 datasets), with data for 148,509,760 pregnant women from 53 countries. The global seroprevalence of HCV Ab in pregnant women was 1.80% (95% CI, 1.72-1.89%) and 3.29% (3.01-3.57%) in overall and sensitivity analyses, respectively. The seroprevalence was highest in the Eastern Mediterranean region (6.21%, 4.39-8.29%) and lowest in the Western Pacific region (0.75%, 0.38-1.22%). Subgroup analysis indicated that the seroprevalence of HCV Ab among pregnant women was significantly higher for those with opioid use disorder (51.94%, 95% CI: 37.32-66.39) and HIV infection (4.34%, 95% CI: 2.21-7.06%) than for the general population of pregnant women (1.08%, 95% CI: 1.02–1.15%), as confirmed by multivariable meta-regression (p < 0.001). A significant decreasing trend was observed with increasing human development index levels. Other important risk factors for HCV seropositivity included older age, lower educational levels, poly sexual activity, history of blood transfusion, hospitalization, surgery, abortion and sexual transmitted diseases, having scarification/tattoo or piercing, and testing hepatitis B positive.

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Interpretation This meta-analysis showed relatively high burden of exposure to HCV infection (2.2–5.3 million) in pregnant women globally. However, due to substantial heterogeneity between studies, our estimates might be different than the true seroprevalence. Our findings highlighted the need to expand HCV screening for women of reproductive age or during pregnancy, particularly in countries with high prevalence; as well as for more studies that assess safety of existing therapeutic drugs during pregnancy or potentially support development of drugs for pregnant women.

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Keywords: Hepatitis C infection; Global seroprevalence; Pregnant women; Systematic review and meta-analysis

Research in context

Evidence before this study

The WHO Global Health Sector Strategy aims to eliminate hepatitis C (HCV) infection by 2030. Reliable estimates of current disease prevalence are needed to inform global and national strategies. We searched international scientific databases for any systematic review and meta-analysis studies on the HCV infection prevalence in pregnant women from January 1, 2000 up to April 1, 2023. The following search terms were used: ("hepatitis C Virus" OR "Hepatitis C" OR "Hepacivirus" OR "Hepatitis C Antibodies" OR "Hepatitis C Antigens") AND (pregnancy" OR "pregnant women" OR "gestation" OR "antenatal clinics) AND ("prevalence" OR "incidence" OR "epidemiology" OR "seroprevalence" OR screen*). We found systematic reviews on HCV infection prevalence in the patients with HIV-infection, children, transgenders, general population, and some other specific population groups but no systematic review specifically estimated HCV infection or seroprevalence in pregnant women

Added value of this study

We analysed data for 192 eligible studies (208 datasets) comprising 148,509,760 pregnant women from 53 countries in all six WHO-defined regions. We estimated the worldwide seroprevalence of HCV Ab among pregnant women to range between 1.72% and 3.57%. The pooled seroprevalence estimates in WHO-defined regions (in descending order, with

the range) were: 6.21% (4.39–8.29%) in the Eastern Mediterranean region; 2.35% (1.89–2.86%) in Africa; 2.09% (1.91–2.27%) in North-America; 1.62% (1.07–2.27%) in the Caribbean and Latin America; 1.48% (1.15–1.84%) in Europe; 0.99% (0.28–2.07%) in South-East Asia; and 0.75% (0.38–1.22%) in the Western Pacific. Our results demonstrated higher seroprevalences of HCV ab in pregnant women living in countries or regions with low-income and low human development indices, as well as those with specific diseases such as HIV-infection, and opioid use disorders. We also identified several risk factors associated with HCV seropositivity in pregnant women.

Implications of all the available evidence

Our findings suggested that the global HCV seroprevalence among pregnant women over the period 2000–23 is relatively high, suggesting potential for an increased, yet preventable, risk of adverse complications for mothers and infants. The data presented here could inform public health research, policy, and programming priorities at global, regional and even national levels. The findings emphasise a need to expand HCV screening for women of reproductive age or during pregnancy, particularly in developing countries; as well as for more studies that assess safety of existing therapeutic drugs during pregnancy or potentially support development of drugs for pregnant women.

Introduction

Hepatitis C virus (HCV) infection is a global health problem affecting millions of people around the world each year.^{1,2} In 2019, the global burden of HCV was estimated at over 58 million people,³ of which 14.9 million HCV infections were in women aged 15–49 years.⁴ HCV is mainly transmitted through infected blood transfusions, therapeutic injections, intravenous drug use or blood products, sexual transmission, and mother-to-child/vertical transmission (MTCT).⁵ While MTCT is generally a less common route of HCV, it has been identified as the main cause of pediatric hepatitis C.⁶⁷ It is estimated that the rate of vertical HCV transmission is 5.8%, rising to 10.8% among HCV/human immunodeficiency virus (HIV) co-infected pregnant women.⁸

HCV in pregnant women has dramatically increased in the past decade. In the United States, for example, this may be attributable to the increasing rate of opioid use, particularly through injection, among women of reproductive age.⁹ Worldwide, up to 8% of pregnant women have HCV infection, with the prevalence being as high as 4% in the United States.¹⁰ Some studies suggest that there is an increased risk of maternal complications for pregnant women with HCV infection.^{11,12} These complications include intrahepatic cholestasis, premature contractions, preterm delivery, placenta praevia, placental separation, premature rupture of membranes, vaginal bleeding, and mortality.^{13–15} Moreover, some studies indicate that infants born to mothers with HCV infection are more likely to experience poor outcomes, such as low birth weight, preterm birth, intrauterine fetal death, and being small for gestational age.^{16–18}

The advent of direct-acting antiviral agents (DAAs) with over 95% effectiveness in treating patients with chronic HCV infection¹⁹ prompted the World Health Organization (WHO) to formulate the "Global Health Sector Strategy on viral hepatitis" with a goal of eliminating HCV infection by 2030.^{20,21} While the use of DAAs for HCV in pregnancy lacks extensive clinical trial evidence,22-26 recent recommendations from the American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA) suggest that DAA treatment may be considered on a case-by-case basis, taking into account potential risks and benefits.27 Moreover, despite recommendations advocating for universal and risk-based HCV screening among adults aged 18 to 79,27,28 with a particular emphasis on pregnant women, the screening for HCV in women of childbearing ages and pregnant women remains uncommon.^{29,30} This is particularly uncommon in low- and middle-income countries and even in highincome countries.^{4,31} In addition, information on the global and regional seroprevalence of HCV antibody (Ab) among pregnant women is also scarce.^{32,33} Against this background, we conducted a systematic review and metaanalysis to estimate the seroprevalence of HCV Ab in pregnant women globally and in WHO-specific regions, with the aim of informing public health policy and progress towards elimination goals.

Methods

Study design

This study was conducted following the systematic review guidelines established by the Cochrane Collaboration.³⁴ We reported our methodology and findings according to the Meta-Analyses and Systematic Reviews of Observational Studies (MOOSE)³⁵ and the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA)³⁶ guidelines (see PRISMA checklist in Text S1). Discrepancies during stages of this study were resolved by consensus. The Protocol was registered in PROSPERO CRD42023423259.

Study eligibility

We included observational studies that reported prevalence of anti-HCV serum antibodies (referred to henceforth as "HCV seroprevalence") in pregnant women or had enough data to compute this estimate (i.e., number of tested pregnant women and HCV seropositive women). We excluded studies that had overlapped datasets or participants, examined nonpregnant women of child-bearing age or women after delivery, had no available full-text even after contacting the corresponding author, as well as reviews, systematic reviews, letters, commentaries, editorials, conference papers, randomised controlled trials with no baseline prevalence measure, case reports, and case-series studies. We also excluded studies that evaluated HCV RNA or viremia, since there were few eligible studies and tested women that could not have been representative of prevalence rates at national or regional level.

Data sources and search strategies

We developed our search strategy in collaboration with a medical library expert (Figure S1). Briefly, we used search terms related to HCV infection (i.e., "hepatitis C Virus" OR "Hepatitis C" OR "Hepacivirus" OR "Hepatitis C Antibodies" OR "Hepatitis C Antigens"); pregnant women (ie, "pregnancy" OR "pregnant women" OR "gestation" OR "antenatal clinics"); and epidemiology (ie, "prevalence" OR "incidence" OR "epidemiology" OR "seroprevalence" OR screen*) and searched PubMed/MEDLINE, Web of Science Core Collection, Embase, Scopus, and SciELO databases for peerreviewed studies between January 1, 2000 and February 1, 2023, without language or geographical restrictions (Figure S1). We updated our literature search on April 1, 2023. The 20 first pages of the Google Scholar search engine, as well as the reference lists of the included studies, and relevant reviews were additionally screened to identify additional studies that could have been missed.

Data extraction and quality assessment

Three researchers (FA, MA, and HB) extracted data independently from eligible studies using a standardised data extraction form in Microsoft Excel (version 2016; Microsoft Corporation, Redmond, USA), and three others (MHB, EM and MJ) independently appraised extracted data. Two researchers also independently evaluated the quality of included studies using the Joanna Briggs Institute (JBI) prevalence critical appraisal tool,37 with a third researcher assisting in resolving any disagreement. We systematically extracted data on participant characteristics (first author's name, number of pregnant women screened and those with test positive result); study design; country; publication date, period of study implementation, type of serological methods, and related risk factors (if available). All countries were classified according to regions or subregions as defined by the WHO,³⁸ World Bank's income category,³⁹ and the human development index (HDI).40 We also recorded gross national income per capita for each country.³⁹

Data synthesis and statistical analysis

We estimated the seroprevalence of HCV Ab in pregnant women at global, regional, and national levels, and reported them separately. For this, we first used the Freeman-Tukey double arcsine transformation⁴¹ for stabilising the variance of individual studies. Then, the DerSimonian and Laird random-effects model (REM)42 was used to pool seroprevalence estimates across studies. Pooled seroprevalences were expressed as percentages with 95% confidence intervals (CIs). The REM was selected considering the heterogeneity across studies, as expected in observational studies.43,44 Such heterogeneity in seroprevalences is caused by differences in study populations (such as age and sex of participants), diagnostic method, setting, and other factors. A REM assumes the observed estimates of seroprevalence can vary across studies because of real differences in the seroprevalence in each study as well as sampling variability (random error). We used "metaprop" in Stata to perform meta-analyses of binomial data. Metaprop builds further on the mean procedure. It allows computation of 95% confidence intervals using the score statistic and the exact binomial method and incorporates the Freeman-Tukey double arcsine transformation of proportions. The program also allows the within-study variability be modelled using the binomial distribution. Between-study heterogeneity was assessed using the Q, and I^2 test statistics.^{45,46} An $I^2 > 75\%$ indicated a high heterogeneity.34,45,46 We used sensitivity analysis to assess the effect of large sample size studies on pooled global seroprevalence through the "leave-oneout" method.47 Leave-one-out meta-analysis performs multiple meta-analyses by excluding one study at each analysis. Large studies may impact the effect sizes. Leave-one-out meta-analysis is useful to investigate the influence of each study on the overall effect-size estimate and to identify influential studies.47 We also assessed "small-study effects" using visual funnel plot based on the logit transformation of effect size and sample size method, as the conventional funnel plot and "small-study effects" tests have limitations for metaanalyses of studies with low prevalence.48

We further conducted subgroup and univariable and multivariable meta-regression analyses to explore sources of heterogeneity in HCV seroprevalence. These were determined a priori and included in subgroup and/or meta-regression analyses as relevant and included WHO-region and subregion, types of serological methods, year of publication, study start date, type of pregnant women population, study design, income and HDI levels, and risk of bias. The Stata software (v.17.0; Stata Corp., College Station, Texas, USA) was used for all statistical analyses. A p-value <0.05 was indicative of statistically significant difference.

Ethics approval and consent to participate Not applicable.

Role of funding source

There was no funding source for this study. The corresponding author (A.R.) had access to the data in the study and had final responsibility for the decision to submit for publication. All authors had full access to all the data in the study and accept responsibility for the decision to submit for publication.

Results

Eligible studies

Fig. 1 illustrates the study selection process. Our search of scientific databases identified 3846 articles. We further obtained 428 records through screening Google Scholar and other literature. Of these, 314 were eligible for fulltext screening after removing duplicates and reviewing titles and abstracts. A total of 192 studies (208 datasets) including 148,509,760 pregnant women from 53 countries were included in the quantitative synthesis (characteristics summarised in Table S1). The rest were excluded for reasons outlined in Fig. 1. We also identified that 50 studies had data on HCV viremia in pregnant women. The highest number of eligible datasets was contributed by the African (n = 57) region and the lowest by the South-East Asian region (n = 6). Most examined pregnant women were from North America (n = 146,412,206). Studied women were mostly general pregnant women $(n = \sim 148.5 \text{ million})$, but 17,229 were HIV-positive, 3958 with opioid use disorder (OUD), and 3292 with other complications (women with female genital cutting [FGC], acute hepatitis, HBsAg-positive and chronic viral-illness, fulminant hepatic failure, jaundice, thalassemia, and thrombocytopenia). Thirty-seven datasets were performed at national level (covering the whole country) and 171 datasets sub-national (representing a city or province within the country) levels. Moreover, 199 datasets screened all pregnant women, while in nine datasets pregnant women were a portion of the population. Studies were classified with either low (n = 114) or moderate (n = 78) risk of bias. More details are presented in Tables 1-3 and Table S1.

Global and regional seroprevalences of HCV Ab in pregnant women

For the 208 datasets, 486,839 of 148,509,760 pregnant women were seropositive to HCV Ab, resulting in an overall, pooled global seroprevalence of 1.80% (95% CI, 1.72–1.89) (Table 1; Fig. 2). There was substantial heterogeneity between studies ($I^2 = 99.8\%$, p < 0.001). A sensitivity analysis excluding four studies^{49–52} from the USA with very large sample sizes (totalling 142,114,213 pregnant women) increased the estimated global seroprevalence of HCV Ab in pregnant women to 3.29% (3.01–3.57%). Pooled seroprevalences for WHO-regions (in descending order, with the range) were: 6.21% (4.39–8.29%) in the Eastern Mediterranean region; 2.35% (1.89–2.86%) in Africa; 2.09% (1.91–2.27%) in



Fig. 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart—indicating the literature search strategy and the numbers of included and excluded studies.

North-America; 1.62% (1.07-2.27%) in the Caribbean and Latin America; 1.48% (1.15-1.84%) in Europe; 0.99% (0.28-2.07%) in South-East Asia; and 0.75% (0.38-1.22%) in the Western Pacific. For WHO subregions defined by mortality strata (A to E), the highest and lowest pooled prevalence were in the subregions EMR-D (7.79%, 5.47-10.48%) and WPR-A (0.21%, 0.11-0.32%), respectively. The countries (those with three or more eligible datasets) with highest seroprevalence estimates were Pakistan (9.02%, 6.19-12.31%), Italy (7.18%, 1.08-17.67%), Ghana (4.92%, 2.67-7.76%), Egypt (3.89%, 2.08-6.20%), Burkina Faso (3.80%, 2.18-5.83%), and Cameroon (3.50%, 1.72-5.83%). Pooled seroprevalence for USA, a country with highest number of tested pregnant women, was 2.45% (2.25-2.66%). More information pertaining to the seroprevalence of HCV Ab in pregnant women in WHO-regions, WHO sub-regions and individual countries are given in Table 1 and Fig. 2. There was no indication of publication bias in the funnel plot used to evaluate "small-study effects" for the pooled prevalence (Figure S2).

Seroprevalence according to a priori-defined subgroups

Table 2 provides estimates for the pooled mean seroprevalence of previously-defined subgroups. Studies published during 2016-2023 (1.46%, 1.36-1.56%) showed lower seroprevalence than those published before 2010 (3.44%, 2.58-4.41%) and 2010-2015 (3.35%, 2.55–4.25%) (p < 0.001); however, after excluding four studies with large sample size (published 2016-2023) in sensitivity analysis, the pooled seroprevalence in 2016-2023 (3.32%, 2.98-3.67%) was relatively similar to other time periods. Trend analyses on years of publication (coefficient [C] = -0.0005; p-value = 0.739) and beginning date of sampling (C = -0.0007, pvalue = 0.996) indicated a non-significant decreasing trend in HCV seroprevalence over time (Supporting Information: Table S2 and Figure S3A and B). However, we observed a non-significant increasing trend in HCV prevalence for African (C = 0.0004, p-value = 0.51) and Eastern Mediterranean (C = 0.0005, p-value = 0.88) regions. Furthermore, non-significant decreasing trends were also observed for all WHO-regions. Subgroup analyses further estimated the highest pooled seroprevalence for lower-middle-income (3.76%, 2.84-4.80%) countries and those with low levels of HDI (3.74%, 2.82-4.78%); while high-income (1.51%, 1.40-1.61%) countries and those with very-high (1.39%, 1.30-1.49%) levels of HDI had the lowest pooled prevalence. Trend analysis indicated a non-significant decreasing trend in seroprevalence of HCV Ab with increasing income (C = -0.0000008, p-value = 0.837; Figure S4A), but a

WHO regions/subregions ^b /country ^a	Number of	Number of women	Number of HCV	Pooled mean prevalence	Heteroge	neity
	datasets	screened (total)	seropositive women	(95% CI)	1 ²	Q
Global	208	148,509,760	486,839	1.80 (1.72-1.89)	99.81	115611.1
Eastern Mediterranean	42	191,863	8848	6.21 (4.39-8.29)	99.57	9738.78
EMR-B	15	74,182	1515	3.81 (1.36-7.29)	99.52	2933.38
Egypt	9	65,958	740	3.89 (2.08-6.20)	98.34	484.20
Iran	4	3424	27	0.79 (0.03-2.25)	89.68	29.09
Kuwait	2	4800	748	9.76 (8.94-10.62)	-	-
EMR-D	27	117,681	7333	7.79 (5.47-10.48)	99.32	3861.04
Pakistan	21	108,361	7119	9.02 (6.19-12.30)	99.35	3121.52
Iraq	2	3645	130	3.33 (2.76-3.95)	-	-
Yemen	2	800	68	8.50 (6.65-10.54)	-	-
Sudan	1	423	3	0.71 (0.15-2.06)	-	-
Afghanistan	1	4452	13	0.29 (0.16-0.50)	-	-
African Region	57	53,349	1374	2.35 (1.89-2.86)	90.62	597.17
AFR-D	37	30,887	868	2.75 (2.16-3.41)	88.45	311.81
Nigeria	19	19,043	549	2.05 (1.34-2.89)	90.65	192.69
Ghana	6	1134	57	4.92 (2.67-7.76)	73.17	18.64
Cameroon	5	7328	162	3.50 (1.72-5.83)	91.61	47.68
Burkina Faso	5	2182	77	3.80 (2.18–5.83)	79.05	19.09
Gabon	1	947	20	2.11 (1.29–3.24)	-	-
Benin	1	253	3	1.19 (0.25-3.43)	_	_
AFR-E	20	22,462	506	1.71 (0.97-2.62)	92.78	263.50
Ethiopia	10	4056	108	2.11 (0.84–3.89)	90.38	93.55
DR Congo	3	2069	52	2.95 (0.81-6.30)	-	_
Rwanda	2	12,985	339	2.33 (2.06-2.61)		
Tanzania					-	-
Malawi	2	838	3	0.35 (0.03-0.92)	-	-
		2349	3	0.08 (0.00-0.27)	-	-
Uganda	1	165	1	0.61 (0.02-3.33)	-	-
North America AMR-A	31	146,412,206	471,519	2.09 (1.91-2.27)	99.96	78660.91
	31	146,412,206	471,519	2.09 (1.91-2.27)	99.96	78660.91
USA	29	146,339,778	470,773	2.45 (2.25–2.66)	99.96	77714.96
Canada	2	72,428	746	0.84 (0.77-0.91)	00 50	4074 70
Caraebian and Latine America	20	235,457	679	1.62 (1.07-2.27)	98.50	1271.79
AMR-B	19	235,431	679	1.71 (1.15-2.37)	98.58	1271.48
Brazil	15	234,796	473	0.52 (0.32-0.75)	96.37	385.70
Mexico	2	341	160	45.32 (40.00–50.68)	-	-
Bahamas	1	30	0	0.01 (0.00-11.57)	-	-
Argentina	1	264	46	17.42 (13.05-22.55)	-	-
AMR-C	1	26	0	0.01 (0-13.23)	-	-
Peru	1	26	0	0.01 (0.00-13.23)	-	-
European	41	1,415,046	3870	1.48 (1.15–1.84)	99.01	4051.02
EUR-A	32	1,276,663	3396	1.81 (1.33-2.36)	99.13	3587.88
Italy	5	13,689	354	7.18 (1.08–17.67)	99.62	1060.52
Spain	5	14,266	78	0.62 (0.19–1.25)	89.94	39.78
England	4	56,987	70	0.13 (0.00-0.41)	93.17	43.95
Slovenia	3	24,919	32	0.13 (0.07–0.21)	-	-
Ireland	3	18,543	9309	0.81 (0.38–1.39)	-	-
Portugal	1	934	13	1.39 (0.74–2.37)	-	-
Wales	2	2283	297	8.20 (7.10-9.37)	-	-
France	2	4471	132	2.78 (2.31-3.30)	-	-
Sweden	1	1,093,969	2056	0.19 (0.18-0.20)	-	-
Scotland	1	30,259	121	0.40 (0.33-0.48)	-	-
Denmark	1	4890	3	0.06 (0.01-0.18)	-	-
Netherlands	1	4563	15	0.33 (0.18-0.54)	-	-
			-		Table 1 continue	

WHO regions/subregions ^b /country ^a	Number of	Number of women	Number of HCV	Pooled mean prevalence	Heterogeneity	
	datasets	screened (total)	seropositive women	(95% CI)	l ²	Q
(Continued from previous page)						
Austria	1	4222	67	1.59 (1.23–2.01)	-	-
Norway	1	1668	3	0.18 (0.04-0.52)	-	-
Belgium	1	1000	2	0.20 (0.02-0.72)	-	-
EUR-B	9	138,383	474	0.89 (0.47-1.42)	98.19	444.33
Turkey	5	121,015	264	0.16 (0.07-0.28)	92.31	51.97
Poland	3	17,091	135	0.95 (0.35-1.81)	-	-
Azerbaijan	1	277	75	27.08 (21.93-32.72)	-	-
South-East Asian	6	15,030	148	0.99 (0.28-2.07)	95.19	104.09
Sear-D	5	12,580	147	1.31 (0.51-2.43)	92.21	51.40
India	5	12,580	147	1.31 (0.51-2.43)	92.21	51.40
Sear-B	1	2450	1	0.04 (0.01-0.23)	-	-
Indonesia	1	2450	1	0.04 (0.00-0.23)	-	-
Western Pacific	11	186,809	401	0.75 (0.38-1.22)	97.76	447.31
WPR-A	3	18,788	44	0.21 (0.11-0.32)	-	-
Japan	2	17,873	41	0.22 (0.16-0.30)	-	-
New Zealand	1	915	3	0.33 (0.07-0.96)	-	-
WPR-B	8	168,021	357	1.08 (0.47-1.92)	98.40	437.68
Thailand	3	3565	149	3.37 (1.72-5.53)	-	-
China	2	161,780	198	0.12 (0.10-0.14)	-	-
Vietnam	2	2166	5	0.12 (0.00-0.37)	-	-
Cambodia	1	510	5	0.98 (0.32-2.27)	-	-

A, very low child mortality and low adult mortality; B, A, low child mortality and low adult mortality; C, low child mortality and high adult mortality; D, high child mortality; and high adult mortality; E, high child mortality and very high adult mortality. The developed countries are at (AMR-A, EUR-A, EUR-A, EUR-A, EUR-A, Iow-mortality developing countries are at (AMR-B, EMR-B, and high-mortality developing countries are at (AFR-D, AFR-E, AMR-D, EMR-D and SEAR-D). ^aThe WHO regions are sorted based on prevalence rates, and countries are sorted based on the number of datasets. ^bSubregions are sorted based on mortality strata (A to E).

Table 1: Global and regional pooled prevalence of HCV infection among pregnant women.

significant decreasing trend in seroprevalence of HCV Ab with increasing HDI values (C = -0.1163, p-value = 0.028; Figure S4B).

Subgroup analyses with respect to 'type of pregnant women' showed that pooled seroprevalence of HCV Ab in general women was 1.08% (1.02-1.15%); while pregnant women with OUD (51.94%, 37.32-66.39%), other complications (13.27%, 4.33-25.89%), and HIV infection (4.34%, 2.21-7.06%), showed higher pooled seroprevalences (p-value <0.001). In sensitivity analysis pooled seroprevalence in general pregnant women was 1.79% (1.59-1.99%). Pooled seroprevalence was highest in studies that used rapid-immunochromatographic (2.56%, 0.88-5.02%) and lowest in studies that use chemiluminescent (0.75%, 0.36-1.28%) assays. With regard to type of participants; studies that study populations exclusively comprised of pregnant individuals showed a seroprevalence of 1.85% (1.77-1.94%), while studies that study populations partially comprised of pregnant individuals showed a lower seroprevalence rates (0.87%, 0.33-1.61%). Considering location level, seroprevalence rates were 1.14% (1.02-1.26%) and 3.44% (3.10-3.79%) for studies conducted as national and sub-national levels, respectively. Subgroup analysis based on risk of bias indicated that the seroprevalence of HCV Ab in studies with a low risk of bias (1.41%,

1.31–1.48%) was significantly lower (p-value <0.001) than in studies with a moderate risk of bias (5.04%, 4.16-6.01%).

Univariable and multivariable meta-regression analyses to identify sources of heterogeneity

Table S2 shows findings of the univariable and multivariable meta-regression analyses investigating association of studies' characteristics with HCV seroprevalence. The univariable analysis revealed that HDI levels ($\beta = -0.1163$, -0.2202 to -0.0123, p-value = 0.023) and type of pregnant women ($\beta = 0.0713$, 0.0575–0.0852, pvalue <0.001) were significantly associated with HCV seroprevalence in pregnant women. Multivariable metaregression analysis identified significant associations for HDI levels ($\beta = -0.1967$, -0.3342 to -0.0592, pvalue = 0.005) and type of pregnant women ($\beta = 0.0697$, 0.0554–0.0839, p-value <0.001) with HCV seroprevalence in pregnant women. The final model could explain 41.96% of the total heterogeneity in HCV seroprevalence.

Meta-analyses on risk factors of HCV seroprevalence in pregnant women

Table 3 provides estimates for the pooled mean sero-
positivity prevalence by key risk factors for HCV sero-
prevalence. Subgroup analyses investigating

Variable subgroup	Number of datasets	Number of women screened (total)	Number of HCV seropositive women	Pooled mean prevalence% (95% CI)	OR between sub-groups	ľ	p-value for subgroup analysis
Publication year	_	-				_	
Before 2010	45	173,175	1941	3.44 (2.58-4.41)	Ref	98.94	<0.001
2010-2015	75	2,109,575	10,456	3.35 (2.55-4.25)	0.43 (0.41-0.46)	99.75	
2016-2023	88	146,227,010	474,442	1.46 (1.36-1.56)	2.87 (2.74-3.01)	99.88	
Type of pregnant women							
General	167	148,485,281	483,144	1.08 (1.02-1.15)	Ref	99.82	<0.001
HIV positive	21	17,229	770	4.34 (2.21-7.06)	1.43 (1.33–1.54)	97.99	
OUD	11	3958	1998	51.94 (37.32-66.39)	31.22 (29.33-33.23)	98.82	
Others ^a	9	3292	927	13.27 (4.33-25.89)	12.01 (11.12–12.95)	98.39	
Type of studies							
Retrospective cohort	38	115,032,862	364,348	1.55 (1.39–1.71)	Ref	99.95	<0.001
Prospective cohort	22	106,207	1713	7.27 (5.10–9.78)	0.51 (0.49–0.54)	99.27	
Cross-sectional	147	33,369,279	120,738	2.87 (2.57-3.18)	0.11 (0.10-0.12)	99.10	
Case-control	1	1412	40	2.83 (2.03-3.84)	0.97 (0.61-1.25)	-	
Type of serological methods							
Chemiluminescent	9	149,047	494	0.75 (0.36-1.28)	Ref	97.88	<0.001
ELISA	173	148,185,825	480,225	1.91 (1.82-2.01)	9.77 (8.94–10.68)	99.82	
Rapid-immunochromatographic assays	20	136,696	5987	2.56 (0.88-5.02)	13.77 (12.56–15.10)	99.72	
Others ^b	6	38,192	133	1.70 (0.45-3.63)	1.05 (0.86-1.27)	97.91	
Type of participants							
Pregnant women as total participants	199	148,500,277	486,782	1.85 (1.77–1.94)	5.43 (4.19-7.05)	99.82	0.012
Pregnant women as partial participants	9	9483	57	0.87 (0.33-1.61)	Ref	86.04	
Location level							
National	37	143,697,150	459,731	1.14 (1.02–1.26)	Ref	99.94	<0.001
Sub-national	171	4,812,610	27,108	3.44 (3.10-3.79)	1.76 (1.74–1.78)	99.65	
ncome							
Low	27	29,481	664	2.43 (1.60-3.43)	Ref	94.76	<0.001
Lower middle	76	224,045	8818	3.76 (2.84-4.80)	1.77 (1.64–1.92)	99.13	
Upper middle	33	526,656	1515	1.51 (1.17-1.88)	0.12 (0.11-0.13)	98.67	
High	72	147,729,578	475,842	1.51 (1.40-1.61)	1.40 (1.29–1.51)	99.91	
HDI							
Low	70	157,976	8338	3.74 (2.82-4.78)	Ref	98.68	<0.001
Medium	19	25,197	501	3.14 (2.22-4.21)	0.36 (0.33-0.39)	93.14	
High	38	472,165	1699	1.67 (1.29–2.09)	0.06 (0.05-0.07)	98.66	
Very high	81	147,854,422	476,301	1.39 (1.30-1.49)	0.58 (0.56-0.59)	- 99.90	
Risk of bias							
Low	125	148,293,477	483,670	1.41 (1.33-1.50)	Ref	99.88	<0.001
Moderate	83	216,283	3169	5.15 (4.26-6.12)	0.45 (0.43-0.47)	98.59	

Abbreviations: CI, confidence intervals; OUD, opioid used disorders; HDI, human development index. ^aThalassemic, Thrombocytopenic, FGC, chronic viral illness, HbsAg positive. ^bImmunoblot assay, Latex agglutination.

Table 2: Pooled prevalence and association of study characteristics with HCV in pregnant women.

associations of risk factors with HCV seroprevalence showed that pregnant women who lived in rural areas (OR 1.67, 95% CI: 1.65–1.70); older ages (OR 1.63, 95% CI: 1.45–1.83); those with primary or less educational levels (OR 7.86, 95% CI: 7.67–8.05); those who were single (OR 4.36, 95% CI: 4.31–4.42); those women with multi-parity (OR 23.32, 95% CI: 21.31–25.52); those who had poly-sexual activity (OR 29.87, 95% CI: 24.60–36.27); those who had history of blood transfusion (OR 20.87, 95% CI: 16.79–25.93), hospitalization (OR 1.76, 95% CI: 1.26–2.47), surgery (OR 2.75, 95% CI: 2.44–3.10), dental procedures (OR 1.33, 95% CI: 1.08–1.63), abortion (OR 1.43, 95% CI: 1.13–1.81), scarification/tattoo (OR 5.01, 95% CI: 4.31–5.81), piercing (OR 4.80, 95% CI: 3.68–6.28), and injection drug use (OR 79.13, 95% CI: 63.26–98.98); those who were positive for HIV (OR 1.64, 95% CI: 1.55–1.74), HBV (OR 2.84, 95% CI: 2.49–3.25), and STD (OR 3.71, 95% CI: 3.61–3.81); and those who were in third trimester of pregnancy (OR 2.32, 95% CI: 1.46–3.68);

Variables	Number of women screened/HCV seropositive women	Pooled mean prevalence (95% CI)	OR between sub-groups	l ²	p-value for subgroup analysis
Age group					
<20	241,407/569	0.01 (0-0.31)	Ref	97.55	<0.001
20-39	1,067,851/1873	1.49 (1.11-1.93)	0.74 (0.67-0.81)	98.78	
30–39	139,471/536	1.27 (0.79–1.83)	1.63 (1.45-1.83)	96.47	
≥40	20,186/126	0.01 (0-0.07)	2.65 (2.19-3.22)	86.18	
Education level					
Primary or less	1,389,931/1377	1.51 (0.35-3.17)	1.62 (1.53-1.72)	98.74	<0.001
Secondary	27,062,120/128,946	0.62 (0.43-0.85)	7.86 (7.67-8.05)	90.58	
College and above	11,826,953/7197	0.85 (0.50-1.26)	Ref	95.90	
Occupation					
Housewife	45,698/326	4.22 (2.33-6.58)	7.97 (6.26-10.15)	98.85	0.080
Working	92,203/83	3.84 (2.01-6.13)	Ref	96.40	
Marital status					
Single	15,325,340/101,943	1.50 (0.66–2.56)	4.36 (4.31-4.42)	99.86	<0.001
Married	22,679,344/34,725	1.10 (0.88-1.35)	Ref	98.62	
Parity					
Nulli-parity	726,049/560	1.43 (0.51-2.68)	Ref	97.96	<0.001
Primi-parity	1,389,931/1377	2.02 (1.44-2.69)	1.28 (1.16-1.41)	98.68	
Multi-parity	1,777,571/3144	1.55 (1.21-1.93)	23.32 (21.31-25.52)	99.16	
Poly sexual					
Yes	1056/201	4.56 (0.01-17.18)	29.87 (24.60-36.27)	96.37	<0.001
No	35,220/275	2.69 (1.46-4.25)	Ref	96.40	
Residence	33, 473			5.1	
Rural	4,853,084/25,150	1.73 (1.29–2.23)	1.67 (1.65-1.70)	99.90	<0.001
Urban	36,626,273/113,284	0.59 (0.43-0.78)	Ref	99.96	-0.001
Blood transfusion	20102012101207		inci	55.50	
Yes	675/224	10.48 (3.72-19.43)	20.87 (16.79-25.93)	96.64	<0.001
No	7873/183	3.79 (2.49-5.34)	Ref	97.60	40.001
Hospitalization	/0/3/105	5.75 (2.45-5.54)	i ci	37.00	
Yes	856/45	4.71 (3.27-6.37)	1.76 (1.26-2.47)	0	<0.001
No	5420/165	3.14 (1.28-5.73)	Ref	94.66	<0.001
History of surgery	5420/105	3.14 (1.20-5.73)	Rei	94.00	
Yes	F602/442	6 90 (2 02 12 11)		07.11	<0.001
	5692/442	6.89 (2.93-12.11) 3.86 (2.27-5.82)	2.75 (2.44-3.10)	97.11	<0.001
No Dental procedure	27,480/815	3.00 (2.27-5.02)	Ref	97.98	
•	2707/455	F 02 (2 01 0 0C)	D-f	02.02	0.001
Yes	3707/155	5.03 (2.01-9.06)	Ref	93.92	<0.001
No	4621/254	4.47 (1.82-8.12)	1.33 (1.08–1.63)	95.92	
Abortion history	4204.04			70	0.000
Yes	4138/101	2.11 (0.78-3.84)	1.43 (1.13-1.81)	78.94	0.006
No	14,031/240	2.31 (1.29–3.55)	Ref	92.58	
Religion			D (
Islam	291/12	3.03 (0.51-6.97)	Ref	53.25	0.365
Christianity	1551/66	2.77 (0.68-6.06)	1.03 (0.55–1.93)	89.82	
Scarification/tattoo					
Yes	3054/297	6.56 (1.27–14.26)	5.01 (4.31-5.81)	96.69	<0.001
No	24,275/511	3.63 (2.31–5.23)	Ref	96.34	
Injection drug use					
Yes	400/225	41.61 (20.51-64.03)	79.13 (63.26–98.98)	90.21	<0.001
No	22,017/352	3.05 (1.59-4.85)	Ref	95.87	
HIV status					
HIV positive	323,412/1393	3.71 (1.97-5.81)	Ref	93.77	<0.001
HIV negative	903,753/6391	1.34 (0.98-1.76)	1.64 (1.55-1.74)	99.21	
				(Table 3	continues on next page

Variables	Number of women screened/HCV seropositive women	Pooled mean prevalence (95% CI)	OR between sub-groups	l ²	p-value for subgroup analysis
(Continued from previou	s page)				
HBV status					
HBV positive	11,468/228	2.77 (0.17-7.23)	2.84 (2.49-3.25)	95.63	<0.001
HBV negative	903,753/6391	1.34 (0.98–1.76)	Ref	99.21	
Trimesters					
First	1460/20	0.97 (0.01-3.05)	Ref	80.84	<0.001
Second	2478/31	0.97 (0.14-2.31)	0.91 (0.51-1.60)	82.29	
Third	6530/204	1.44 (0.44-2.85)	2.32 (1.46-3.68)	89.78	
STD status					
STD positive	367,517/5984	0.96 (0.71-1.24)	3.71 (3.61-3.81)	73.81	<0.001
STD negative	28,336,857/125,769	0.08 (0.01-0.65)	Ref	97.07	
Piercing					
Yes	1272/155	4.41 (0.01–14.51)	4.80 (3.68-6.28)	96.55	<0.001
No	3245/91	0.57 (0.01-3.43)	Ref	92.49	
Abbreviations: CI, confide	nce intervals; HIV, human immunodeficiency virus; HB	V, hepatitis B; STD, sexual transmi	tted disease.		

were more likely to be seropositive to HCV Ab compared with other pregnant women. Details are given in Table 3.

Discussion

This comprehensive systematic review and metaanalysis provided estimates for the seroprevalence of HCV Ab among pregnant women globally and regionally by analyzing 208 seroprevalence surveys including over 148 million pregnant women; although it should be noted that about 142.1 million of examined pregnant women were from four large studies performed in USA.^{49–52} Our findings indicated that the pooled overall worldwide seroprevalence of HCV among pregnant women (2000–2023) was in the range of 1.72–1.89%, however, a sensitivity analysis excluding four large studies from USA yielded a higher seroprevalence estimate in the range of 3.01–3.57%. To present a conservative interpretation, we estimated that a range of 1.72–3.57% of pregnant women worldwide have been exposed to HCV. According to these estimates and the estimated 140 million births per year globally (2021), we forecasted that between that 2.2 and 5.3 million babies will be born to HCV-seropositive mothers each year. This high burden of HCV seropositivity in pregnant



Fig. 2: Geographical distribution of HCV seroprevalence in pregnant women worldwide—based on data from eligible, peer-reviewed studies published from January 1, 2000 to February 1, 2023.

women could be also associated with an increased risk of adverse maternal and neonatal complications. Therefore, our findings underscore the critical importance of universal screening for HCV infection in all women of reproductive age, with a particular emphasis on pregnant women. Early detection and management of HCV in pregnant women may not only prevent future complications in mothers but also significantly reduce the risk of vertical transmission and subsequent severe health complications in their infants, thereby alleviating the overall healthcare burden.^{29,53} Despite the initial costs involved, universal HCV screening in pregnant women emerges as a judicious investment in public health, promising substantial economic and societal benefits in the long term.54,55 Currently, there are no approved HCV drugs for use during pregnancy.56 However, a growing body of research is exploring the use of DAA agents in pregnant individuals. Notably, Chappell and colleagues conducted a phase 1 study with ledipasvir/sofosbuvir (Harvoni, Gilead) during the second and third trimesters, reporting positive outcomes with no significant adverse events.25 Additionally, the CDC's Coalition for Global Hepatitis Elimination established the TiP-HepC registry to collect real-world data on DAA treatment in pregnant women, aiming to provide essential safety and efficacy information.57 Furthermore, an ongoing larger study in the United States is evaluating sofosbuvir/velpatasvir (Epclusa, Gilead) treatment in pregnant women.58,59

Our estimated range for HCV seroprevalence in pregnant women (1.72-3.57%) is slightly (~1.5 fold) higher than seroprevalence range (1.4-2.3%) in the general population reported from a recent global metaanalysis.60 Moreover, our findings corroborate other evidence indicating the importance of injecting drug use, HIV-infection and other high-risk behaviors or viral coinfections in driving the HCV epidemic.61-63 Our findings indicated significant higher seroprevalence rates in high-risk women such as those with OUD (51.9%), HIV-infection (4.34%) and those with other complications (13.2%) than general pregnant women (1.79% in sensitivity analysis). These findings are in agreement with previous estimates in people who use IV drugs (52.3%, 42.4-62.1%),⁶¹ pregnant women or heterosexually people who are HIV-positive (4.0%, 1.2-8.4%),62 people who are transgender (9%, 3-15%),64 patients undergoing hemodialysis (20.7%, 18.9-22.6%),65 and patients with cirrhosis (21%).63 These findings emphasise the urgent need for global HCV prevention interventions in high-risk pregnant women, particularly in regions with high HCV seroprevalences and those with OUD. These interventions could include needle or syringe exchange programmes, opiate substitution ther-DAA and therapies before intended apy, pregnancies.62,66,67

Our findings showed that different WHO regions had different rates of HCV Ab seroprevalence among pregnant women. The highest prevalence was observed in the Eastern Mediterranean (6.21%) region, while the African (2.35%), North American (2.09%), Caribbean and Latin American (1.62%), and European (1.48%) regions showed moderate prevalence, and the South-East Asian (0.99%) and Western Pacific (0.75%) regions had the lowest pooled prevalence. These estimates are consistent with previous global estimates for general populations.^{60,68,69} A modeling study by Dugan et al.⁴ estimated global HCV viraemic prevalence in 2019 among women of childbearing age, and similar to our study, the Eastern Mediterranean (1.75%) had the highest prevalence, although it should be noted that our estimates are about HCV antibody prevalence and differed to viraemic prevalence. Due to the lack of information on risk behaviors, it is difficult to compare these variations in HCV prevalence throughout the world.70 Differences in risk behaviors such as injection drug use, blood transfusion, unprotected sex, differences in HCV laboratory testing, national socioeconomic status, healthcare policies, and cultural practices like tattooing and piercing could contribute to differences in prevalence worldwide.68,71

Pakistan, as one of the countries in the Eastern Mediterranean region, had one of the highest prevalence rates (9.02%) among pregnant women in our study. A meta-analysis conducted in 2018 estimated HCV pooled prevalence in Pakistan at 6.2% among the general population (populations at low risk) including pregnant women.72 This disparity may be attributed to the fact that our study exclusively focused on pregnant women, whereas Al Kanaani et al.72 included pregnant women alongside other low-risk populations, such as blood donors, children, refugees, household-based survey participants, and national army recruits. The greatest HCV prevalence worldwide was seen in Egypt and Pakistan before 2015,73 but since then, Egypt has made significant progress in lowering HCV prevalence through mass DAA treatment for HCV-infected persons.74 This change in Egypt's HCV treatment and prevention strategy may explain the wide difference in HCV prevalence between Pakistan (9.02%) and Egypt (3.89%). Our research further showed an elevated seroprevalence of HCV, particularly in the Eastern Mediterranean and Africa, in addition to other regions with low income and HDI levels. These results were confirmed by our meta-regression analyses. Medical iatrogenic exposures such as unsafe and non-sterile therapeutic procedures, contaminated blood product transfusions, and unsafe drug injection techniques are the primary causes of HCV transmission and are prevalent in low- or middle-income countries.75-78 Interestingly, substantial HCV seroprevalence among pregnant women was also found in high-income regions, namely North America and Europe. It is considered that rising injection drug use in Europe and the US has contributed to increasing HCV infection rates over the past decade.⁷⁹ HCV infection prevalence ranges between 40 and 80% among people who inject drugs in Eastern Europe.⁸⁰ Another explanation might be that the USA and developed countries have better perinatal HCV screening programs. This can result in more diagnoses of HCV prevalence in developed countries compare to developing nations.⁴

Another finding, based on our meta-regression analysis, was the non-significant decreasing seroprevalence of HCV Ab in pregnant women over time. Although non-significant, this decrease could be explained by efforts to improve diagnosis, treatment, and prevention for HCV infection especially after the advent of highly effective DAA medications in 2014.81 This may have reduced HCV acquisition among women of reproductive age in recent years and therefore HCV prevalence among pregnant women. More studies are however needed to confirm this trend as our sensitivity analysis excluding four large sample size studies, all conducted post 2016 in USA and comprising 140 million pregnant women,49-52 yielded a pooled prevalence of 3.0% between 2016 and 2023, which is comparable to estimates from earlier years.

Several risk factors exist for HCV infection in the general population and pregnant women. These include intravenous drug use, intranasal cocaine usage, tattoos, body piercing, risky sexual activity, multiple partners, needle stick injuries, incarceration, a history of blood transfusions, HIV co-infection, chronic hemodialysis, and organ transplantation.28,82-84 Consistent with the literature, our findings also showed that injected drug use, polysexuality, a history of surgery, blood transfusion, hospitalization, dental procedures, tattooing, and piercing are potential risk factors associated with HCV seropositivity in pregnant women. We also found that HCV seroprevalence was highest among pregnant women between the ages of 20 and 39 (1.49%), who are possibly are more sexually active and may engage in more high-risk behaviors. Moreover, similar to previous studies, our findings indicate that HIV- and HBV- coinfected pregnant women had a greater seroprevalence of HCV Ab infection than those with no coinfections.7,85 Living in a rural area and having a low education level are also associated with higher HCV seroprevalence among pregnant women. It has been established that injection drug users who experience homelessness or unstable housing have a higher risk of HCV infection.86 It seems that a higher seroprevalence of HCV Ab in rural areas is associated with lower availability of healthcare services and less educational information about this virus and its transmission.

To the best of our knowledge, this is the first worldwide systematic and meta-analysis study of the seroprevalence of HCV Ab in pregnant women. We performed a comprehensive search and used a rigorous methodology to conduct this study. As a result, we have now established an enormous database with information on more than 150 million pregnancies around the world. This wide range of datasets enabled global, regional, and national HCV seroprevalence calculations. Nevertheless, this study has limitations. Only about 26% of the world's countries were represented geographically in our analysis (53/200), which compromises somewhat the interpretation of findings from the present study. Only 37 included studies were performed at national level, therefore, our estimates at country-level may not necessarily be representative of all pregnant women in that country especially for sub-national studies with small sample size. Additionally, our estimates might be influenced by an upward bias, which could be attributed to the composition of pregnant women in the included studies, where those sampled were more likely to have a higher prevalence of HCV. Although the size of this bias is unknown and is anticipated to be relatively small. To overcome this problem, we categorised the recruited pregnant women in included studies based on risk of HCV, and as indicated in Table 2 seroprevalence rates in general (1.08%) pregnant women was lower than those with OUD, HIV infection and other complications. Secondly, as expected in this type of research, our results showed significant heterogeneity across WHO regions and other subgroups. Sub-group analyses showed that almost all variables in Table 2 could be a source of heterogeneity. Meta-regression analyses were also conducted to investigate sources of heterogeneity in HCV seroprevalence among pregnant women. Our final multivariable metaregression model explained 41.96% of the total heterogeneity in HCV seroprevalence and types of pregnant women was determined as significant source of heterogeneity. Another important limitation of this study is the lack of data on HCV viremia, which is essential for determining the true prevalence of HCV. Although we identified 50 measures for HCV viremia, these were insufficient to calculate representative regional and national estimates of HCV prevalence in pregnant women.

In conclusion, this study found that HCV seroprevalence is relatively high among pregnant women. The burden of HCV seropositivity in pregnant women and its implications on maternal and child health, especially in the absence of safe and accurate treatment for pregnant women with HCV, suggests that MTCT is unlikely to be reduced without adequate HCV screening for women considering pregnancy. While further studies are needed to determine the cost-effectiveness of different screening strategies, our findings suggest that HCV screening may be worthy for women in reproductive age in areas of high HCV seroprevalence and for women at high-risk of acquiring the infection. Research aiming at assessing the safety of currently approved drugs during pregnancy or that support the development of novel therapeutic drugs that can be safely administered to pregnant women are also warranted. Our findings emphasised that in order to attain the

WHO's ambitious goal of HCV infection elimination by 2030, it is imperative for policymakers and healthcare planners to consider a multifaceted approach, particularly with a focus on pregnant women. This approach encompasses expanded universal screening programs, enhanced education and awareness initiatives, streamlined testing and early detection protocols, improved access to HCV treatment options, the integration of HCV services into maternal and child health programs, rigorous research and data collection efforts, the development of evidence-based policies, healthcare provider capacity building, community engagement, rigorous monitoring and evaluation systems, international collaboration, and adequate resource allocation.^{27,87}

Contributors

FA, MA, MFM, and AR conceived and designed this study. FA, FA, KBM, HB, MHB, MJT, SR, KB and MR searched databases and extracted data from eligible articles. MA, MR, MS and AR performed the statistical analyses. FA, MA, MFM, MS and AR assessed and verified all the data included in this study. FA, MA, AFN, and AR wrote the original draft of the manuscript. FA, MFM, HC, and AR contributed to the interpretation of the data and the writing of the manuscript. All authors reviewed and approved the final version before submission. All authors had access to all data used in this study, approved the final version of the manuscript, and accepted the responsibility for the decision to submit the manuscript for publication.

Data sharing statement

The all data are presented in the manuscript and Additional files. Further data that supports the findings of this study are available from the corresponding authors upon reasonable request.

Declaration of interests

The authors declare no competing interests.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2023.102327.

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