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Review Article

The Worldwide Epidemiology of Hepatitis B, Hepatitis C, and Herpes Simplex Virus Type 2 in Female Sex Workers: A Systematic Review and Meta-Analysis

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Abstract

Background and Aims: Female sex workers are vulnerable and at high risk to acquire sexually transmitted infections, and act as a bridge in the transmission of sexually transmitted infections (STIs) to the general population. This study was conducted to determine the prevalence of the main viral pathogens responsible for STIs, including Hepatitis B virus (HBV), Hepatitis C virus (HCV), and Herpes simplex virus type 2 (HSV-2) in female sex workers in the world.

Materials and Methods: A systematic search was carried out for relevant literature in international databases from database inception to September 25, 2019. The pooled prevalence for each STI of interest was estimated by a DerSimonian-Laird random-effects model using the inverse variance method.

Results: The lowest pooled prevalence of HBV, HCV, and HSV-2 infections was seen in the Republic of Mauritius (0.17%; 95% CI: 0.01%-2.64%), Panama (0.20%; 95% CI: 0.05%-0.80%), and Iran (14.12%; 95% CI: 6.66%-27.48%), respectively. The highest pooled prevalence of HBV infection was found in Slovakia (22.22%; 95% CI: 8.60%-46.47%), while for HCV and HSV-2 infections was observed in Scotland (64.29%; 95% CI: 54.35%-73.13%) and Indonesia (90.30%; 95% CI: 84.76%-93.97%), respectively.

Conclusion: A decreasing trend was observed in the prevalence of STIs of interest among female sex workers during recent years. However, the prevalence has remained high in some regions, and therefore it is important to improve prevention programs and conduct surveillance regularly in all parts of the world to decrease the risk of transmission of infections to the general population.

Keywords: Female sex worker; Prostitute; sexually transmitted infection; Hepatitis; Herpes simplex virus; Meta-Analysis

Introduction

Female sex workers are defined as women who offer sexual services in return for money, goods, or other markers of economic remuneration. However, female sex workers are a heterogeneous population group who work in varied work environments and community organizations. Street-based sex workers are mainly illegal workers who solicit clients on the street or in public settings such as markets, parks, cinema halls, and service them in alleys, or the clients' cars. Another group is indoor-based sex workers who are employed to work in brothels, hotels, massage parlors, saunas, and lodges (1-3).

Female sex workers are known to be a high-risk group for the acquisition of sexually transmitted infections (STIs) due to the risk factors associated with their occupation, such as multiple sexual partners, low adherence to condom use, and unsafe sexual practices. This population has long been recognized as a major driver of growing epidemics of STIs in several countries.

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These epidemics are initially triggered by female sex workers and subsequently generalized to their clients and partners (4, 5).

To date, there are more than 30 different sexually transmissible agents, including viruses, bacteria, and parasites. Among them, three bacterial (Chlamydia trachomatis, Neisseria gonorrhoeae, Treponema pallidum), a parasitic (Trichomonas vaginalis), and six viral (Hepatitis B virus (HBV), Hepatitis C virus (HCV), Human immunodeficiency viruses (HIV), Herpes simplex virus type 2 (HSV-2), and Human papillomavirus (HPV) and Human T-cell leukemia virus type 1 (HTLV-1) infections account for the majority of STIs globally (6, 7).

According to the last reports of the world health organization (WHO), HIV, HBV and HCV are major public health concerns which have significant impacts on human health and human life. It is estimated that approximately 38 million are HIV-infected (8), 257 million are HBV-infected (9), and 71 million have chronic HCV infections worldwide (10). It has been well documented that persistent infections with HCV and HBV are a leading cause of cirrhosis and hepatocellular carcinoma (11, 12). Besides, female sex workers are also exposed to the risk of genital ulcers caused by infection with HSV-2. In recent years, an increasing prevalence of HSV-2 has been found around the world, particularly among high-risk groups such as female sex workers (13). Several clinical and epidemiological studies offered evidence for multiple interactions between HIV and HSV-2 (14, 15).

In some meta-analysis and epidemiological studies, it has been demonstrated that HSV-2 can be regarded as a risk factor for HIV infection (16, 17). Furthermore, the status of antibodies to HSV-2 can be considered as a serological marker for the vulnerability to HIV infection in order to surveillance of infection controls (18, 19).

Considering the critical role of viral sexually transmitted infections and their complications and subsequences among female sex workers and their clients which pose a great burden on society and public health, it is worth investigating the prevalence of these infections in this high-risk group. Despite the numerous studies investigating the prevalence of STIs among female sex workers, there is no available study designed to characterize the global epidemiology of major viral STIs among this high-risk population. To the best of our knowledge, this is the first meta-analysis that aims to characterize the epidemiology of the three most important viral pathogens, including HBV, HCV, and HSV-2 among female sex workers around the world.

Methods

The protocol of this systematic review and meta-analysis was in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guideline (20).

Search strategy : We carried out an electronic literature search to identify relevant publications on the prevalence of STIs including HBV, HCV, and HSV-2 infections in female sex workers in the world. Articles were identified through searches in electronic databases, including PubMed, Scopus, Google Scholar, Web of Science, and Embase from database inception to September 25, 2019.

Also, we manually searched relevant articles and bibliographic reference lists of the publiccations selected for inclusion in our meta-analysis.

All searched publications were imported to EndNote software version X8 (Thomson Reuters, California, USA) for further management.

Selection criteria: Studies were deemed eligible for inclusion if they reported: (1) original data published in peer-reviewed journals in the English language regarding the prevalence measure for each STI of interest among female sex workers; (2) the prevalence of hepatitis B surface antigen (HBsAg), anti-HCV antibody, anti-HSV-2 antibody in blood and saliva; (3) editorials, letters, commentaries, short reports, and English abstracts with sufficient data.

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Table 1. The characteristics of all eligible studies in this systematic review and meta-analysis

Author (Ref.)	Publication Year	Study Period	Location	Virus	Total sample size	No. HBV positive	No. HCV positive	No. HSV-2 positive
Frade (25)	2019	2015-2017	Brazil	HBV	153	3	-	-
Puga (26)	2018	2009-2010	Brazil	HCV	402	-	2	-
Ferreira-Júnior (27)	2018	2016	Brazil	HBV/HCV	4245	16	38	-
Julien (28)	2018	2017	Rwanda	HBV/HCV	3930	126	177	-
Zhu (29)	2017	2014	China	HSV-2	585	-	-	268
Zhu (30)	2017	2014-2015	China	HSV-2	1058	-	-	537
Vu (31)	2017	2013	Tanzania	HSV-2	1903	-	-	1095
Niama (32)	2017	2011-2012	Republic of Congo	HBV/HCV	805	34	6	-
Mutagoma (33)	2017	2015	Rwanda	HBV/HCV	1978	50	28	-
de Matos (34)	2017	2009-2010	Brazil	HBV/HCV	402	6	3	-
Han (35)	2016	2012	China	HSV-2	1487	-	-	414
Yu (36)	2016	2010-2014	China	HCV	1026	-	27	-
Shen (37)	2016	2014	China	HCV	653	-	13	-
Adisesh (38)	2016	2010	India	HBV/HCV/ HSV-2	2532	58	53	72
Moayedi-Nia (39)	2015	2012-2013	Iran	HBV/HCV	161	2	13	-
Fan (40)	2015	2012-2013	China	HCV	622	-	44	-
Salyuk (41)	2015	2013	Ukraine	HCV	4806	-	841	-
Chen (42)	2015	2010-2012	China	HCV	51790	-	516	-
Luo (43)	2015	2012	China	HSV-2	833	-	-	570
Bugssa (44)	2015	2013	Ethiopia	HBV	319	19	-	-
Tang (45)	2014	2010	China	HCV	12622	-	128	-
Aho (46)	2014	2005-2006	Guinea	HSV-2	201	-	-	169
Kazerooni (47)	2014	2010-2011	Iran	HSV-2	278	-	-	27
Zhang (48)	2014	2011	China	HBV	600	74	-	-
Lwin (49)	2014	2009-2010	Myanmar	HCV	150	-	7	-
Li (50)	2014	NR	China	HSV-2	460	-	-	198
Fu (51)	2014	NR	China	HSV-2	575	-	-	176
Wang (52)	2014	2008-2012	China	HCV	759783	-	6021	-
Vandenhoudt (53)	2013	2008	Kenya	HSV-2	479	-	-	404
Zohrabyan (54)	2013	2009-2010	Moldova	HBV/HCV	658	60	149	-
Zhou (55)	2013	2010	China	HCV	12622	-	126	-
Valadez (56)	2013	2010	Libya	HBV/HCV	69	2	5	-
Schuelter-Trevisol (57)	2013	2009	Brazil	HBV/HCV	134	5	12	-
Chen (58)	2013	2009	China	HSV-2	2453	-	-	1347
Praseeda (59)	2013	2007	India	HBV/HCV	250	19	7	-
Kotaki (60)	2013	2012	Indonesia	HBV/HCV	200	8	1	-
Johnston (61)	2013	2010	Republic of Mauritius	HBV/HCV	295	0	140	-
Hakre (62)	2013	2009-2011	Panama	HBV/HCV/	999	6	2	741

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				HSV-2				
Sarna (63)	2013	2010	India	HSV-2	529	-	-	321
Prestileo (64)	2013	1999-2008	Italy	HBV/HCV	239	7	4	-
Mollik (65)	2013	NR	Bangladesh	HBV	196	18		
Ghosh (66)	2012	NR	India	HBV/HSV-2	45	0	-	13
Zermiani (67)	2012	1999-2007	Italy	HBV/HCV	345	12	3	-
Navadeh (68)	2012	2010	Iran	HSV-2	139	-	-	28
Wong (69)	2012	2005-2007	Hong Kong	HBV	503	43	-	-
Dunford (70)	2012	2008-2009	Vietnam	HBV	1000	99	-	-
Wang (71)	2012	2009	China	HSV-2	345	-	-	201
Dunford (72)	2012	2008-2009	Vietnam	HCV	1000	-	87	-
Cárcamo (73)	2012	2002-2003	Peru	HSV-2	4485	-	-	2718
Barua (74)	2012	2006	India	HCV	426	-	41	-
Delgado (75)	2011	2009	Nicaragua	HSV-2	825	-	-	641
Qyra (76)	2011	2008	Albania	HBV	92	7	-	-
Yang (77)	2011	2008	China	HSV-2	793	-	-	375
Kassak (78)	2011	2007-2008	Lebanon	HBV/HCV	103	0	0	-
Hemalatha (79)	2011	2005-2006	India	HSV-2	322	-	-	225
Kassaian (80)	2011	2009-2010	Iran	HBV/HCV	91	1	9	-
Braunstein (81)	2011	NR	Rwanda	HSV-2	800	-	-	478
Znazen (82)	2010	2007	Tunisia	HBV/HCV/ HSV-2	183	1	2	105
Todd (83)	2010	2006-2008	Afghanistan	HBV/HCV	520	34	10	-
Zermiani (84)	2010	1999-2008	Italy	HBV/HCV	395	12	3	-
Shethwala (85)	2009	2005-2006	India	HBV	300	10	-	-
Wang (86)	2009	2006	China	HSV-2	737	-	-	502
Cavlek (87)	2009	2003-2006	Croatia	HCV	272	-	11	-
Shahmanesh (88)	2009	2004-2005	India	HSV-2	326	-	-	182
Bautista (89)	2009	2000-2002	Argentina	HCV	625	-	26	-
Uusküla (90)	2008	2005-2006	Estonia	HCV	191	-	15	-
Yun (91)	2008	2003	South Korea	HSV-2	188	-	-	162
Ngo (92)	2008	2004	China	HCV/ HSV-2	310	-	24	140
Xu (93)	2008	2006	China	HSV-2	96			68
Forbi (94)	2008	2006-2007	Nigeria	HBV	720	123	-	-
Linhart (95)	2008	NR	Israel	HSV-2	300	-	-	180
Wang (13)	2008	2006	China	HSV-2	737	-	-	502
Taylor (96)	2008	1999	Scotland	HCV	98	-	63	-
Gul (97)	2008	2005	Turkey	HBV/HCV/ HSV-2	130	4	1	8 (IgM), 104 (IgG)
Barua (98)	2008	NR	India	HCV	426	-	41	-
Monsalve-Castillo (99)	2007	2004-2005	Venezuela	HCV	47	-	0	-
Passos (100)	2007	NR	Brazil	HBV	449	3	-	-
Vandepitte (101)	2007	2002	Republic of Congo	HSV-2	501	-	-	293
Davies (102)	2007	1999-2000	Indonesia	HSV-2	165			149
Papadogeorgaki	2006	2005	Greece	HBV/HCV/	299	4	7	208

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(103)				HSV-2				
Theng (104)	2006	2003-2004	Singapore	HSV-2	300	-	-	237
Pando (105)	2006	2000-2002	Argentina	HCV	602	-	26	-
Nigro (106)	2006	2001-2002	Italy	HBV/HCV	118	2	0	-
Dolar (107)	2006	NR	Turkey	HSV-2	483	-	-	290
Kweon (108)	2006	2004	South Korea	HBV/HCV	1527	102	21	-
Fox (109)	2006	1985-2000	UK	HSV-2	453	-	-	272
Cwikel (110)	2006	NR	Israel	HBV/HCV	43	3	4	-
O'Farrell (111)	2006	2002-2003	Vietnam	HSV-2	904	-	-	251
Didelot-Rousseau (112)	2006	2003-2004	Burkina Faso	HSV-2	379	-	-	264
Inciardi (113)	2006	2001-2003	USA	HCV	533	-	158	-
Chen (114)	2005	1999-2000	China	HSV-2	505	-	-	327
del Amo (115)	2005	2002	Spain	HBV/HCV	734	2	1	-
Nigam (116)	2005	NR	India	HBV	60	5	-	-
Nessa (117)	2004	2002	Bangladesh	HSV-2	400	-	-	138
Belza (118)	2004	1999-2000	Spain	HCV	579	-	5	-
Taketa (119)	2003	1996	Thailand	HBV/HCV	100	11	2	-
Uribe-Salas (120)	2003	1998	Mexico	HSV-2	468	-	-	401
Miyazaki (121)	2003	1999-2001	Japan	HBV/HCV	171	0	2	-
Qutub (122)	2003	NR	Bangladesh	HSV-2	463	-	-	438
Valdivia (123)	2003	NR	Peru	HCV	98	-	0	-
Risbud (124)	2003	1994-1999	India	HCV	933	-	13	-
Huo (125)	2003	2001-2002	Taiwan	HBV/HCV	1045	126	86	-
Camejo (126)	2003	1999	Venezuela	HBV/HCV	212	8	1	-
Bystrická (127)	2003	NR	Slovakia	HBV/HCV/ HSV-2	18	4	0	9
Uribe-Salas (128)	2002	1998	Mexico	HBV	461	6	-	-
Miyazaki (129)	2002	1999-2000	Japan	HBV/HCV	135	0	1	-
Othman (130)	2002	NR	Syria	HBV/HCV	102	11	2	-
Laurent (131)	2001	1988	Republic of Congo	HCV	1144	-	76	-
Ishi (132)	2001	NR	Japan	HBV/HCV	308	2	10	-
Rahman (133)	2000	1998	Bangladesh	HSV-2	203	-	-	127
Limpakarnjanarat(134)	1999	1991-1994	Thailand	HSV-2	500	-	-	378
Ghebrekidan (135)	1999	1995	Eritrea	HSV-2	107	-	-	86
Conde-Glez (136)	1999	1992	Mexico	HSV-2	997	-	-	606
Suganuma (137)	1998	1996	Thailand	HCV	100	-	2	-
Juárez-Figueroa (138)	1998	1992	Mexico	HBV	1498	3	-	-
Dada (139)	1998	1990-1991	Nigeria	HSV-2	796			470
Ghebrekidan (140)	1998	1995	Eritrea	HBV/HCV	107	3	3	-
McDonnell (141)	1998	1991-1997	Ireland	HBV/HCV	99 (for HCV),	6	8	-

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					124 (for HBV)			
Uribe-Salas (142)	1997	1992	Mexico	HBV/HSV-2	778 (for HBV), 757 (For HSV-2)	3	-	493
Tsakris (143)	1997	NR	Greece	HBV	230	8	-	-
Luksamijarulkul (144)	1997	1995	Thailand	HCV	200	-	19	-
Mesquita (145)	1997	1986-1990	Brazil	HBV/HCV	686	34	105	-
Sattar (146)	1996	NR	Bangladesh	HBV	164	16	-	-
Nakashima (147)	1996	1989-1992	Japan	HCV	604	-	61	-
Weber (148)	1995	1991-1993	Germany	HCV	364	-	5	-
Watts (149)	1994	1990	Somalia	HCV	236	-	4	-
Gotuzzo (150)	1994	1991-1992	Peru	HSV-2	399	-	-	328
Develouxl (151)	1994	1990	Niger	HCV	250	-	19	-
Wu (152)	1993	1988-1990	Taiwan	HCV	622	-	74	-
Ndumbe (153)	1993	1990-1992	Cameroon	HCV	104	-	16	-
Echevarria (154)	1993	1990	Spain	HCV	121	-	15	-
Tuncel (155)	1992	NR	Turkey	HBV	101	9	-	-
Orduna (156)	1992	NR	Spain	HBV/HCV	227	14	20	-
Gutierrez (157)	1992	NR	Spain	HCV	227	-	20	-
Wu (158)	1991	NR	Taiwan	HCV	223	-	23	-
Lee (159)	1991	1988-1999	Taiwan	HBV/HCV	196	42	14	-
Ramachandran (160)	1990	1988	Malaysia	HBV	98	6	-	-
Mak (161)	1990	1988-1989	Belgium	HBV/HCV	123	0	3	-
Hyams (162)	1990	1988	Mexico	HBV	354	3	-	-
Caballero (163)	1987	NR	Spain	HBV	80	8	-	-
Jama (164)	1987	1985-1986	Somalia	HBV	85	17	-	-
Goh (165)	1985	1982	Singapore	HBV	239	15	-	-
de Hoop (166)	1984	1982	Netherlands	HBV	128	3	-	-
Kaklamani (167)	1980	1978-1979	Greece	HBV	198	22	-	-
Frosner (168)	1975	1973	Germany	HBV	258	6	-	-

NR: Not reported; HBV: Hepatitis B virus; HCV: Hepatitis C virus; HSV-2: Herpes simplex virus 2.

Studies that met any one of the following criteria were excluded: (1) studies investigating the incidence of STIs among female sex workers; (2) publications about the incidence and the prevalence of STIs among trans-genders, male sex workers, men who have sex with men, lesbians, clients of female sex workers (3) studies evaluating the prevalence of occult hepatitis B (OBI) among female sex workers. (4) Case reports, posters, review articles, and conference abstracts; (5) publications in languages other than English with non-English abstracts.

Data extraction and quality assessment: Two authors independently extracted data from eligible studies onto a pre-designed data extraction form using Microsoft Excel 2013 (Microsoft Corporation, Redmond, Washington, USA), and any disagreements were resolved by a third author.

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Table 2. Subgroup analysis of the prevalence of HBsAg in female sex workers

Characteristics	Categories	No. of Studies	Pooled prevalence (%) (95% CI)	Heterogeneity test I^2 %, *p*-value	Differences between subgroups; χ^2 test (*p*-value)
Overall		67	3.76 (2.99-4.72)	93.2%, *P*<0.01	
Detection method	ELISA	49	3.39 (2.62-4.38)	92.7%, *P*<0.01	***P*<0.01†**
	Latex agglutination	1	8.33 (3.51-18.51)	NA, NA	
	Passive agglutination	2	0.3 (0.05-2.28)	0%, *P*= 0.91	
	Passive hemagglutination	2	3.16 (1.86-5.33)	3.9%, *P*= 0.31	
	Radioimmunoassay	7	9.93 (5.97-16.07)	84.8%, *P*<0.01	
	Rapid Test	3	1.89 (0.4-7.27)	97.8%, *P*<0.01	
Study location	Afghanistan	1	6.54 (4.71-9.01)	NA, NA	***P*<0.01†**
	Albania	1	7.61 (3.67-15.11)	NA, NA	
	Bangladesh	2	9.45 (6.83-12.93)	0%, *P*= 0.85	
	Belgium	1	0.40 (0.03-6.11)	NA, NA	
	Brazil	6	1.57 (0.53-4.57)	93.7%, *P*<0.01	
	China	1	12.33 (9.93-15.21)	NA, NA	
	Eritrea	1	2.80 (0.91-8.33)	NA, NA	
	Ethiopia	1	5.96 (3.83-9.15)	NA, NA	
	Germany	1	2.33 (1.05-5.08)	NA, NA	
	Greece	3	4.01 (1.16-12.96)	90.3%, *P*<0.01	
	Hong Kong	1	8.55 (6.40-11.33)	NA, NA	
	India	5	4.20 (2.10-8.21)	84.9%, *P*<0.01	
	Indonesia	1	4.00 (2.01-7.79)	NA, NA	
	Iran	2	1.19 (0.39-3.63)	0%, *P*= 0.92	
	Ireland	1	4.84 (2.19-10.35)	NA, NA	
	Israel	1	6.98 (2.27-19.51)	NA, NA	
	Italy	4	3.06 (2.18-4.27)	0%, *P*= 0.82	
	Japan	3	0.52 (0.17-1.59)	0%, *P*= 0.85	
	Lebanon	1	0.48 (0.03-7.21)	NA, NA	
	Libya	1	2.90 (0.73-10.86)	NA, NA	
	Malaysia	1	6.12 (2.78-12.96)	NA, NA	
	Mexico	4	0.57 (0.24-1.33)	63.1%, *P*= 0.04	
	Moldova	1	9.12 (7.14-11.57)	NA, NA	
	Netherlands	1	2.34 (0.76-7.01)	NA, NA	
	Nigeria	1	17.08 (14.51-20.01)	NA, NA	
	Panama	1	0.60 (0.27-1.33)	NA, NA	
	Republic of Congo	1	4.22 (3.03-5.85)	NA, NA	
	Republic of Mauritius	1	0.17 (0.01-2.64)	NA, NA	
	Rwanda	2	2.92 (2.32-3.66)	52.0%, *P*= 0.15	
	Singapore	1	6.28 (3.82-10.15)	NA, NA	
	Slovakia	1	22.22 (8.60-46.47)	NA, NA	
	Somalia	1	20.00 (12.81-29.84)	NA, NA	
	South Korea	1	6.68 (5.53-8.05)	NA, NA	
	Spain	3	3.05 (0.67-12.83)	90.0%, *P*<0.01	
	Syria	1	10.78 (6.07-18.43)	NA, NA	
	Taiwan	2	15.99 (8.85-27.18)	91.7%, *P*<0.01	
	Thailand	1	11.00 (6.20-18.78)	NA, NA	

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	Tunisia	1	0.55 (0.08-3.77)	NA, NA	
	Turkey	2	5.59 (1.94-15.05)	70.0%, *P*= 0.07	
	Venezuela	1	3.77 (1.90-7.36)	NA, NA	
	Vietnam	1	9.90 (8.20-11.91)	NA, NA	

NA: Not applicable; ELISA: Enzyme-Linked Immunosorbent Assay. † Statistically significant

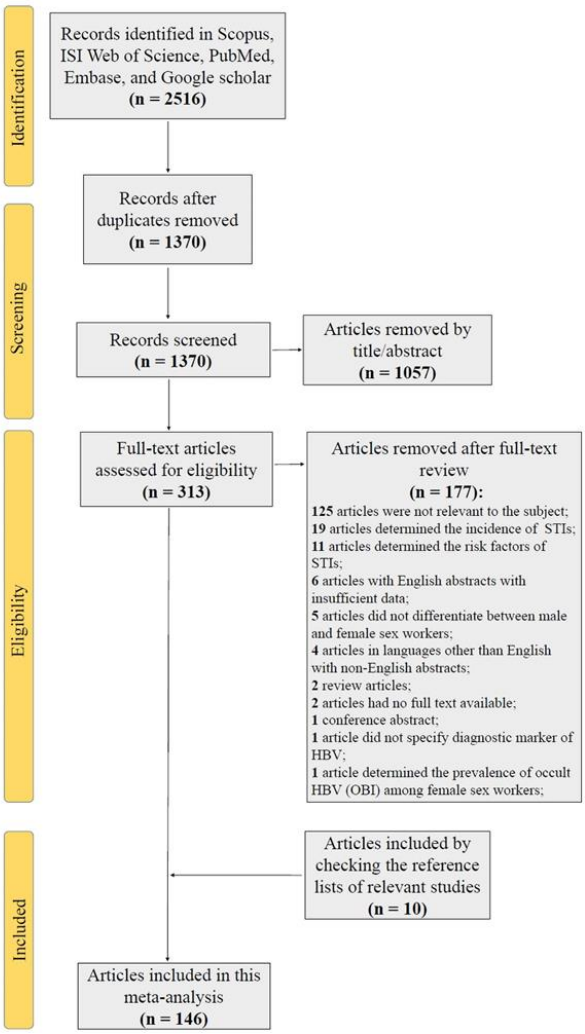

Fig. 1. Flowchart presenting the steps of literature search and selection

The following characters were extracted from each eligible study: the first author's last name, publication date, study date, study location, total sample size, type of sample, number of HBV, HCV, and HSV-2 -positive cases, diagnostic methods, and diagnostic indexes (for HSV-2).

A quality assessment of the retrieved studies was conducted using a modified checklist based on the guidelines of the strengthening the reporting of observational studies in epidemiology (STROBE). The checklist was comprised of 12 questions covering different methodological perspectives. Studies were deemed eligible for the main meta-analysis if they achieved a validity score of at least 8 out of a maximum of 12. Data extraction was undertaken independently by two authors, and any discrepancies at this stage were resolved by discussion and consultation with a third author.

Statistical analysis: To estimate the pooled prevalence for each STI among female sex workers, a DerSimonian-Laird random-effects meta-analysis using the inverse variance method was conducted (21). The logit transformation was applied to stabilize the variance and normalize their distribution, and the Clopper-Pearson method was applied to calculate the 95% exact confidence intervals (CIs) for proportions (22). To identify the possible sources of heterogeneity, subgroup analyses were performed, based on the diagnostic method, study location, and diagnostic indexes. A time-trend graph was produced using GraphPad Prism 7.1 for Windows (GraphPad Software, La Jolla California USA). To measure the heterogeneity among the included publications, I-square statistics (I^2) was carried out, in which the result is presented as a percentage. I^2 values of 25%, 50%, and 75% are indicative of low, moderate, and high levels of heterogeneity, respectively (23). All analyses were implemented in the R package Meta (24) (version 3.5.3 [2019-03-11], R Foundation for Statistical Computing, Vienna, Austria), and for all statistical tests, *P* values of less than 0.05 were considered statistically significant.

Results

Literature search: In the initial search, 2516 articles were identified from five electronic international databases. A total of 1146 duplicates was excluded, and then 1370 articles

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were screened by title and abstract, which led to the elimination of 1057 articles.

The remaining 313 articles were checked for agreement with the inclusion and exclusion criteria by the full-text review.

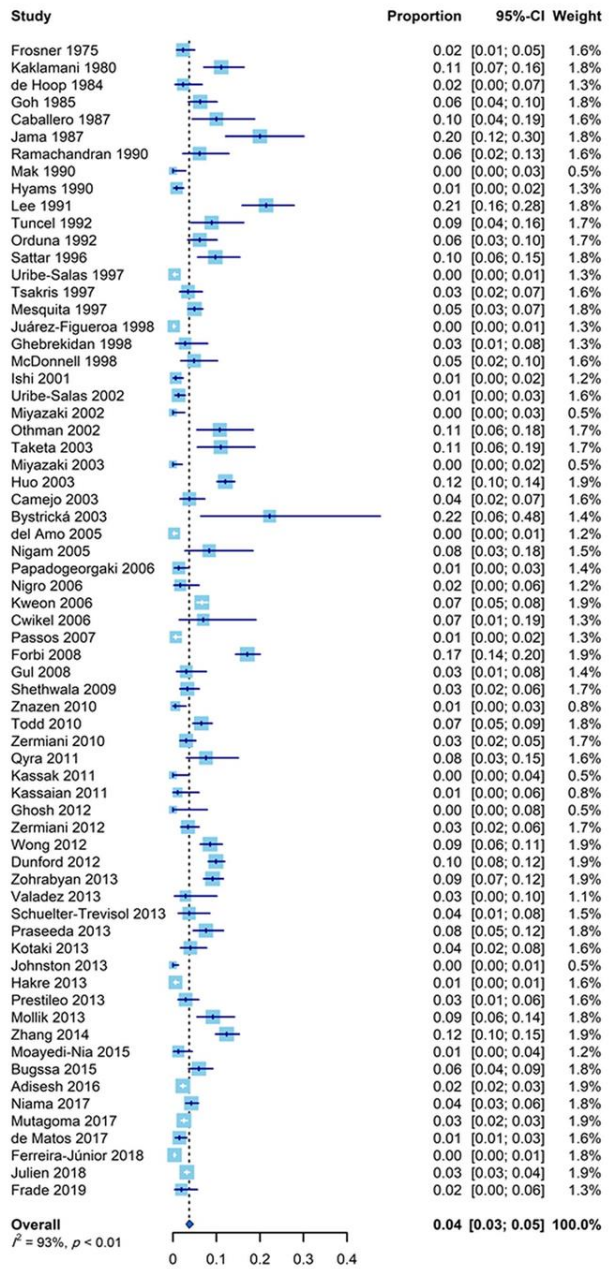

Fig. 2. Forest plot of the prevalence of HBsAg among female sex workers.

After the full-text screening, 177 articles were excluded due to the following: 1) articles which were not relevant to the subject (n = 125), 2) articles which were determined the incidence of STIs (n = 19), 3) articles which were determined the risk factors of STIs (n = 11), 4) articles with English abstracts with insufficient data (n = 6), 5) articles which did not differentiate between male and female sex workers (n=5), 6) articles in languages other than English with non-English abstracts (n=4), 7) review articles (n=2), 8) articles which had no full-text available (n=2), 9) conference abstract (n=1), 10) article which did not specify diagnostic marker of HBV (n=1), and 11) article which was determined the prevalence of occult HBV (OBI) among female sex workers.

Also, 10 relevant articles were found and included by a manual search of the reference lists of the identified articles. Based on the modified STROBE checklist, all papers were deemed to have good quality (obtained scores of 8 and above), and none of the papers was failed to reach score of 8. Finally, 146 articles were included in this systematic review and meta-analysis. Fig. 1 represents the process of literature retrieval and screening using a flow chart.

Study characteristics: The characteristics of eligible studies in this systematic review and meta-analysis are summarized in Table 1. One hundred forty-six studies with a total of 917816 female sex workers were included in this meta-analysis. The studies' publication dates ranged from 1975 to 2019, and they examined the population of 55 countries. The largest study included 759783 and the smallest included 18 female sex workers. Out of 146 studies included, 67 studies assessed HBsAg (in 34048 participants), 77 studies assessed anti-HCV antibodies (in 879725 participants), and 51 studies assessed anti-HSV-2 antibodies (in 34230 participants).

Most studies investigating the prevalence of HBsAg, anti-HCV antibody, and anti-HSV-2 antibodies were from Brazil (n=6), China (n=8), and China (n=14), respectively.

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Table 3. Subgroup analysis of the prevalence of HCV infection in female sex workers

Characteristics	Categories	No. of Studies	Pooled prevalence (%) (95% CI)	Heterogeneity test I^2 %, *p*-value	Differences between subgroups; χ^2 test (*p*-value)
Overall		77	3.39 (2.30-4.97)	99.5%, *P*<0.0001	
Detection method	CLEIA	2	1.00 (0.32-3.07)	0%, *P*=0.71	*P*=0.19
	ELISA	68	3.69 (2.53-5.36)	99.3%, *P*<0.0001	
	Passive hemagglutination	2	2.71 (0.13-36.54)	89.4%, *P*<0.01	
	Rapid Test	4	2.65 (0.37-16.52)	99.5%, *P*<0.01	
Sample type	Blood	76	3.22 (2.19-4.71)	99.5%, *P*<0.0001	***P*<0.01†**
	Saliva	1	64.29 (54.35-73.13)	NA, NA	
Study location	Afghanistan	1	1.92 (1.04-3.54)	NA, NA	***P*<0.01†**
	Argentina	2	4.24 (3.24-5.52)	0%, *P*=0.89	
	Belgium	1	2.44 (0.79-7.29)	NA, NA	
	Brazil	5	2.34 (0.45-11.33)	98.5%, *P*<0.01	
	Cameroon	1	15.38 (9.64-23.65)	NA, NA	
	China	8	1.91 (1.33-2.72)	98.3%, *P*<0.01	
	Croatia	1	4.04 (2.25-7.15)	NA, NA	
	Eritrea	1	2.80 (0.91-8.33)	NA, NA	
	Estonia	1	7.85 (4.79-12.62)	NA, NA	
	Germany	1	1.37 (0.57-3.62)	NA, NA	
	Greece	1	2.34 (1.12-4.83)	NA, NA	
	India	5	3.88 (1.67-8.76)	96.1%, *P*<0.01	
	Indonesia	1	0.50 (0.07-3.46)	NA, NA	
	Iran	2	8.77 (5.84-12.96)	0%, *P*=0.62	
	Ireland	1	8.08 (4.09-15.33)	NA, NA	
	Israel	1	9.30 (3.54-22.30)	NA, NA	
	Italy	4	1.04 (0.57-1.89)	0%, *P*=0.63	
	Japan	4	2.96 (0.95-8.84)	88.5%, *P*<0.01	
	Lebanon	1	0.48 (0.03-7.21)	NA, NA	
	Libya	1	7.25 (3.05-16.26)	NA, NA	
	Moldova	1	22.64 (19.61-26.00)	NA, NA	
	Myanmar	1	4.67 (2.24-9.46)	NA, NA	
	Niger	1	7.60 (4.90-11.61)	NA, NA	
	Panama	1	0.20 (0.05-0.80)	NA, NA	
	Peru	1	0.51 (0.03-7.56)	NA, NA	
	Republic of Congo	2	2.34 (0.26-17.80)	96.4%, *P*<0.01	
	Republic of Mauritius	1	47.46 (41.82-53.16)	NA, NA	
	Rwanda	2	2.57 (0.82-7.79)	97.0%, *P*<0.01	
	Scotland	1	64.29 (54.35-73.13)	NA, NA	
	Slovakia	1	2.63 (0.16-30.96)	NA, NA	
	Somalia	1	1.69 (0.64-4.43)	NA, NA	
	South Korea	1	1.38 (0.90-2.10)	NA, NA	
	Spain	5	3.70 (1.41-9.35)	91.4%, *P*<0.01	
	Syria	1	1.96 (0.49-7.50)	NA, NA	
	Taiwan	4	9.49 (7.50-11.95)	60.0%, *P*=0.06	
	Thailand	3	3.89 (1.11-12.79)	76.6%, *P*=0.01	

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	Tunisia	1	1.09 (0.27-4.26)	NA, NA	
	Turkey	1	0.77 (0.11-5.25)	NA, NA	
	Ukraine	1	17.50 (16.45-18.60)	NA, NA	
	USA	1	29.64 (25.92-33.66)	NA, NA	
	Venezuela	2	0.61 (0.12-2.99)	0%, *P*=0.65	
	Vietnam	1	8.70 (7.10-10.61)	NA, NA	

CLEIA: Chemiluminescence enzyme immunoassay; ELISA: Enzyme-Linked Immunosorbent Assay; NA: Not applicable.
† Statistically significant

Table 4. Subgroup analysis of the seroprevalence of HSV-2 in female sex workers

Characteristics	Categories	No. of Studies	Pooled prevalence (%) (95% CI)	Heterogeneity test I^2 %, *p*-value	Differences between subgroups; χ^2 test (*p*-value)
Overall		51	60.48 (55.43-56.31)	98.6%, *P*<0.0001	
Detection method	ELISA	43	57.47 (51.71-63.03)	98.7%, *P*<0.0001	***P*=0.02†**
	Immunoelectrotransference	1	65.13 (61.66-68.44)	NA, NA	
	Rapid Test	2	72.54 (41.06-90.92)	97.9%, *P*<0.01	
	Western blotting	4	77.13 (63.82-86.58)	97.6%, *P*<0.01	
Detection index	IgM antibody	5	10.31 (3.88-24.66)	96.7%, *P*<0.01	***P*<0.01†**
	IgG antibody	47	64.84 (60.73-68.75)	98.1%, *P*<0.0001	
Study location	Bangladesh	3	71.19 (29.00-93.73)	99.2%, *P*<0.01	***P*<0.01†**
	Burkina Faso	1	69.66 (64.84-74.08)	NA, NA	
	China	14	53.10 (45.54-60.51)	98.3%, *P*<0.01	
	Eritrea	1	80.37 (71.76-86.84)	NA, NA	
	Greece	1	69.57 (64.11-74.52)	NA, NA	
	Guinea	1	84.08 (78.35-88.51)	NA, NA	
	India	5	35.84 (9.82-74.13)	99.6%, *P*<0.01	
	Indonesia	1	90.30 (84.76-93.97)	NA, NA	
	Iran	2	14.12 (6.66-27.48)	88.2%, *P*<0.01	
	Israel	1	60.00 (54.35-65.40)	NA, NA	
	Kenya	1	84.34 (80.81-87.33)	NA, NA	
	Mexico	3	71.90 (57.67-82.78)	97.6%, *P*<0.01	
	Nicaragua	1	77.70 (74.73-80.41)	NA, NA	
	Nigeria	1	59.05 (55.59-62.41)	NA, NA	
	Panama	1	74.17 (71.37-76.79)	NA, NA	
	Peru	2	72.57 (47.39-88.60)	98.5%, *P*<0.01	
	Republic of Congo	1	58.48 (54.11-62.72)	NA, NA	
	Rwanda	1	59.75 (56.31-63.10)	NA, NA	
	Singapore	1	79.00 (74.02-83.24)	NA, NA	
	Slovakia	1	50.00 (28.42-71.58)	NA, NA	
	South Korea	1	86.17 (80.46-90.41)	NA, NA	
	Tanzania	1	57.54 (55.31-59.74)	NA, NA	
	Thailand	1	75.60 (71.64-79.17)	NA, NA	
	Tunisia	1	57.38 (50.11-64.34)	NA, NA	
	Turkey	2	74.99 (42.70-92.34)	96.4%, *P*<0.01	
	UK	1	60.04 (55.46-64.46)	NA, NA	
	Vietnam	1	27.77 (24.94-30.78)	NA, NA	

ELISA: Enzyme-Linked Immunosorbent Assay; NA: Not applicable; † Statistically significant.

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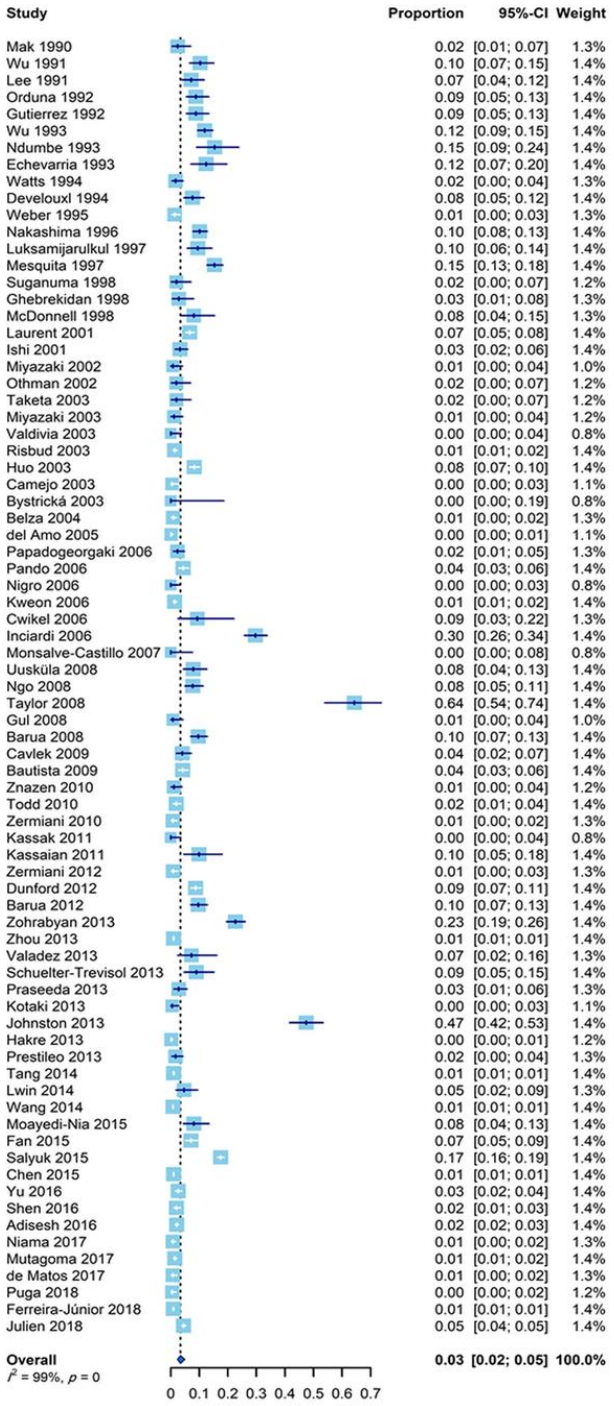

Fig. 3. Forest plot of the prevalence of HCV infection among female sex workers.

Prevalence of HBsAg marker among female sex workers: The pooled prevalence of HBsAg was determined amongst 34048 female sex workers from 41 countries in the world. The overall prevalence of HBsAg was 3.76% (95% CI: 2.99%–4.72%), and the details are presented in a forest plot (Fig. 2). However, there was significant heterogeneity between the studies (I^2 = 93.2%, P< 0.01), and the studies met the random-effects model. Table 2 shows subgroup analyses of the prevalence of HBsAg in female sex workers stratified by detection method and study location. Subgroup analysis according to study location showed that the lowest pooled prevalence of HBsAg was seen in the Republic of Mauritius (0.17%; 95% CI: 0.01%-2.64%), while the highest pooled prevalence was found in Slovakia (22.22%; 95% CI: 8.60%-46.47%).

The majority of studies on the prevalence of HBsAg in female sex workers was conducted in Brazil (6 studies), followed by India (5 studies), Italy (4 studies), and Mexico (4 studies). According to the subgroup analysis results for detection method, the pooled prevalence of HBsAg was higher using the radioimmunoassay (9.93%; 95% CI: 5.97%-16.07%) than using the latex agglutination (8.33%; 95% CI: 3.51%-18.51%), ELISA (3.39%; 95% CI: 2.62%-4.38%), passive hem-agglutination (3.16%; 95% CI: 1.86%-5.33%), and Rapid Test (1.89%; 95% CI: 0.4%-7.27%), and the differences were statis-tically significant (P<0.01). In all studies, blood samples were used to evaluate the presence of HBsAg, and thus, there is no subgroup analysis of sample type.

Prevalence of HCV infection among female sex workers: The pooled prevalence of HCV infection was calculated amongst 879725 female sex workers from 42 countries across the world. The overall prevalence of HCV infection was 3.39% (95% CI: 2.30%–4.97%), and outputs of meta-analyses are depicted in a forest plot (Fig. 3). However, a high degree of heterogeneity existed among the included studies (I^2 = 99.5%, P<0.0001), and therefore, the studies met the random-effects model. Table 3 presents subgroup analyses of the prevalence of HCV infection among female sex workers stratified by detection method, sample type, and study location.

In the subgroup analysis according to study location, the highest prevalence was observed in Scotland (64.29%; 95% CI: 54.35%-73.13%), whereas the lowest prevalence was found in Panama (0.20%; 95% CI: 0.05%-0.80%).

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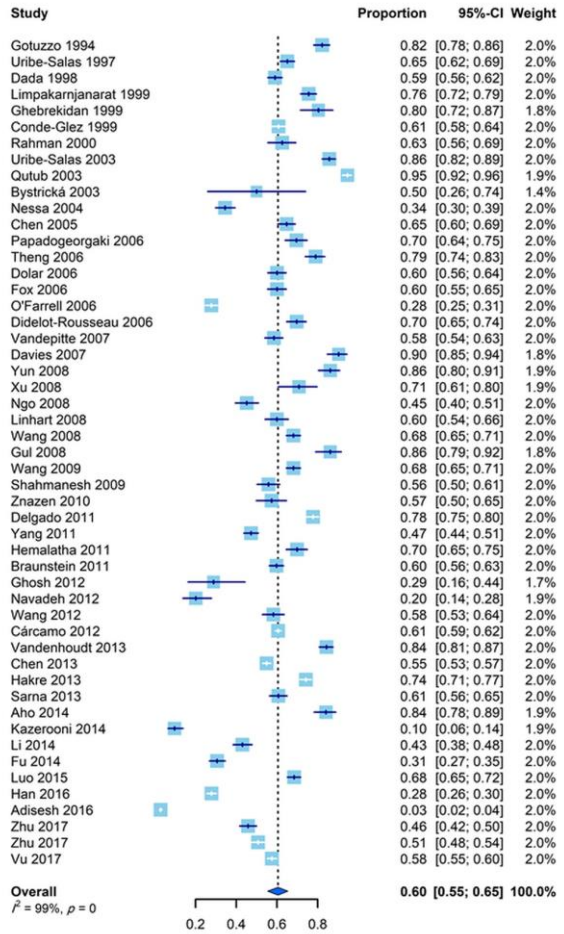

Fig. 4. Forest plot of the seroprevalence of HSV-2 among female sex workers.

Most of the studies investigating the prevalence of HCV infection among female sex workers were performed in China (8 studies), followed by Brazil (5 studies), India (5 studies), and Spain (5 studies). Based on the subgroup analysis results for detection method, more HCV positive cases were detected by ELISA (3.69%; 95% CI: 2.53%-5.36%) than passive hemagglutination (2.71%; 95% CI: 0.13%-36.54%), Rapid Test (2.65%; 95% CI: 0.37%-16.52%), chemiluminescence enzyme immunoassay (CLEIA) (1.00%; 95% CI: 0.32%-3.07%). However, the differences were not statistically significant (P=0.19).

Furthermore, our subgroup analysis of sample type revealed that the prevalence of HCV infection was higher using the saliva samples (64.29%; 95% CI: 54.35%-73.13%) compared to the blood samples (3.22%; 95% CI: 2.19%-4.71%), and the difference was statistically significant (P<0.01).

Prevalence of HSV-2 infection among female sex workers: A random-effects meta-analysis was performed to estimate the pooled seroprevalence of HSV-2 in 34230 female sex workers from 27 countries throughout the world. The pooled seroprevalence of HSV-2 was 60.48% (95% CI: 55.43%–65.31%). Totally, 47 studies (in 31236 participants) were conducted on the seroprevalence of IgG antibody, and 5 studies (in 3124 participants) were assessed the seroprevalence of IgM antibody. The overall prevalence of HSV-2 IgG and IgM antibodies worldwide was 64.84% (95% CI: 60.73%–68.75%) and 10.31% (95% CI: 3.88%–24.66%), respectively, and the results of the meta-analysis are visually illustrated in a forest plot in Fig. 4. Table 4 displays subgroup analyses of the seroprevalence of HSV-2 among female sex workers, based on antibody class and study location. The seroprevalence of HSV-2 ranged from 2.84%-28.89% for IgM antibody and 27.77%-94.60% for IgG antibody.

In the subgroup analysis according to study location, the highest seroprevalence of HSV-2 was observed in Indonesia (90.30%; 95% CI: 84.76%-93.97%), whereas the lowest seroprevalence was found in Iran (14.12%; 95% CI: 6.66%-27.48%), respectively.

Time trend analysis: Time trend analysis was performed to investigate changes in the prevalence of STIs of interest over time in the world (Fig. 5). According to this analysis, the prevalence of HBsAg was the highest (11.11%; 95% CI: 7.43%-16.30%) between the years 1975 and 1979. From 2010 until 2019, the number of HBsAg-positive cases among female sex workers was decreased, and the lowest prevalence was seen between the years of 2015 and 2019 (1.58%; 95% CI: 0.69%-3.60%). Regarding HCV infection, the prevalence was high between the years of 1985 and 1994 (~8%). However, a dramatic decrease was observed during the period 1995-1999 (3.4%; 95% CI: 0.48%-20.51%), and from 2005 to 2019, a decreasing trend was observed in HCV prevalence among female sex workers.

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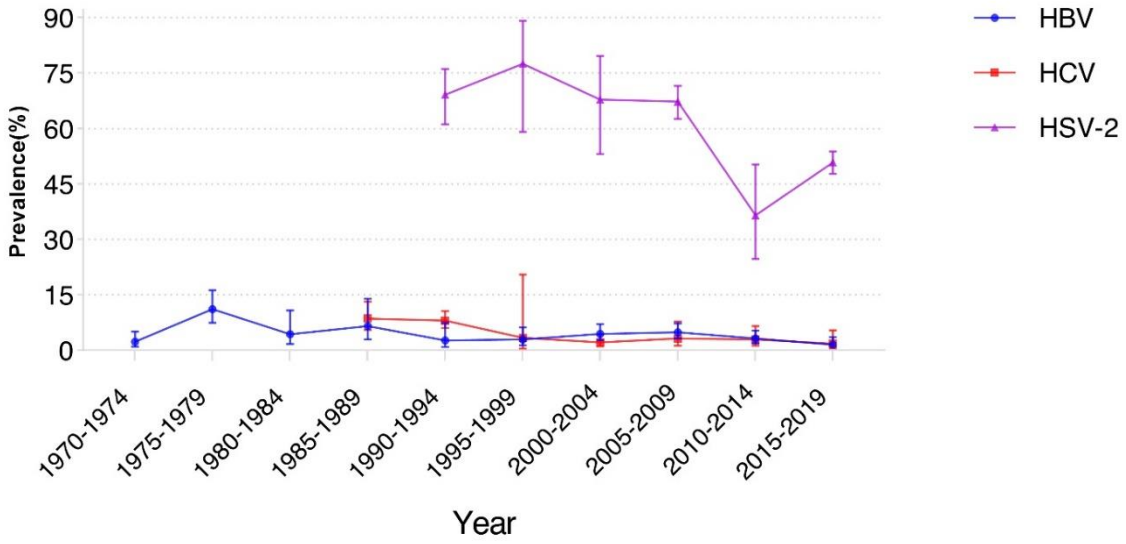

Fig. 5. Time trends in the prevalence of each STI of interest among female sex workers.

Our results have shown that similar to HBsAg, the prevalence of HCV infection was the lowest between the years of 2015 and 2019 (1.81%; 95% CI: 0.59%-5.42%).

Furthermore, we found there was no remarkable change in the seroprevalence of HSV-2 among female prostitutes during the period 1990-2009. Nonetheless, a decrease in the seroprevalence was observed between the years 2010-2014.

Discussion

Female sex workers or prostitutes are considered as one of the high-risk groups for sexually transmitted diseases and transmission of STIs and blood-borne infections like HBV and HCV. The large majority of prostitutes has been involved in unsafe sexual practice, generally owing to the lack of skills of condom use by their sexual partners. The prevalence estimates of HBsAg in female sex workers calculated in our current meta-analysis indicate that in most countries, the number of HBsAg-positive cases is significantly higher than those observed in the general population. For instance, our meta-analysis indicated that the pooled prevalences of HBsAg among Chinese and Thai female prostitutes were 12.3% and 11%, respectively, whereas according to the results of the previous meta-analysis, the estimates in the general population were 6.8% and 5.1%, respectively (169, 170).

According to the results of our meta-analysis, the highest prevalence rates of HBV infection were mainly observed among female sex workers in the Asia-Pacific and sub-Saharan Africa regions. In comparison with other countries, China (12.3%), Taiwan (16%), Thailand (11%), Hong Kong (8.5%), Malaysia (6.1%), Singapore (6.2%), Bangladesh (9.4%), Vietnam (10%) (From Asia-Pacific region), Somalia (20%) and Nigeria (17%) (From sub-Saharan Africa region) had a higher prevalence of HBV infection among female sex workers. This arises from the fact that HBV is endemic in many parts of the Asia–Pacific and sub-Saharan Africa regions (171).

Similarly, our meta-analysis also revealed the HCV infection occur at a higher rate among female sex workers than the general population. For example, according to our meta-analysis results, the pooled prevalence of HCV infection among Iranian, Chinese, and Cameroon female sex workers was 8.7%, 1.9%, and 15.3%, respectively, while the correspon-ding values in the general population calculated in

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previous meta-analyses were 0.3% (172), 0.9% (173), and 3.6% (174), respectively.

Regarding the aforementioned results, it can be confirmed that female sex workers are at increased risk of both HBV and HCV acquisition.

Some countries such as Belgium, Japan, Mexico, and Brazil, have lower prevalences of HBV and HCV infections in female sex workers compared to the other countries. The explanation for these low prevalence estimates can be attributed to some influential factors such as prostitutes' knowledge and awareness about STDs transmission and prevention modes, regular STD screening by rapid qualitative tests, using barrier methods such as condoms, and HBV vaccination of sex workers. For example, the Ministry of Health of Brazil has been developed campaigns to distribute free condoms at health centers (26).

Nevertheless, condom failure (breakage or slippage) is a common problem among female sex workers, especially those who have experienced client-perpetuated violence.

Condom breakage is estimated to be 0.8% to 40.7%, and condom slippage during sexual intercourse is estimated to be 13.1% and 19.3% (175).

The risk of STD infection among female sex workers is significantly related to the type of sex work environments. The current meta-analysis showed that the pooled prevalences of HBV and HCV infection among Japanese prostitutes are low. In Japan, the most common workplace for female sex workers is massage parlors with cell baths (121). Street-based female sex workers are more likely than indoor-based sex workers to experience poverty, poor health, and social exclusion (176). A similar situation has been reported for Mexican female sex workers so that women working at street sites had higher rates of STIs such as HSV-2 and HBV compared to women working in bars and massage parlors (142). It should be noted that due to anal tissue is more prone to tears, the practice of anal sex with female sex workers is associated with an increased risk of STIs transmission (177, 178). Since that anal sex was an infrequent practice among Japanese and Mexican female sex workers included in this meta-analysis (121, 129, 138), it might justify lower prevalences of HBV and HCV among female sex workers in these countries. Another explanation for the low prevalence of viral hepatitis in Mexican prostitutes may partly be due to the absence of injecting drug use (138). Injection drug use is an important public health concern and a major risk factor for increasing the prevalence of STIs among female prostitutes (34).

The overall pooled seroprevalence of HSV-2 was 60.5% among female sex workers, indicating a high exposure of the population to the infection. The seroprevalence of HSV-2 ranged from 14.1% in Iran to 90.3% in Indonesia. HSV-2 infection is one of the most common STIs worldwide and is a major causative agent of genital ulcers (58). The virus can infect anogenital regions and creates a potential and lifelong source of viral transmission to sexual partners (179). In previous studies, strong multiple interactions observed between HSV-2 and HIV, and also HSV-2 recognized as a risk factor for HIV infection. For example, in the meta-analysis carried out by Freeman et al., infection with HSV 2 was associated with a three times increase in the risk of acquiring HIV in the general population (180). The results presented by Schacker et al. also confirmed an increased efficiency of the sexual HIV transmission with genital herpes infection (181). Furthermore, the HSV-2 antibody status is often used as a serological marker of HIV susceptibility (58).

Hence, routine screening of HSV-2 antibody status can be used as a predictive factor of high-risk behaviors in female sex workers and will be helpful to develop efficient intervention and surveillance programs.

The present study has some limitations; (1) there were no data regarding the prevalence of HBV, HCV, and HSV-2 among female sex workers especially for countries in Northern America and Europe. We did not find any published articles for countries such as Canada, Cuba, Haiti, and El Salvador from Northern America, and France, Sweden, Norway, Poland, Romania, Portugal, Russia, and many other countries from Europe; (2) the number of studies was limited in countries such as USA,

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UK, and Germany, with only one study included; (3) In more conservative settings and Islamic countries such as Pakistan, Iran, Saudi Arabia, UAE, and Afghanistan, female sex workers have extensively remained as a hidden population. Most female sex workers in these countries do not attend public STD clinics, and therefore, estimation of the prevalence of the STIs of interest is not precise in our meta-analysis. (4) Included studies in this meta-analysis have used different diagnostic kits for measuring the prevalence of viral infections. It should be noted that the sensitivity and specificity of each kit are varied, and therefore, the difference between results can be attributed partly to this feature.

Conclusion

This meta-analysis concluded that the prevalence of STIs including HBV, HCV, and HSV-2 infections among female sex workers is considerably high, particularly in some regions, and highlights the importance of STIs screening of this high-risk, vulnerable, and neglected group to public health.
It is required for female sex workers to implement comprehensive health promotion programs, develop inexpensive, sensitive, and rapid tests, improve prevention programs such as vaccination (for HBV), and using barrier methods like condoms.

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Conflict of interest

The authors have no conflict of interest.

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