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SYSTEMATIC REVIEW AND META-ANALYSIS

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Transmission of Hepatitis B and C Virus Infection Through Body Piercing

A Systematic Review and Meta-Analysis

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Abstract: Hepatitis B and hepatitis C are 2 types of potentially life-threatening liver diseases with high infection rate. Body piercing represents a progressively popular sociocultural phenomenon which is also a potential exposure approach for hepatitis B virus (HBV) and hepatitis C virus (HCV). Conclusions from those researches with statistically risk assessment of body piercing on HBV and HCV transmission are contradictory.

Systematically analyze the association between body piercing and the risk of transmitting hepatitis B virus and hepatitis C virus for general population. Make evidence-based recommendations to the current practice and wake up public awareness of this health-threatening behavior.

Comprehensive and high sensitivity search strategies were performed to exhaustively search related studies before 15 January 2015 (MEDLINE, EMBASE, WANFANG, CNKI datasets for published literatures, and Google and Google scholars for related grey articles). Two authors identified relevant studies for the review, abstracted data, and assessed literature quality independently and critically according to the selection criteria and quality assessment standard. Odds ratio (OR) and corresponding 95% confidence interval (CI) were used to estimate risk of HBV and HCV infection in relation to body piercing status. Subgroup analysis and sensitivity analysis were conducted to examine the source of heterogeneity and test the robust of the results.

A total of 40 studies were included in this systematic review (10 for Hep-B, 26 for Hep-C, 4 for both Hep-B and Hep-C), the pooled OR (95% CI) for the association between body piercing and transmission of HBV/HCV is 1.80 (1.18, 2.75) and 1.83 (1.27, 2.64), respectively. Subgroup analysis suggested that highest risk of body piercing related to hepatitis C infection was for former soccer and veterans with OR of 4.63 (2.65, 8.10), while strongest association between body piercing and hepatitis B was for samples derived from students/community with OR of 2.40 (1.44, 4.02).

The current systematic review and meta-analysis suggests that body piercing is significantly associated with the transmission of HBV as well as HCV, having body piercing probably can increase the risk of getting infected. Evidence from this study strongly recommends that comprehensive and effective programs should be established to provide safer piercing practice.

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Abbreviations: CI = confidence interval, HBV = hepatitis B virus, HCV = hepatitis C virus, Hep-B = hepatitis B, Hep-C = hepatitis C, NOS = Newcastle-Ottawa scale, OR = odds ratio, RevMan = Review Manager, RR = risk ratio.

INTRODUCTION

Hepatitis B is a potentially life-threatening liver infection caused by the hepatitis B virus (HBV). Overall, there are estimated 2 billion people across the world with this virus, and more than 350 million are chronic carriers.[1] Infected symptoms vary between acute and chronic infection and include chronic liver disease to cirrhosis of the liver and liver cancer. In the 2010 Global Burden of Disease study, HBV infection ranked in the top health priorities and was the tenth leading cause of death (780,000 deaths each year).[2] HBV is majorly transmitted through infected blood or other body fluids so that its well-known transmission modes include vertical transmission (mother-to-child), sexual transmission, unsafe injections, and blood transfusions or dialysis.[3] Even though transmission modes have been well explored and strategies exist to protect humans from it, statistics still suggested that about half the total liver cancer mortality in 2010 was attributed to HBV infection, and from 1990 to 2010, about 30% of the

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world's population shows serological evidence of current or past HBV infection.[3]

This uncommon phenomenon indicates that far more is needed than to rely on clinical treatment, hepatitis B vaccine, and limited health regulations to prevent people getting infected with HBV and improve their prognosis. Other transmission modes should be examined in order to draw public attention and improve global health.

Hepatitis C is a blood-borne liver disease caused by hepatitis C virus (HCV), which can cause both acute and chronic infection and increase the risk of developing cirrhosis of liver and liver cancer. According to the incomplete estimation, the global prevalence of HCV infection has increased to 2.8% by 2010,[4] which indicates that three to four million persons are newly infected every year, and about 170 million people are chronically infected and at risk of developing cirrhosis of liver and liver cancer. Approximately 350,000 people die each year due to all HCV-related causes.[5] The most common modes of transmission for HCV are through unsafe injection practices, inadequate sterilization of medical equipment, and unscreened blood and blood products.[6] Without an available vaccine, strategies for controlling HCV transmission have been limited to practical issues such as serious sterilization, hand hygiene, blood screening, safe handling, and disposal of sharps and waste. Body piercing, a form of body modification, is the practice of puncturing or cutting a part of the human body, creating an opening in which jewelry can be worn.[7] Nowadays, not only the most popular type of ear piercing and nose piercing, lip, tongue, nipple, and genital piercings are all getting popular throughout the world and across all-ages.[8–11] However, the potential health risk of this beauty behavior has been gradually noticed by the public but far more than enough. When piercing, instruments can be contaminated by infected blood or body fluids from other subjects and hence, if these instruments are not properly sterilized, another source of transmission for HBV and HCV can be created. Well-identified complications for body piercing so far are mostly body-site-specific, such as local infections, keloid formation, traumatic tearing, foreign body rejection, allergic contact dermatitis.[12] No specific estimates concentrate on the percentage of persons who have experienced complications related to body piercing. There are studies supporting the hypothesis with the conclusion body piercing can be an independent risk factor for transmitting hepatitis B and C virus.[13,14] Some studies, however, argue that the correlation between body piercing and HBV and HCV are not significant,[15,16] some even obtain an outcome indicating body piercing is a protective factor.[17] Based on these inconsistence, the current systematic review and meta-analysis was conducted aiming to summarize and critically analyze related information to detect the risk of body piercing on transmission of HBV and HCV, furthermore, make evidenced recommendations to the public and health supervision departments about the future programs for preventing and controlling the infection of HBV and HCV.

OBJECTIVE

Systematically review and critically analyze related studies to detect the association between body piercing and transmission of HBV or HCV separately, furthermore, wake up public awareness of this health-threaten behavior by the evidence-based information and make recommendations to the current practice for preventing HBV and HCV infection.

METHODS

Inclusion and Exclusion Criteria

Include when

(1) Clearly identified persons with HBV/HCV as participants in one of the main groups and examined their infection status as either the primary or secondary outcome.
(2) Clearly defined body piercing as one of the exposure factors.
(3) Present risk ratio (RR) or OR and their corresponding 95% confidence interval (CI), or provided enough data for us to calculate.

Exclude when

(1) The study population is injected drug users, prisoners, blood transfusion, sex workers or others who are well identified as high risk populations.
(2) Sample size is smaller than 50.
(3) The exposure data provided are for body piercing or tattooing, without available data specific for body piercing.

Search Methods for Identification of Studies

We formulated a comprehensive, exhaustive search strategy, trying to identify all relevant studies regardless of publication status. We searched electronic worldwide databases (MEDLINE, EMBASE, WANFANG, CNKI for published literatures, and Google and Google scholars for related grey literatures). We also hand searched Chinese traditional medicine journals. Search strategies were designed based on Cochrane highly sensitive search strategies for observational studies. No language restriction was applied for English databases. Appendix shows the detailed search strategies, http://links.lww.com/MD/A525.

Data Collection and Analysis

Two authors identified relevant studies for the review, abstracted data, and assessed literature quality independently. We contacted authors of included studies to obtain further information as necessary.

Selection of Studies

Identified studies were assessed for eligibility for inclusion in the review based on scanning the titles, abstracts, and keywords of every record retrieved. The selection of studies was independently carried out by 2 authors, based on the on the criteria of inclusion and exclusion. We retrieved the full-text of any literature with unclear information in the title or abstracts. For all papers fulfilling the inclusion criteria, further assessment was carried out by reviewing full-text. At the end of the study selection, all studies selected by the 2 authors were checked and compared. For studies selected only by 1 author, their eligibility for inclusion was discussed for final decision.

Data Extraction and Management

Data extraction was independently carried out by 2 authors with a standard form predesigned for this review. The study characteristics recorded mainly focus on study design, study population, type of the risk factors or confounding adjusted for, and the risk assessment. We resolved any disagreements by referring to source papers and through further discussion. If

there was any unclear or missing information, we contacted the authors for clarifications or additional information. The study was included only after full consensus was achieved.

Dealing With Unavailable Data

If the estimation of correlation between body piercing and HBV/HCV transmission was mentioned or concluded, but the data were not available from the full text, we tried to contact the authors for original data. If these data could not be obtained, excluded the study and provided the reason behind it.

Quality Assessment of the Included Studies

Two authors independently assessed the quality of the included studies according to the Newcastle-Ottawa Scale (NOS). Any discrepancies were further discussed or resolved by a third author.

Measures of Exposure Effect

Review Manager (RevMan) Version5.3 was used to analyze data statistically. For the provided OR and 95% CI, we used the data directly but if only the original categorical data are available, 2 authors independently calculated the crude OR and 95% CI and then all of the crude ORs were combined to estimate the overall crude risk. Besides, provided adjusted OR (95%CI) were extracted to further examine the influence of controlling for confounding factors.

Assessment of Heterogeneity

We tested heterogeneity by considering the variability in participant factors among trials. We used Chi^2 test and I^2 test to test whether statistical heterogeneity exists.[18] If P of Chi^2 test is less than significance level 0.1, we consider the heterogeneity is statistically significant. For I^2 statistic, 0% to 40%: heterogeneity might not be important; 30% to 60%: may represent moderate heterogeneity; 50% to 90%: may represent substantial heterogeneity; 75% to 100%: considerable heterogeneity. If high levels of heterogeneity among the trials exist ($I^2 \geq 50\%$ or $P < 0.1$), we will analyze the study design and characteristics of the included studies.[18] Subgroup analysis and sensitivity analysis was conducted to explain the source of heterogeneity.

Assessment of Reporting Biases

Funnel plots were drawn to assess the reporting bias, if funnel plots are asymmetrical, and egger statistic shows significant P, the results will be carefully interpreted.

Assessment of Effect Size

Forest plots were drawn to assess overall OR and corresponding 95% CI. If tests of heterogeneity are not significant, we will use Mantel–Haenszel method for the fixed-effect model, if statistical heterogeneity is presented ($I^2 \geq 50\%$ or P for Chi^2 test < 0.1), we will choose the random-effects model. If heterogeneity is substantial, we will do subgroup analysis to explore the source of heterogeneity, if failed, meta-analysis will not be performed, instead, a narrative, qualitative summary will be carried out. For all analyses, we weighted the study-specific adjusted log ORs by the inverse of their variances.

Subgroup Analysis and Investigation of Heterogeneity

We carried out subgroup analyses using crude ORs to explore possible sources of heterogeneity, based on sample population source which were classified as samples thought to closely represent the general population risk (sample from community, school, health-related institution, health blood donors) or those populations with higher risk (sample comes from street youths, tattooing conventions, detentions, etc.), and level of social development (developed country, developing country, least developing country).

Sensitivity Analysis

Sensitivity analysis was performed in order to explore the source of heterogeneity in terms of quality components and risk of bias. By omitting studies that are judged to be at high risk of bias or those illustrating their sample population is less of representativeness. We will have a clearer picture about how the correlation is influenced by including studies with a great risk of bias.

RESULTS

Selection of Studies

In total, up to January 15, 2015, we identified 1079 citations related to body piercing and Hep-B and Hep-C. A total of 238 were excluded as duplicates, 622 were excluded after reviewing titles and abstracts, and 175 were excluded after reviewing the full text. Figure 1 shows the specific reasons for excluding those studies during each stage. Finally, 40 papers (10 for Hep-B,[14,15,19–26] 26 for Hep-C,[13,16,27–50] 4 for both Hep-B and Hep-C[51–54]) from 18 countries were included in this systematic review (Fig. 1).

Data Extraction

Characteristics of the 40 studies are presented in Tables 1 and 2 for Hep-B and Hep-C, respectively. Fourteen studies for Hep-B contain 33,201 participants in total and were conducted in 11 different countries, sample source can be summarized into 5 main categories: community, blood donors, tattooing conventions, children, and students. A total of 157,743 participants from 8 main sample populations (blood donors; community; hospital; adolescents; veterans; street youths; homeless and margically house persons; former soccer players) were involved in the 30 studies for Hep-C which were conducted in 17 countries.

Quality Assessment of the Included Studies

Two authors independently assessed the quality of the included studies according to the NOS for case–control study and cross-sectional study, respectively. Most of the studies have acceptable quality to do this systematic review and meta-analysis (Tables 3 and 4).

Measures of Effect Size

Body Piercing and Risk of Hepatitis B

When all crude odds ratios (CORs) from 14 studies were combined (Fig. 2), the forest plot indicate a strong association between body piercing and hepatitis B (overall OR 1.80, 95% CI: 1.18, 2.75). Result of heterogeneity test is 87% which indicate that there are significant heterogeneity between these 14 studies, Figure 3 presents the combined adjusted OR from 4 studies which indicating a stronger risk estimation of body piercing with OR 2.48 and 95% CI (1.57, 3.91). Funnel plot shows that most studies are under the funnel standard line and

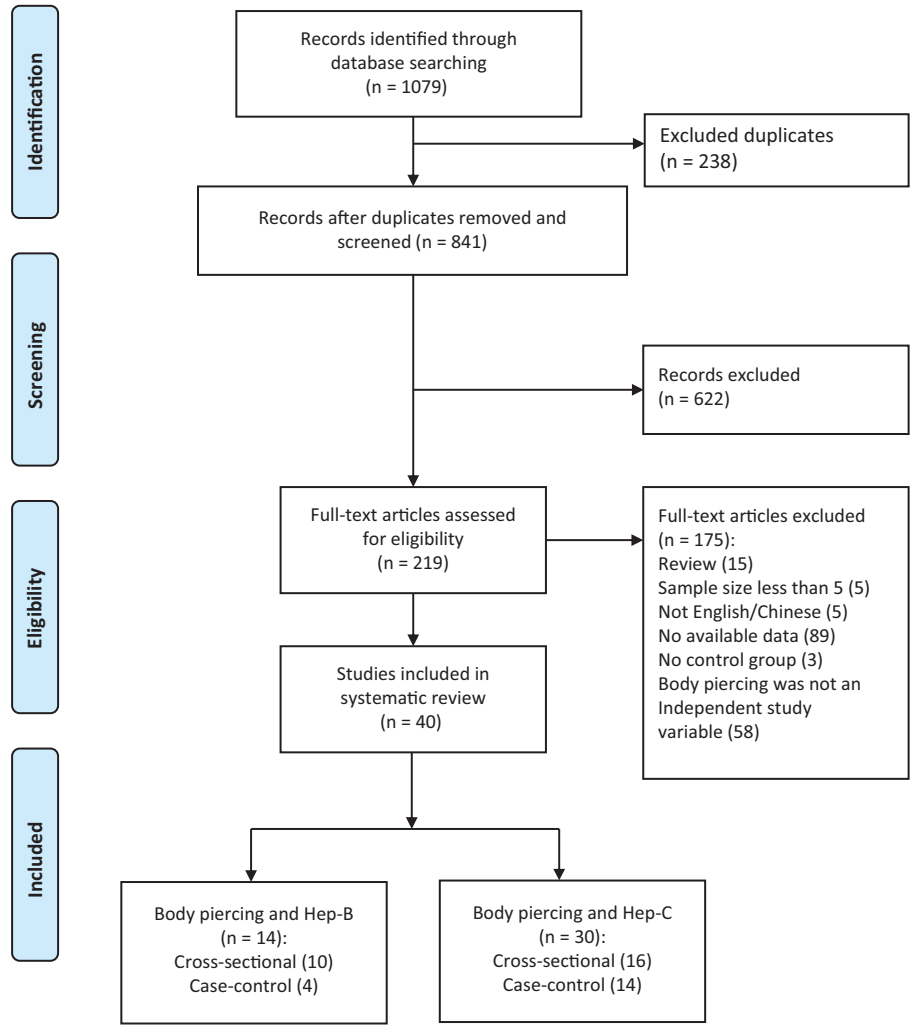

FIGURE 1. This flow chart shows the inclusion and exclusion process of potential eligible literatures.

hold good precision, Egger test ($P < 0.001$) indicating that there are significant publication bias, this may mostly due to the 3 obvious outliers (Ashraf 2010 with OR = 4.97 (2.83, 8.71), Luksamijarulkul 1995 with OR = 8.48 (1.02, 70.44), Liu Fang 2007 with OR = 8.83 (5.08, 15.35)) (Fig. 4).

Body Piercing and Risk of Hepatitis C

CORs from 30 studies were combined (Fig. 5), compared with hepatitis B, a stronger association was seen between body piercing and hepatitis C (overall OR 2.21, 95% CI: 1.60, 3.06). Heterogeneity test (I2 = 87%) indicated these 30 studies differs a lot from each other. Available adjusted OR was combined for 9 studies and the outcome presented in Figure 6 (pooled adjusted OR 1.83, 95% CI: 1.27, 2.64) indicated the significantly high risk effect of body piercing on hepatitis C. Funnel plot seems generally symmetrical besides 2 significant outliers with poor precision (Conry 1996 OR = 54.13 (3.3, 887.2), Channa 2011 OR = 17.35 (9.11, 33.01)), *P* less than 0.001 also showed there was significant publication bias (Fig. 7).

Subgroup Analysis and Investigation of Heterogeneity

Subgroup analyses were conducted based on study population source (Medical institution which includes blood donors, hospital-based population and sample from healthcare-related apartments; community/school-based population; former soccer players/veterans; homeless person/people from tattooing convention or in detention/street youths), level of social development (developed country, developing country, least developed country).

There was significantly strong difference between 3 subgroups with different study population source (Fig. 8, $I^2 = 70.4\%$, P = .03). Strong association between body piercing and hepatitis B for samples derived from School/community (OR 2.40, 95% CI: 1.44, 4.02; $P < 0.001$). No significant association was found in sample population of medical institution and street youth/people from tattooing conventions. Subgroups from different level of social development not significantly differ from each other (Fig. 9, $I^2 = 50.3\%$, $P = 0.13$).

TABLE 1. Characteristics of Included Studies for the Association Between Body Piercing and Hepatitis B

Ref No.	Study ID	Study Location	Study Design	Sample Size	Sample Source	Age (Years)	COR (95% CI)†	AOR (95% CI)
54	Roy 2001	Canada	CC	437	Street youths	Mean (range): 19.5 (14–25)	2.18 (1.13, 4.21)	1.60 (0.80, 3.20)
53	Mariano 2004	Italy	CC	10,185	Community	Range 15–55	1.34 (1.07, 1.68)	1.40 (0.90, 2.20)
19	Nuchprayoon 1992	Thailand*	CC	2626	Blood donors	Range 17–60	0.98 (0.96, 0.99)	NR
20	Akhtar 2005	Pakistan	CC	324	Blood donors	Range 18–64	0.70 (0.20, 3.10)	NR
52	Mele 1995	Italy	CC	11,274	Community	NR	2.20 (1.51, 3.22)	2.12 (1.62, 2.77)
23	Urbanus 2011	Netherlands	CC	434	Tattooing conventions/ hospital	Mean (range): 28 (23–37)	0.40 (0.16, 1.11)	NR
21	Ashraf 2010	Bangladesh	CC	1254	Community	Mean (SD): 24 (14)	4.97 (2.83, 8.71)	4.97 (2.79, 9.10)
22	Abdool 1988	Umlazi	CC	1170	Children	<14	2.93 (1.25, 6.86)	NR
15	Lucus 1999	Solomon island*	CC	598	Blood donors	Mean = 24	1.65 (0.83, 3.29)	NR
14	Luksamijarulkul 1995	Thailand*	CC	165	Children	Range 6–14	8.48 (1.02, 70.44)	NR
51	Hwang 2006	USA	CC	NR	Students	Median (range): 21 (>18)	0.74 (0.54, 1.02)	NR
24	Mahtab 2008	Bangladesh	CC	1018	Community	Any age	1.68 (0.82, 3.43)	NR
25	Liu YI 2014	China*	CC	919	Students	Mean (SD) = 18.97 (4.49)	1.89 (1.18, 3.05)	2.97 (1.72, 5.12)
26	Liu Fang 2007	China*	CC	2797	Students	Mean = 18	8.83 (5.08, 15.35)	

AOR = adjusted odds ratio; CC = case–control study; CI = confidential interval; COR = crude odds ratio; NR = not reported; OR = odds ratio; SD = standard deviation.
* Hepatitis B endemic country.

Similar subgroup analysis was done for hepatitis C (Figs. 10 and 11). Significant subgroup difference was found between studies of different study population source ($I^2 = 80.3\%$, $P < 0.01$), highest risk effect was for former soccer/veterans with OR = 4.63 (2.65, 8.10) and $P < 0.001$, followed by sample grabbed from medical institution with OR = 2.34 (1.49, 3.68) and $P < 0.001$, body piercing was also significantly risk factor for community/school sample with OR = 2.01 (1.17, 3.45). No difference was seen between studies from different level of social development (OR and 95% CI for developed country, developing country, and least developing country was 2.38 (1.77, 3.21), 2.02 (0.84, 4.90), 1.05 (0.11, 10.39) accordingly).

Sensitivity Analysis

Sensitivity analysis was performed to examine the robust of results and attempted to identify studies which responsible for the heterogeneity in all significantly meaningful subgroups. Presented in Table 5, we compared pooled OR with 95% CI and I^2 pre- and postsensitivity analysis and found that after identifying the studies that contributes to large proportion of heterogeneity (2 main standardizations for identifying these omitting studies: poor quality studies scored by quality assessment tool; the outliers discovered by funnel plot), specific reasons are provided in Table 6. After omitting them, heterogeneity test (I^2) decreased to the level that the heterogeneity can be ignored, postcombined OR was not influenced significantly by omitting these studies. Based on this, the overall effect was robust with all of these 40 studies including.

DISCUSSION

Results of this systematic review suggested an increased risk of both hepatitis B and hepatitis C among people who have body piercing. Overall, risk effect of body piercing on hepatitis B and hepatitis C are both significant with OR equals to 1.79 and 1.83, respectively (based on the smaller one of pooled crude or adjusted), this risk effect was consistent through almost all of the stratified subgroups, for hepatitis B, strongest risk of body piercing was found in students/community-based sample population, while for hepatitis C, the effect of risk among former soccer/veterans reached as large as 4.63.

Comparing with the evidence-based risk effect of tattooing on transmitting HBV, HCV, and HIV,[55,56] body piercing is a more common body art action for the purpose of wearing jewelry, the procedure can be as simple as using a needle to create a hole on any part of skin, it can be done almost anywhere so that make it impossible to regulate. The risk of this behavior is worth attention and exploring, this systematic review aimed to provide evidence for the general population and public institutes, we multinational, comprehensively and exhaustively searched in both English and Chinese datasets, till now we can conclude that people who experienced body piercing can increase their risk of getting infected with HBV and HCV.

Besides the overall conclusion, there were several studies worthy of note, these studies can be clarified into 2 types, first, studies who got nonsignificant pooled risk estimations and unexpected results which indicating protective effect of body piercing,[20,23,51] for example, OR from Felippe 2009 is 0.29, which indicating significant protective effect of body piercing which may result from the control group contain most participants from larger cities with better health services which can lead to their safer body piercing procedure.[16] Urbanus 2011 provided OR = 0.43, it also discussed the reason behind this

TABLE 2. Characteristics of Included Studies for the Association Between Body Piercing and Hepatitis C

Ref No.	Study ID	Study Location	Study Design	Sample Size	Sample Source	Age (Years)	COR (95% CI)	AOR (95% CI)
54	Roy 2001	Canada	CC	437	Street youths	Mean (range): 19.5 (14–25)	1.46 (0.69, 3.11)	NR
50	Seong 2013	South Korean*	CC	1707	Adults	Mean = 55.4	1.37 (1.09, 1.71)	1.66 (1.04,2.65)
49	Yi He 2011	China*	CC	915	Blood donors	Mean = 28	9.12 (5.24, 15.87)	7.34 (3.29, 16.33)
53	Mariano 2004	Italy	CC	7819	Community	Range 15–55	2.36 (1.68, 3.32)	2.40 (1.20, 4.80)
48	Kim 1996	South Korean*	CC	192	Blood donors and liver patients	Any age	1.50 (0.71, 3.21)	NR
47	Balasekaran 1999	New Mexico	CC	116	Hospital	Mean (SD) = 42.3	1.00 (0.45, 2.22)	NR
46	Neal 1994	UK	CC	224	Blood donors	Mean = 34.6–37.6	3.70 (1.90, 7.40)	1.40 (0.70, 2.90)
45	Conry 1996	USA	CC	273	Blood donors	Mean = 41	54.13 (3.3, 887.2)	NR
44	Lasher 2005	USA	CC	921	Community	NR	1.50 (0.40, 1.60)	NR
52	Mele 1995	Italy	CC	5242	Community	NR	2.76 (1.31, 5.82)	2.22 (1.20, 4.13)
43	Kerzman 2007	Israel	CC	178	Blood donors; former Soviet Union	Any age	2.68 (1.34, 5.37)	0.80 (0.40, 1.80)
42	Thaikruea 2004	Thailand*	CC	495	Blood donors	Mean = 29.4	2.42 (1.20, 4.89)	NR
41	Murphy 2000	USA	CC	1797	Blood donors	Any age	4.60 (3.20, 6.60)	2.00 (1.10, 3.70)
13	Channa 2011	Pakistan	CC	289	Community	Any age	17.35 (9.11, 33.01)	NR
40	C. Alvarad 2005	Brazil*	CC	97	Former soccer players	Mean = 59.2	1.98 (0.2, 18.81)	NR
39	Hermanstyne 2012	USA	CC	427	Homeless and margically house persons	Mean = 44	1.02 (0.62, 1.69)	1.12 (0.56, 2.21)
38	F. Ahmed 2012	Pakistan	CC	2000	Community	Range 18–96	0.51 (0.34, 0.75)	NR
37	Maclennan 1994	UK	CC	871	Blood donors	NR	4.51 (2.79, 7.3)	NR
36	Dominitz 2005	USA	CC	1288	Veterans	Any age	5.70 (2.90, 11.20)	1.50 (0.40, 5.10)
35	Bair 2005	USA	CC	1002	Adolescents in detention	Mean (range): 15 (10–18)	3.92 (0.52, 29.50)	NR
34	Lee 2003	TAIWAN*	CC	713	Adolescents	Range 13–16	3.60 (1.18, 10.97)	NR
33	Vickery 2009	Australia	CC	1381	Hospital	Median = 52.3	2.98 (1.30, 6.86)	NR
51	Hwang 2006	America	CC	5282	Students	Median (range): 21 (>18)	0.76 (0.36, 1.62)	NR
32	King 2009	France	CC	14,416	Health insurance system	Range 18–81	1.40 (0.70, 2.80)	NR
31	Khin 2010	Myanmar	CC	65,240	Blood donors	Mean (range): 29.5 (16–60)	0.33 (0.08, 1.31)	NR
24	Mahtab 2010	Bangladesh	CC	1018	Community	Any age	3.38 (0.08, 13.68)	NR
16	Felippe 2009	Brazil*	CC	130	Blood donors	Range 18–70	0.29 (0.11, 0.74)	NR
29	T.C.R. 2011	Brazil*	CC	97	Former soccer players	Mean = 59.2	1.98 (0.20, 18.81)	NR
28	Wigand 2013	German	CC	10,973	Hospital	NR	2.73 (1.49, 5.02)	NR
27	Sun Dingyong 2014	China*	CC	32,203	Community	Range 1–79	1.49 (1.06, 2.09)	NR

AOR = adjusted odds ratio; COR = crude odds ratio; SD = standard deviation; OR = odds ratio; CI = confidential interval; CC = case–control study; NR = not reported.
* Hepatitis C endemic country.

TABLE 3. Quality Assessment of Included Studies for the Association Between Body Piercing and Hepatitis C

Ref.	Studies	Study Design	Selection	Comparability	Outcome
54	Roy E 2001	CC	**	**	**
50	Seong M.H. 2013	CC	**	*	*
49	Yi He 2011	CC	*	**	*
53	Mariano 2004	CC	**	**	*
48	Kim 1996	CC	**	*	**
47	Balasekaran 1999	CC	**	**	*
46	Neal 1994	CC	**	**	*
45	Cathy 1996	CC	**	*	**
44	Lasher 2005	CC	—	—	—
52	Mele 1995	CC	**	**	*
43	Kerzman 2007	CC	*	**	**
42	Thaikruea 2004	CC	**	**	**
41	Murphy 2000	CC	**	**	*
13	Channa NA2011	CC	**	*	*
40	C. Alvarad 2005	CS	****	—	***
39	Hermanstyne 2012	CS	***	**	***
38	F. Ahmed 2012	CS	***	**	***
37	Maclennan 1994	CS	***	**	***
36	Dominitz 2005	CS	***	**	***
35	Bair 2005	CS	****	*	**
34	Lee 2003	CS	***	—	**
33	Vickery 2009	CS	***	**	***
51	Hwang 2006	CS	***	**	***
32	King 2009	CS	***	**	***
31	Khin 2010	CS	***	**	***
24	Mahtab 2010	CS	***	—	**
16	FeliPe 2009	CS	**	—	***
29	T.C.R. 2011	CS	***	—	***
28	Wigand 2013	CS	—	—	—
27	Sun Dingyong 2014	CS	***	**	***

CC, case–control study design; CS, cross-sectional study design; CO, cohort study design.
*, **, and *** are scores each included study could get in the Newcastle-Ottawa Quality Assessment Scale (NOS). * means the study got 1 score in the perspective. - means information in the included study was not enough to make the decision on the methodology quality assessment.

nonnormal result by stating that hygiene guideline supervising the procedure of body art was applied in that city,[23] making the effect of body piercing related less to the blood or body fluid transmitting diseases. Most of this kind of studies discussed the reasons behind, to sum up, participants in these studies are less like to represent the general population. Second, 2 studies with unexpected large effect measurements: OR = 54.13 (3.30, 887.2) for Conry 1996[45] due to there were no one exposed

TABLE 4. Quality Assessment of Included Studies for the Association Between Body Piercing and Hepatitis B

Ref.	Studies	Study Design	Selection	Comparability	Outcome
54	Roy E 2001	CC	**	**	**
53	Mariano 2004	CC	**	**	*
19	Nuchprayoon 1992	CC	**	**	*
20	Akhtar, S 2005	CC	*	*	*
52	Mele 1995	CS	**	**	*
23	Urbanus AT 2011	CS	**	**	***
21	Ashraf 2010	CS	**	**	***
22	Abdool 1988	CS	***	—	***
15	Lucus 1999	CS	***	—	**
14	Luksamijarulkul 1995	CS	***	**	***
51	Hwang 2006b	CS	***	**	***
24	Mahtab 2008	CS	***	—	**
25	Liu YI 2014	CS	***	**	***
26	Liu Fang 2007	CS	***	*	***

CC, case–control study design; CS, cross-sectional study design; CO, cohort study design.
*, **, and *** are scores each included study could get in the Newcastle-Ottawa Quality Assessment Scale (NOS). * means the study got 1 score in the perspective. - means information in the included study was not enough to make the decision on the methodology quality assessment.

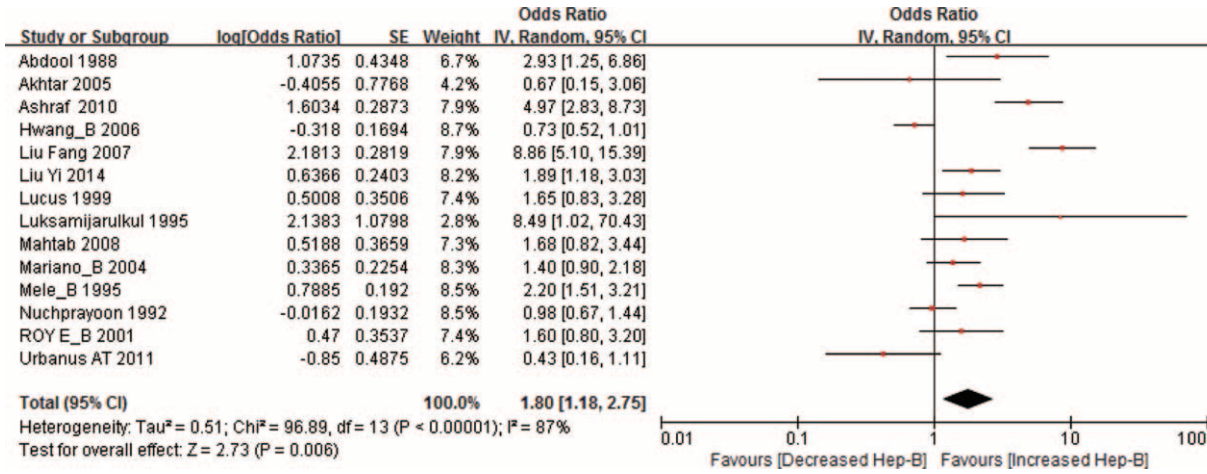

FIGURE 2. This forest plot shows the crude OR for body piercing and risk of hepatitis B in each individual study and pooled crude OR of all the included studies.

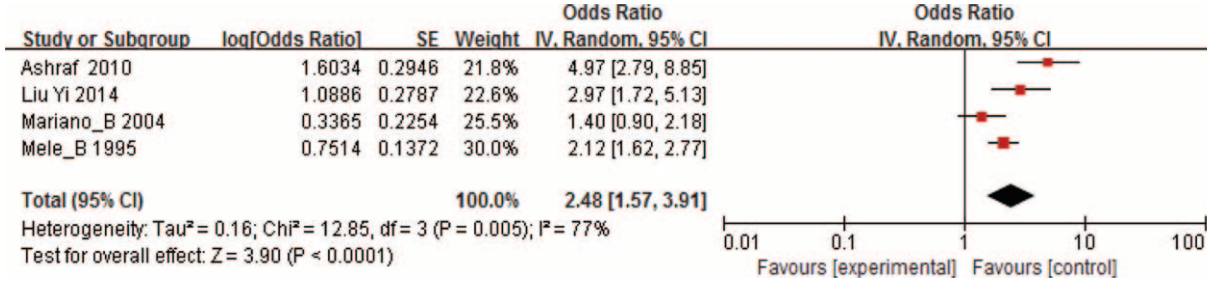

FIGURE 3. This forest plot shows the adjusted OR for body piercing and risk of hepatitis B in each individual study and pooled adjusted OR of all the included studies.

to body piercing in control group, OR = 17.35 (9.11, 33.04) for Chana 2011,[13] this study was conducted in the city of Tando Allahyar, Pakistan which has very poor public health condition.

This systematic review have several strengths, it focused on hepatitis B and hepatitis C simultaneously, making it available for us to compare the different effect size of body piercing on HBV and HCV transmission, body piercing held stronger risk effect on hepatitis C when compared with hepatitis B (2.21 vs. 1.80), this may due to there are mutual vaccination protective strategy for hepatitis B and better public awareness of this infectious disease. Besides, quality of the included studies was critically assessed to provide information of doing sensitivity

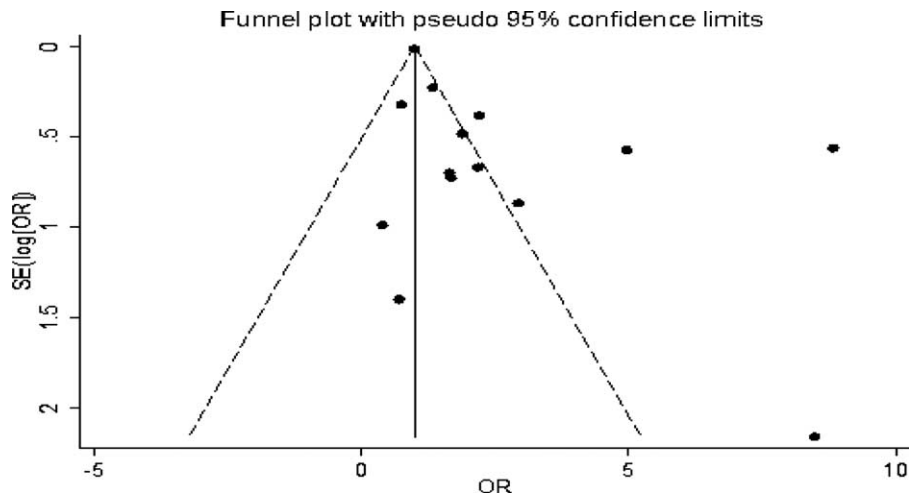

FIGURE 4. This figure shows the funnel plot for body piercing and risk of hepatitis B. The asymmetric plot may be caused by 3 outliers (Ashraf 2010, Luksamijarulkul 1995, and Liu Fang 2007). Horizontal axis represents the observed adjusted log OR in each individual study and the vertical axis represents the standard error of adjusted log OR in each individual study.

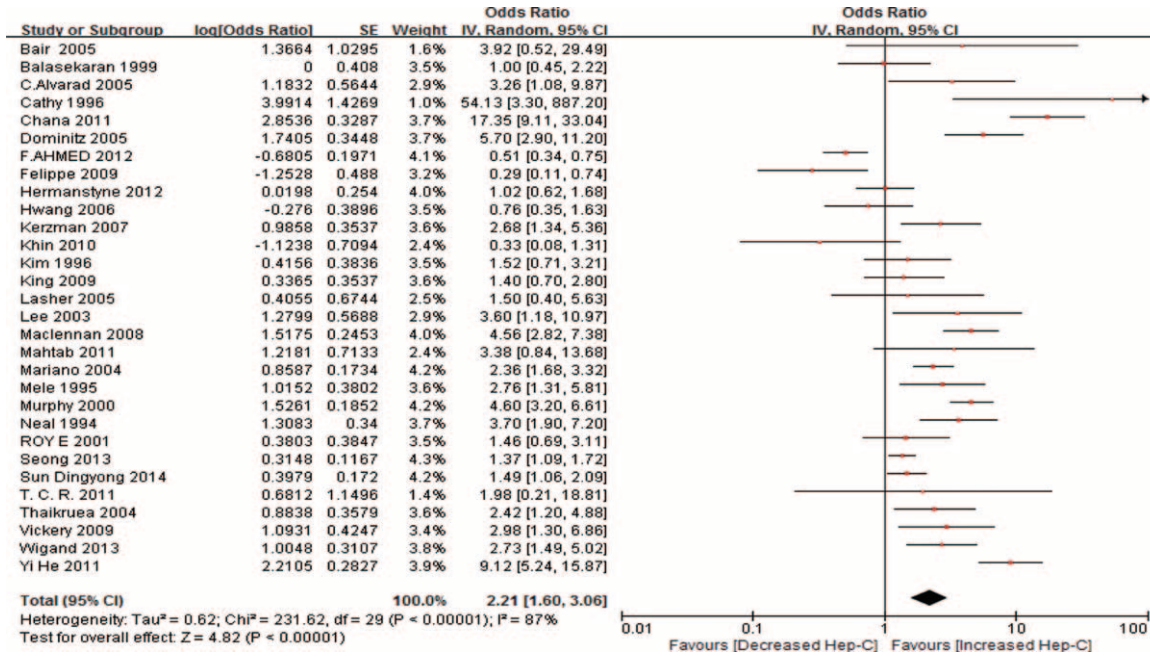

FIGURE 5. This forest plot shows the crude OR for body piercing and risk of hepatitis C in each individual study and pooled crude OR of all the included studies.

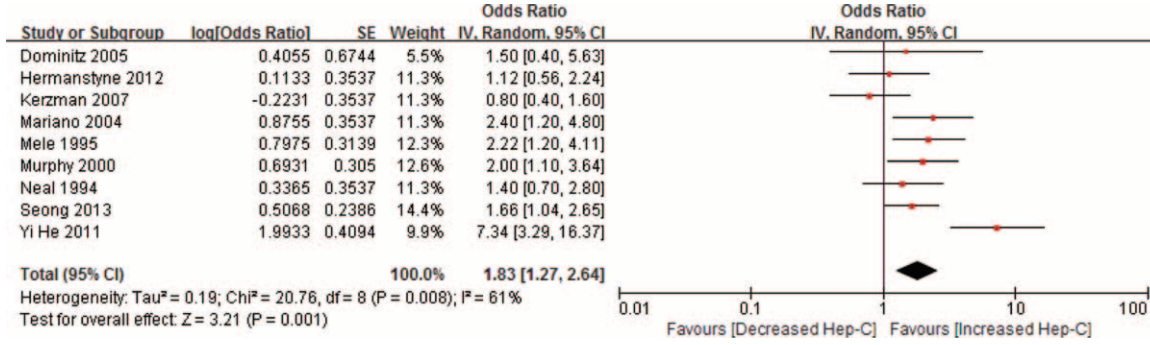

FIGURE 6. This forest plot shows the adjusted OR for body piercing and risk of hepatitis B in each individual study and pooled adjusted OR of all the included studies.

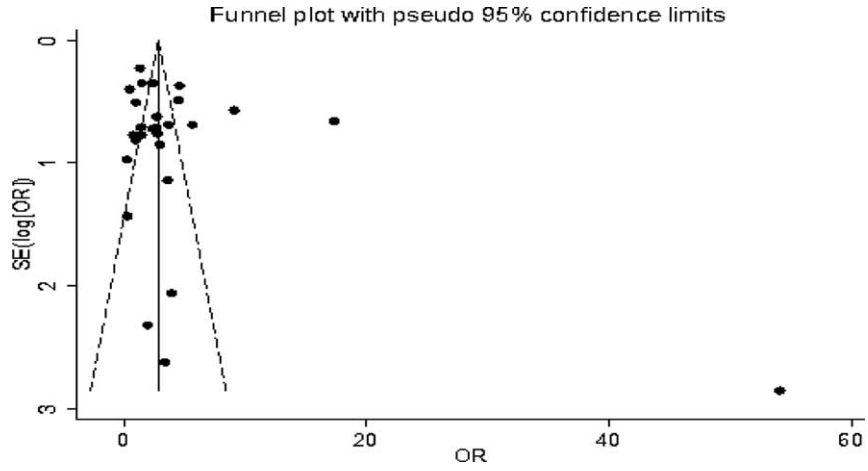

FIGURE 7. This figure shows the funnel plot for body piercing and risk of hepatitis C. The asymmetric plot may be caused by 2 outliers (Conry 1996 and Channa 2011). Horizontal axis represents the observed adjusted log OR in each individual study and the vertical axis represents the standard error of adjusted log OR in each individual study.

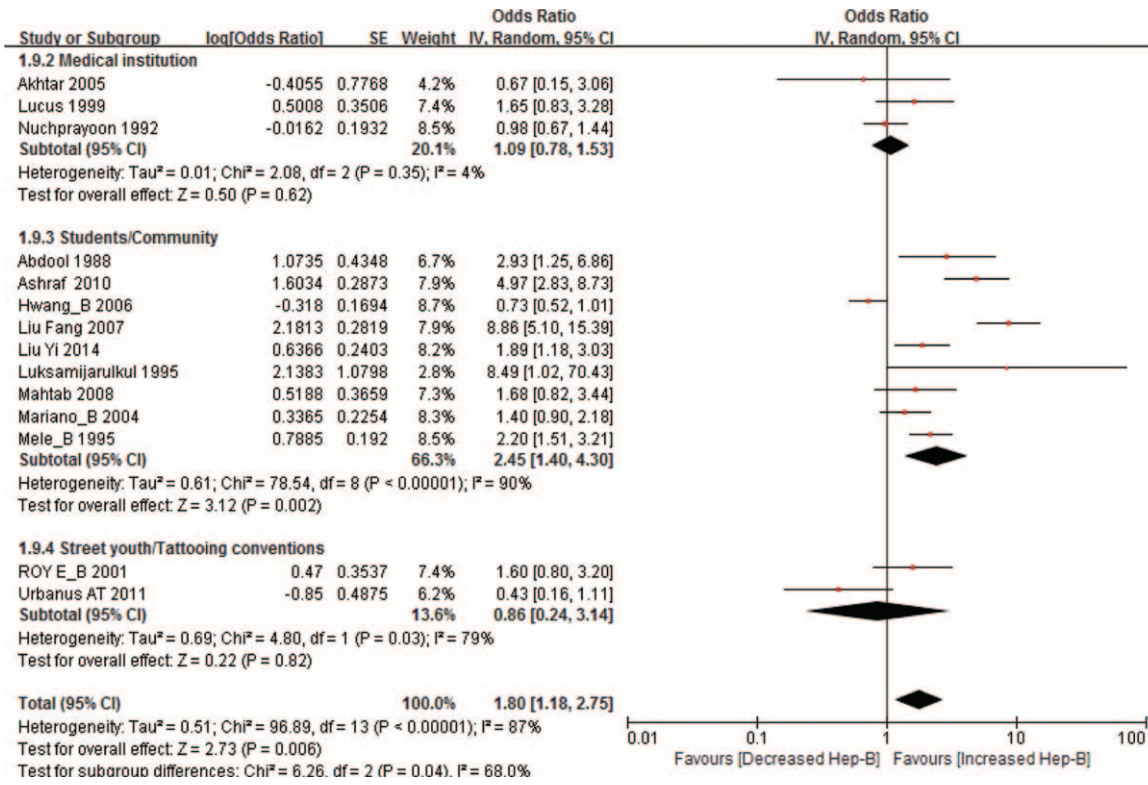

FIGURE 8. This forest plot shows the adjusted OR for body piercing and risk of hepatitis B in each individual study and pooled adjusted OR of all the included studies by subgroups based on study population source.

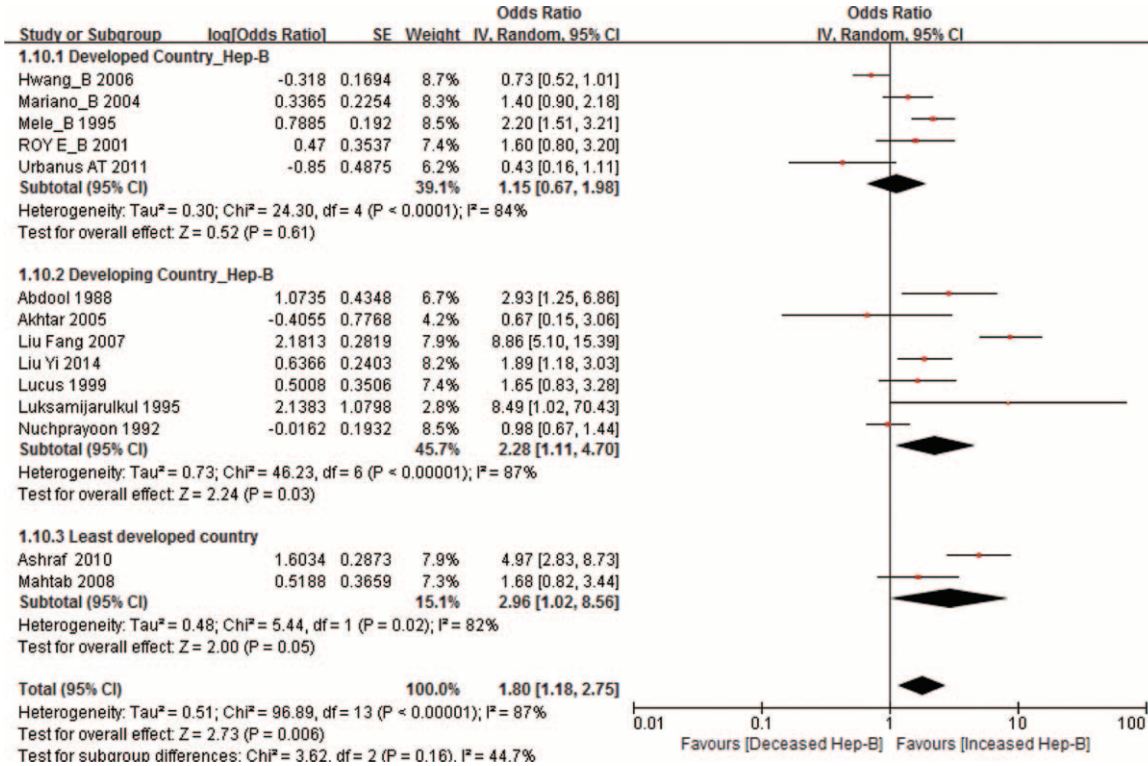

FIGURE 9. This forest plot shows the adjusted OR for body piercing and risk of hepatitis B in each individual study and pooled adjusted OR of all the included studies by subgroups based on level of social development.

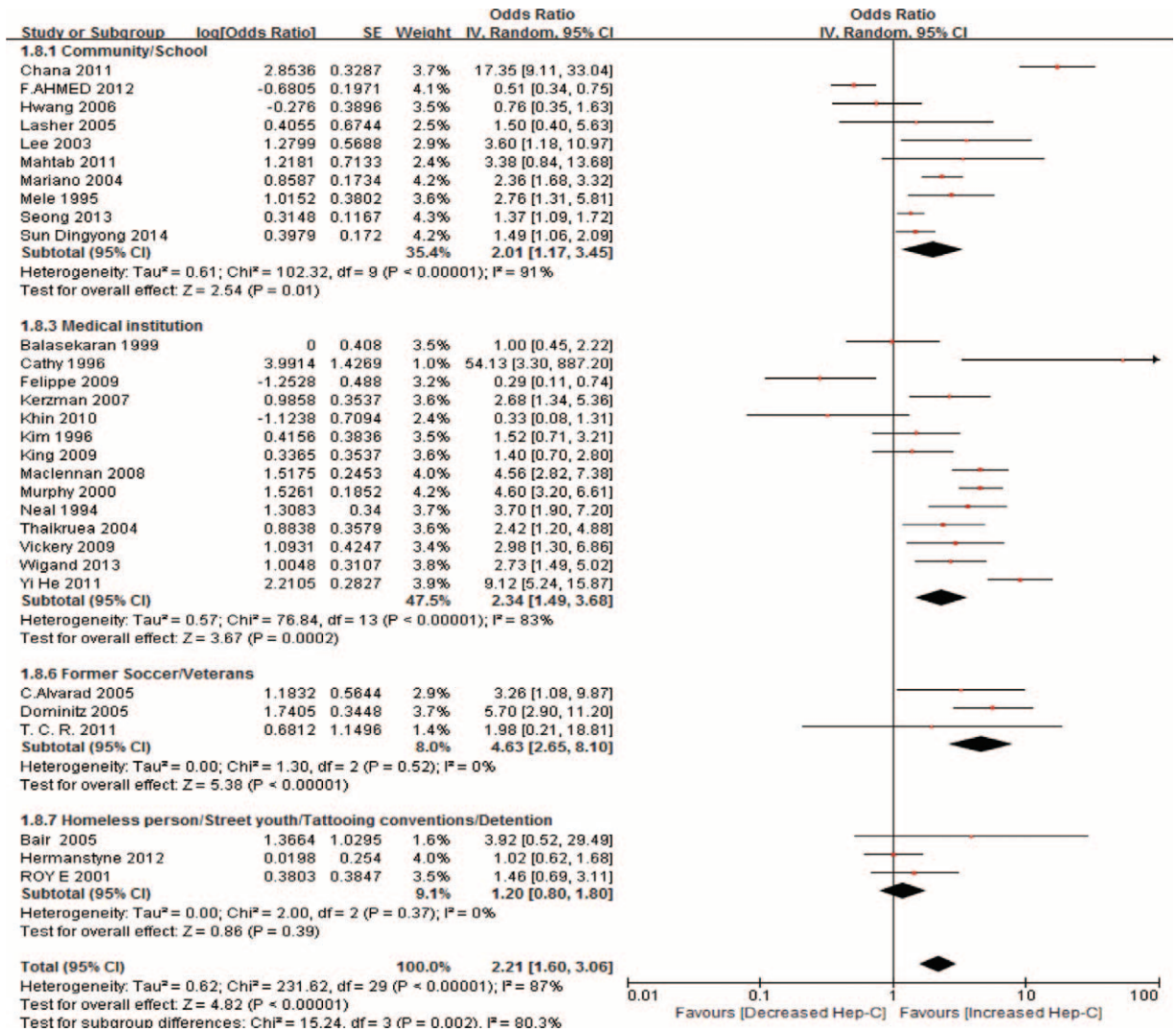

FIGURE 10. This forest plot shows the adjusted OR for body piercing and risk of hepatitis C in each individual study and pooled adjusted OR of all the included studies by subgroups based on study population source.

analysis and combining risk estimates using evidence from different level of strength. Subgroup analysis was conducted based on multiple angles to explore potential sources of heterogeneity sources on a maximum extent, finally, we found that different study population sources can most likely to explain the heterogeneity of this study.

Limitations of this systematic review were mostly due to the observational nature of the included studies, there have been no cohort studies available for this research question so far, even though several literatures included in this systematic review are basically cohort-designed, studies that are basically cross-sectional designed are all turned out to be case–control designed when came to in terms of the association between body piercing and hepatitis infection, fortunately, recall bias is not a severe problem for our question since it is less likely to recall a serious biased body piercing experience. Even so, studies seldom primarily focused on the risk of body piercing, the precision, accurate, and quality of information about this behavior may not poorly asked, recorded and managed, resulted in nonreliable outcome of each individual study.

In sum, based on the overall risk estimates, establishing comprehensive and effective programs that provide safer piercing practice is in urgent throughout the world. To illustrate the risk of body piercing in a more accurate manner in the future, studies are expected to conduct primarily focusing on the risk estimation for body piercing, this may be tough due to many other strong risk factors for HBV and HCV transmission, these factors can mask the effect of body piercing, additionally, there are many potential covariates and confounders when study on hepatitis B or C and it is impossible to comprehensively control for them within one study and also hard to uniformly control for them through different studies. However, it is meaningful and be worthy of our hard working on it, since the high prevalence of getting body piercing,[8] body piercing is becoming increasingly popular especially among young generations,[57] the prevalence of hepatitis B and hepatitis C maintained high in the last few years even though many effective preventive strategies were taken. Because of this, independent risk factors especially those under awareness of the public are in need to be examined, body piercing was proved to be one of the potential independent risk

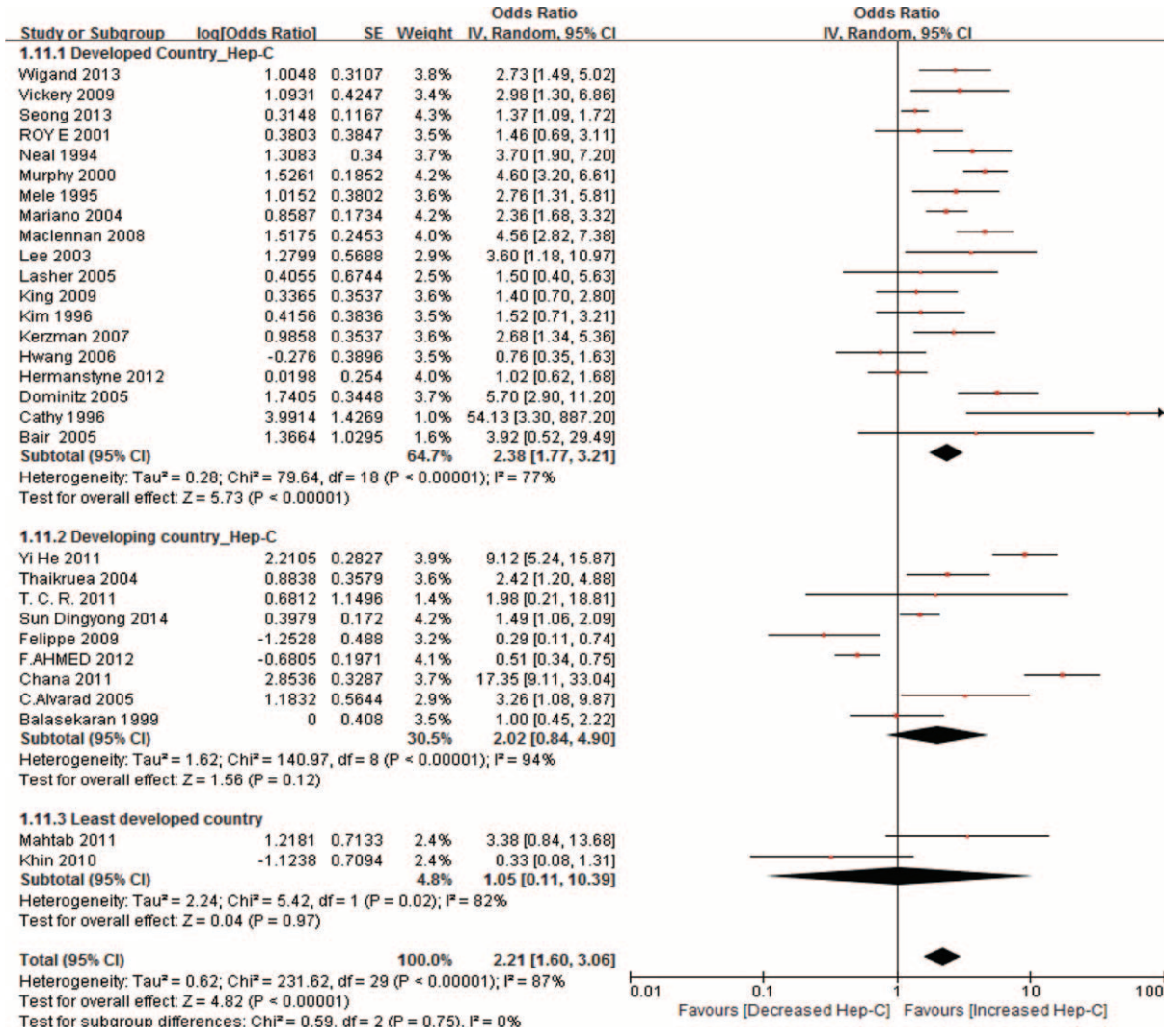

FIGURE 11. This forest plot shows the adjusted OR for body piercing and risk of hepatitis C in each individual study and pooled adjusted OR of all the included studies by subgroups based on level of social development.

TABLE 5. Pre- and Prosensitivity Analysis for Heterogeneity Test

		Presensitivity Analysis			Postsensitivity Analysis			
		No. of Studies	OR (95% CI)	I^2 (%)	No. of Studies	OR (95% CI)	I^2 (%)	Studies Identified as the Source of Heterogeneity
HBV	School/ community	9	2.40 (1.44, 4.02)	90	5	2.13 (1.64, 2.75)	0	Refs.[21,26,51,53]
HCV	School/ community	10	2.04 (1.17, 3.45)	91	5	1.52 (1.23, 1.88)	10	Refs.[13,34,38,51,53]
	Medical institution	14	2.34 (1.49, 3.68)	83	7	2.39 (1.84, 3.11)	0	Refs.[29,30,37,41,45,47,49]

TABLE 6. Reasons for Omitting Studies During Sensitivity Analysis

Study Population	Ref. Study ID	Reasons for Omitting
HBV_School/community	53 Mariano 2004	Outcome measurement is poor
	21 Ashraf 2010	Very poor city
	55 Hwang 2006	Very low prevalence of HCV, low-risk population
	26 Liufang 2007	Comparability is poor
HCV_Medical institution	28 Yi He 2011	(1) A large number of rural workers entered cities; this population once lived in the rural areas with very poor hygiene conditions and was very lack of relevant medical and health knowledge; (2) selection and outcome quality assessment got poor result
	30 Balasekaran 1999	Outcome quality assessment got poor result
	32 Cathy 1996	No one in control group had body piercing
	36 Murphy 2000	Outcome quality assessment got poor result
	40 Maclennan 2008	Blood donors 43% IVDU
	47 Mahtab 2010	Not enough information to assess comparability
	49 T.C.R. 2011	Not enough information to assess comparability
HCV_School/community	53 Mariano 2004	Outcome measurement is poor
	14 Channa 2011	Very poor city
	39 F. Ahmed 2012	Resident living in that district, men were under-representative since going out to work, residents are more babies and elders
	43 Lee 2003	An HCV-hyperendemic area

factors, so the association between body piercing and transmission of HBV and HCV are expected to be measured. According to the above results, the public need safe body piercing and being protected from infectious disease like hepatitis B and hepatitis C which can heavily affect the living quality of individual and population, it is expected to conduct large sample size studies focusing on this topic in order to provide more evidence-based health recommendations to the general public and medicine departments.

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