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REVIEW

Epidemiology of hepatitis B in pregnant Iranian women: a systematic review and meta-analysis

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Abstract Perinatal transmission is one of the most common routes of hepatitis B virus (HBV) transmission. This study aims to identify the epidemiological features of HBV among pregnant Iranian women. This study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. Two authors independently searched several online databases without time limit until May 2017. The databases include Magiran, Iranmedex, SID, Medlib, IranDoc, Scopus, PubMed, Science Direct, Cochrane, Web of Science and Google Scholar. The data were analyzed based on a random-effects model using Comprehensive Meta-Analysis software version 2. Thirty-seven studies were included in the meta-analysis. The prevalence of HBV among pregnant Iranian women was 1.18% (95% CI: 0.09%-1.53%). The prevalence of HBV among pregnant women living in urban and rural areas was 1.60% (95% CI: 0.06%-4.30%) and 1.70% (95% CI: 0.09%-3.2%), respectively. The prevalence of HBV among housewives and working pregnant women was 4.3% (95% CI: 1.4%-12.5%) and 1.2% (95% CI: 0.02%-5.8%), respectively. The risk of developing an HBV infection was significantly associated with illiteracy ($p = 0.013$), abortion ($p = 0.001$), blood transfusion ($p < 0.001$) and addicted spouse ($p = 0.045$). However, no significant relationship was observed between HBV infection and urbanization ($p = 0.65$), occupation ($p = 0.37$), history of surgery ($p = 0.32$) or tattooing ($p = 0.69$). Vaccination coverage (receiving at least a single dose) in pregnant women was 9.8% (95% CI: 5.3%-17.5%). The prevalence of HBV among pregnant women is lower than in the general population of Iran. HBV vaccination coverage was low among pregnant Iranian women. Therefore, health policymakers are recommended to enforce immunization programs for HBV vaccination among high-risk pregnant women.

Introduction

Hepatitis B is one of the most common infectious diseases worldwide [1]. According to the World Health Organization (WHO) in 2012, approximately 2 billion people are infected by HBV, more than 240 million suffer from chronic liver

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disease, and 600,000 deaths occur each year due to acute and chronic liver dysfunction [2, 3]. Iran is considered to be a low-endemic country in terms of HBV [4]. Perinatal transmission is one of the most common routes of transmission [5]. HBV screening of pregnant women has been recommended by WHO [6]. The risk of developing HBV among children born to women with $HBsAg^+$ (hepatitis B surface antigen) and $HBeAg^+$ (hepatitis B virus early antigen) status is 70-90% or more, and over 85% of them become chronic carriers [7]. In addition, cirrhosis and hepatocellular carcinoma leads to death in 25% of these children [7].

Preventing HBV transmission from mother to child is only possible when the disease is diagnosed during pregnancy or before delivery. Therefore, the key elements for controlling the infection and establishing prevention programs for this disease include epidemiological patterns, prevalence, and the risk factors.

Previous studies have assessed the prevalence and risk factors of HBV in pregnant Iranian women [9–13]. However, the results were not consistent among the different studies, and thus, a systematic review and meta-analysis seems necessary.

In meta-analysis, as the number of studies and sample size increases, the confidence interval becomes smaller, and therefore, the results become more reliable [14–16]. Therefore, the present study aims to investigate the epidemiological features of HBV among pregnant women through a systematic review and meta-analysis.

Materials and methods

Study protocol

This study followed the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines [16]. Two authors independently screened the databases and determined which studies were eligible for inclusion. Disagreements were resolved by a third researcher.

Search strategy

Two authors independently searched Iranian and international databases, including Iranmedex, Magiran, SID (Scientific Information Database), IranDoc, Medlib, Scopus, PubMed, Science Direct, Cochrane, Web of Science and also Google Scholar search engine, to identify potentially relevant studies. Languages were restricted to English and Persian. There was no time limit until May 2017. Our search included MeSH keywords "Epidemiology", "Prevalence", "Hepatitis", "Pregnant women", "Pregnancy", " Gestational", "Hepatitis B Surface Antigens", "Vaccination", "Vaccines" and "Risk Factors". Moreover, we reviewed the references of the selected articles to identify further relevant studies.

Definitions

The target population included studies whose subjects were pregnant women. The criterion for defining HBV infection was disease diagnosis in patients with positive blood test results in an enzyme-linked immunosorbent assay (ELISA) [17, 18].

Inclusion and exclusion criteria

The inclusion criteria in this study were investigations of the epidemiology of HBV among pregnant Iranian women published in either Persian or English. The exclusion criteria were non-random sampling methods, studies irrelevant to the topic, studies on animals, editorials, case reports, interventions, and reviews.

Quality assessment of identified studies

Two authors independently screened the identified studies according to the STROBE checklist [19]. STROBE consists of 22 sections that evaluate studies in terms of sampling method, measurement, statistical analysis, and study objectives. Each item includes 0 to 2 points. A score of 16 was chosen as the cutoff point to choose studies for final inclusion, and any disagreement was resolved by a third researcher.

Data extraction

Two authors (Milad Azami, Shoboo Rahmati) independently extracted the data using a pre-prepared checklist. The checklist included the author's name, date of publication, place, type of study, year of study, overall HBV prevalence, HBV prevalence based on place of residence and occupation, vaccination, $HBsAg^+$ and potential risk factors for HBV in pregnant women.

Statistical analysis

Binomial distribution was used to estimate the prevalence of HBV in each study. Pooled odds ratios (OR) were used to measure the effects for potential risk factors of HBV (if the factor was mentioned in two studies or more) in cross-sectional and case-control studies. We used Cochran's Q test and I^2 index to assess heterogeneity. If the p-value of the I^2 index was >50% and the Q test value was <0.05, heterogeneity was assumed and a random effects model was used. If heterogeneity was not found, a fixed effects model was adopted [20, 21]. Subgroup analysis was performed to find

the source of heterogeneity in HBV prevalence. Sensitivity analysis was carried out to assess the stability of the data. Publication bias was assessed using Egger and Begg's tests [22]. We used meta-regression to investigate the relationship between prevalence of HBV and year of study. Data were analyzed through meta-analysis based on the random effects model using Comprehensive Meta-Analysis software version 2 (Biostat, Englewood, NJ, USA). $p < 0.05$ was considered statistically significant.

Results

Search results

Searching online databases identified 364 studies. After careful consideration for inclusion and exclusion criteria and quality assessment (using the STROBE checklist), 37 studies were included in the meta-analysis (Fig. 1).

Characteristics of the included studies

The 37 studies were published in 1990-2016, and included 71,550 pregnant Iranian women. Ten, two, five and nine studies were conducted in central, eastern, northern and southern Iran, respectively, and the ELISA technique was used in all studies for HBV diagnosis. The mean age of the pregnant women was estimated to be 25 years. Table 1 shows the details of the studies in this meta-analysis.

The overall prevalence of HBV

The prevalence of HBV among pregnant women in Iran was 1.18% (95% confidence interval [CI]: 0.09%-1.53%) and the heterogeneity index was $I^2 = 99.06$ ($p < 0.0001$). The lowest

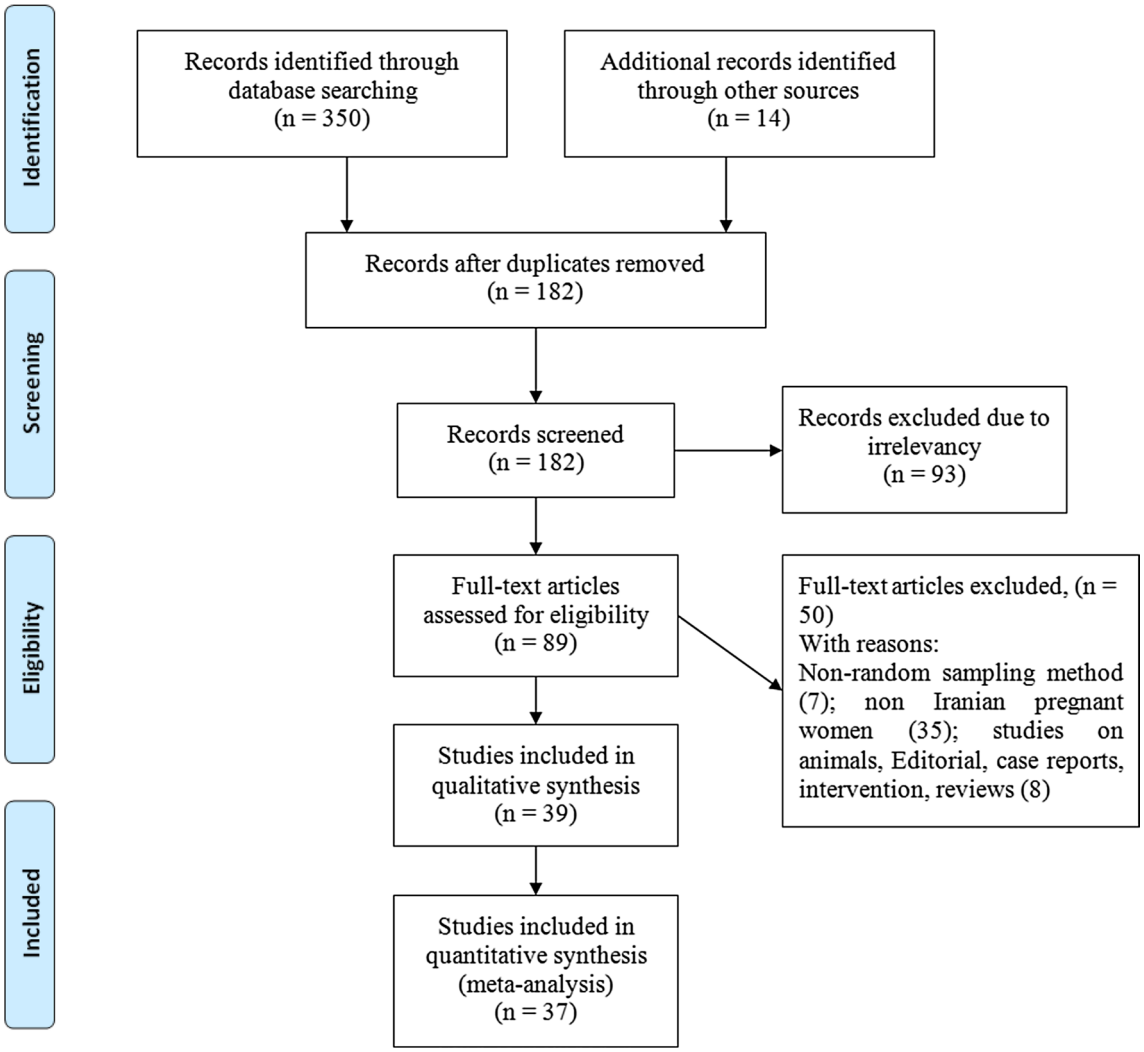

Fig. 1 Study selection process

Table 1 Detail of studies included into this meta-analysis

References	First author, publication year	Place	Year of study	Sample size	Age (mean ± SD)	Diagnostic criteria	Hepatitis B prevalence (%)	Vaccination coverage (%)
[8]	Yadegari D, 1998	Zanjan	1996	600	24.5 ± 5.6	HBsAg	1	
[9]	Aminzadeh Z, 2004	Rafsanjan	2003	600	26.2 ± 5.3	HBsAg	1.3	1
[10]	Moradi B, 2003	Tehran	1999	339		HBsAg	4.71	
[11]	Ghalenoee M, 2003	Kerman	1996	232	25.37 ± 5.0	HBsAg	2.58	
[12]	Sharifi M, 2000	Qazvin	2000	323		HBsAg	3.4	
[13]	Aali B. Sh, 1998	Kerman	1997	1002	26.52 ± 5.8	HBsAg	2.3	
[23]	Mirghaforvand M, 2007	Tabriz	2006	187		HBsAg	3.2	
[24]	Salimi S, 2014	Ardebil	2009	9321		HBsAg	1.7	
[25]	Sarifi-halat B, 2005	Zahedan	2002	200	21 ± 5.0	HBsAg	6.5	
[26]	Tabasi Z, 2003	Kashan	2002	2000	24.65 ± 6.2	HBsAg	0.35	
[27]	Motazakker M, 2014	Orumieh	2011	368	25.9 ± 5.5	HBsAg	0.80	
[28]	Cheraghali F, 2011	Gorgan	2008	1553		HBsAg	1	
[29]	kavosi A, 2015	Aqqala	2010	1057		HBsAg	1.6	
[30]	Mohammad Jaffari R, 2004	Ahvaz	1998	120	28.9 ± 5.0	HBsAg	1.7	5.8
[31]	Mobaien A, 2014	Zanjan	2011	1317	26.7 ± 5.8	HBsAg	0.40	8.6
[32]	Behjati Ardekani R, 2000	Yazd	2000	1904		HBsAg	0.84	
[33]	Mohebbi SR, 2011	Lorestan	2007	827	26.1 ± 5.4	HBsAg	0.70	
[34]	Motamedifar M, 2012	Shiraz	2009	238		HBsAg	0.85	22.8
[35]	Ahmadi M, 2011	Isfahan	2009	1078	26.1 ± 4.9	HBsAg	0.50	12.5
[36]	Jalali P, 1999	Hamedan	1998	1000		HBsAg	1.2	
[37]	Hassanjan Roshan M. 1994	Babol	1994	1456		HBsAg	2	
[38]	Ebrahim Pour S, 1993	Tabriz	1988	460		HBsAg	2.17	
[39]	Ahansaz M, 2000	Gorgan	1999	246		HBsAg	1.21	
[40]	Nasrirazin B, 2000	Tehran	1999	1000		HBsAg	1.7	
[41]	Aghighi M, 2000	Tehran	1995	1429		HBsAg	4	
[42]	Ryazi Z, 2007	Torbat Heydarieh	2004	1830		HBsAg	1.2	
[43]	Moradi HR, 2000	Tehran	1998	1000		HBsAg	1.7	
[44]	Sahaf F, 2007	Tabriz	2006	680		HBsAg	2.5	
[45]	Shoghli A, 2015	Seven provinces	2011	5261	27.8 ± 5.0	HBsAg	1.21	
[46]	Dehghani Zahedani M, 2010	Bandar Abbas	2008	680		HBsAg		28.1
[47]	Afzali H, 2015	Kashan	2012	768	24.65 ± 4.0	HBsAg	1.56	
[48]	Yahyapour Y, 2011	Amol	2005	6442		HBsAg	0.16	
[48]	Yahyapour Y, 2011	Amol	2004	5939		HBsAg	0.40	
[48]	Yahyapour Y, 2011	Amol	2006	6315		HBsAg	0.40	
[48]	Yahyapour Y, 2011	Amol	2008	6057		HBsAg	0.51	
[48]	Yahyapour Y, 2011	Amol	2007	6488		HBsAg	0.62	
[49]	Bayani M, 2016	Babol	2014	1065		HBsAg	0.18	
[50]	Kheiri L, 2015	Dehloran	2011	850		HBsAg	0.59	

prevalence was reported in the city of Amol (Yahyapour et al.), with 0.16%, and the highest prevalence was reported in the city of Zahedan, with 6.5% (Sharifi et al.) (Fig. 2).

Sensitivity analysis

Removing any single study did not affect the combined results for HBV prevalence (Fig. 3).

Subgroup analysis based on region and province

Table 2 and Figure 4 show the geographical distribution of HBV among pregnant women in Iran. As shown in Table 2, the lowest prevalence was found in northern Iran (0.69% [95% CI: 0.42%-1.12%]), and the highest prevalence was found in eastern Iran (2.8% [95% CI: 0.52%-13.7%]).

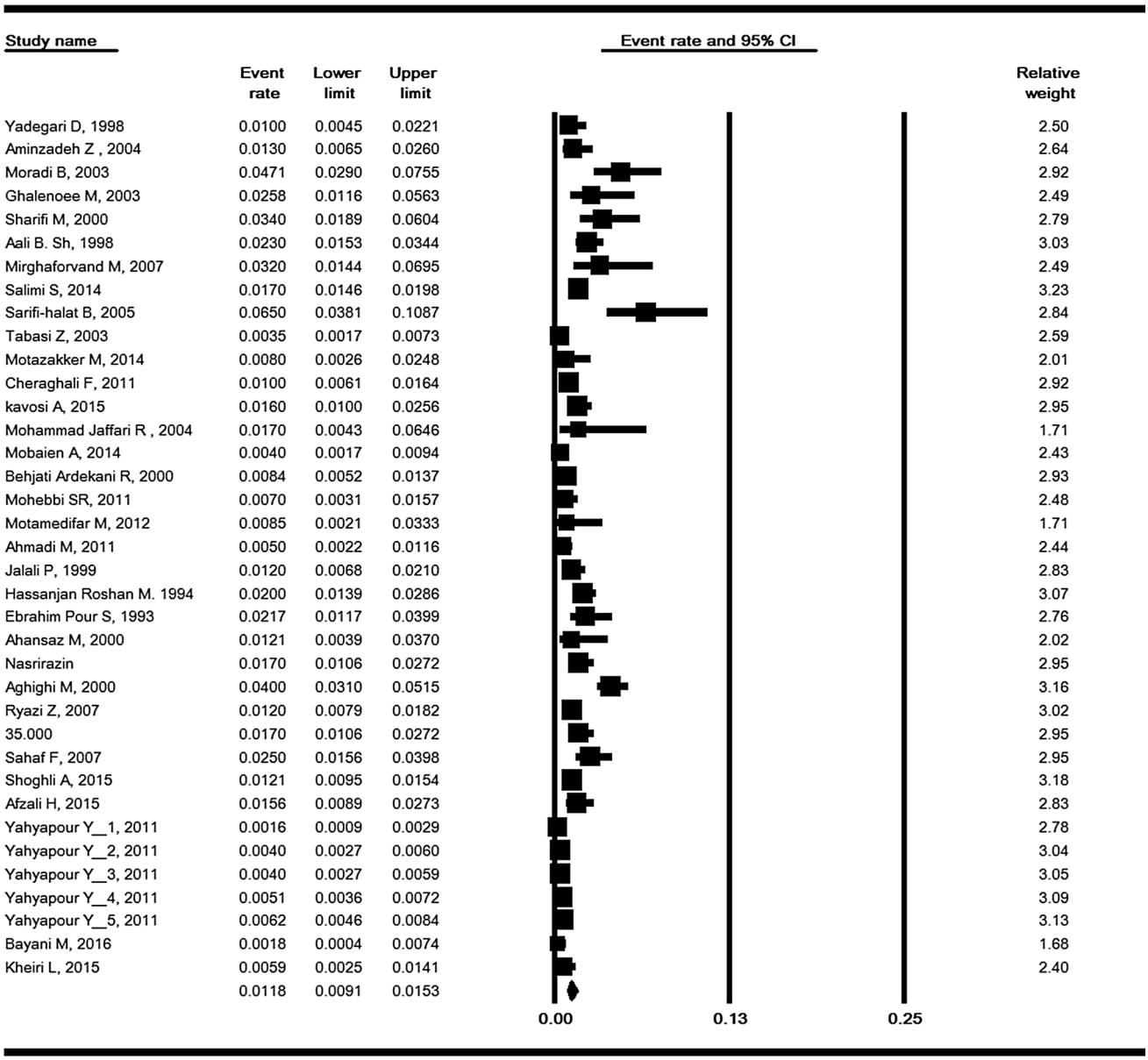

Fig. 2 Forest plot of prevalence of HBV infection among pregnant Iranian women according to the random-effects model

Prevalence of HBV infection based on place of residence and occupation

The prevalence of HBV infection among pregnant women living in urban and rural areas was 1.60% (95% CI: 0.06%-4.30%) and 1.70% (95% CI: 0.09%-3.2%), respectively (p-value for difference = 0.96). The prevalence of HBV among housewives and working pregnant women was 4.3% (95% CI: 1.4%-12.5%) and 1.2% (95% CI: 0.02%-5.8%), respectively (p-value for difference = 0.37) (Table 2).

Hepatitis B vaccination coverage and HBsAb$^+$

Six studies examined vaccination coverage and reported that 9.8% (95% CI: 5.3%-17.5%) of pregnant women had received at least a single dose of HBV vaccine. The prevalence of HBsAb$^+$ in pregnant Iranian women was 43.3% (95% CI: 33.3%-53.9%). (Fig. 5).

Risk factors for hepatitis B in pregnant women

The risk of developing an HBV infection was significantly associated with illiteracy (p = 0.013), abortion

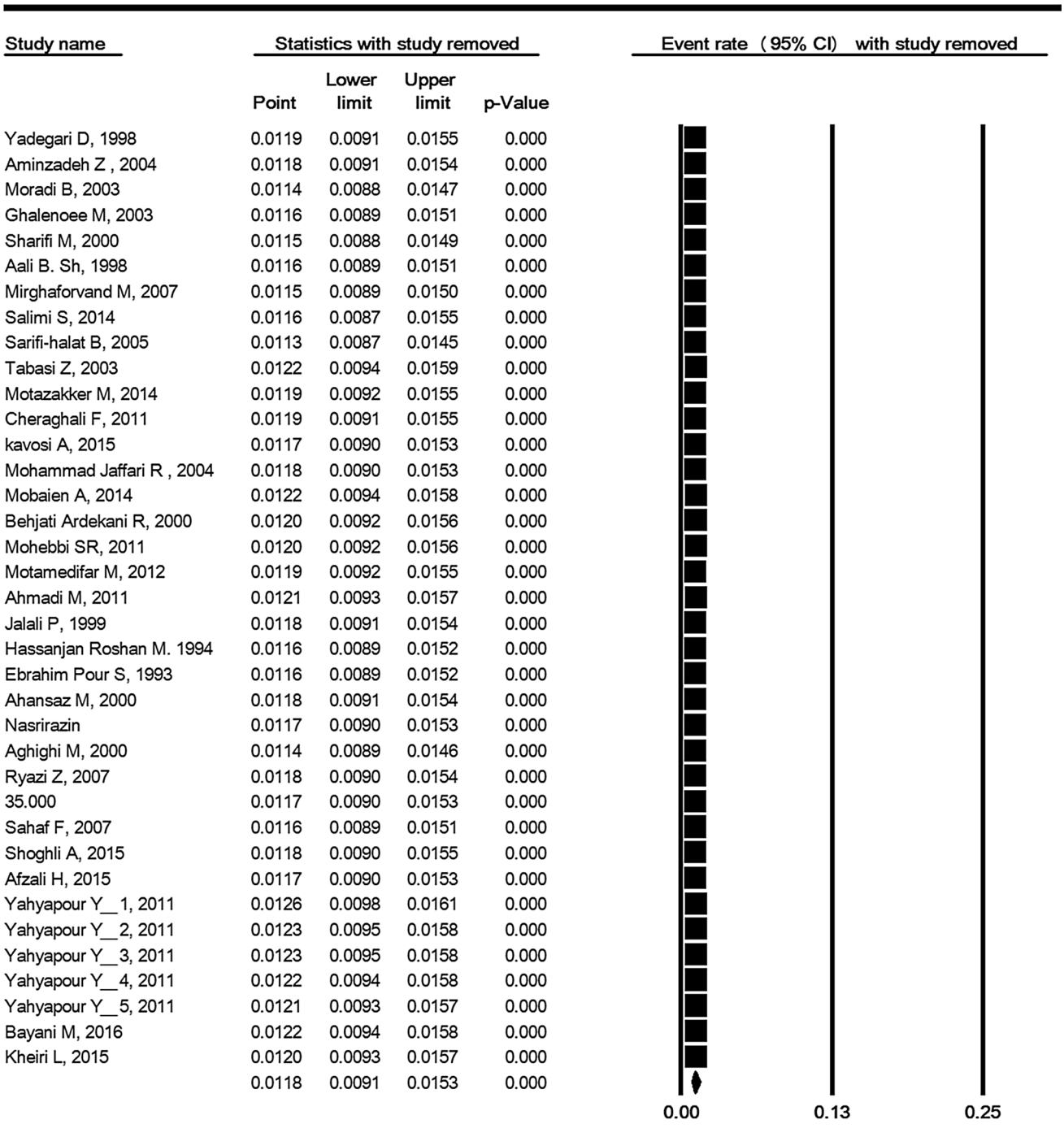

Fig. 3 Sensitivity analysis of the prevalence of HBV infection among pregnant Iranian women according to the random-effects model

($p = 0.001$), blood transfusion ($p < 0.001$) and addicted spouse ($p = 0.045$). However, no significant relationship was observed between HBV infection and urbanization ($p = 0.65$), occupation ($p = 0.37$), history of surgery ($p = 0.32$) or tattooing ($p = 0.69$) (Table 3).

Meta-regression

In order to assess the relationship between the prevalence of HBV and the year in which the study was performed, we used meta-regression model (Fig. 6). Our results revealed a

Table 2 Subgroup analysis of HBV prevalence based on region, province, place of residence, and occupation

Variables	Studies (N^a)	Sample (N)	Heterogeneity		95% CI[b]	Overall (%)
			I^2	p-value		
Region						
Center	10	9841	90.84	< 0.0001	0.92–2.73	1.59
East	2	2030	95.78	< 0.0001	0.52–13.7	2.8
North	5	2190	0	0.42	0.42–1.12	0.69
South	9	6289	72.15	< 0.0001	0.75–1.87	1.18
Test for subgroup differences: $Q = 15.39$, $df(Q) = 5$, $p = 0.009$						
Province						
Khuzestan	1	120	–	–	0.43–6.46	1.7
Mazandaran	7	33762	91.67	< 0.0001	0.27–0.83	0.47
Golestan	3	2856	0	0.403	0.92–1.76	1.27
Ardebil	1	9321	–	–	1.46–1.98	1.7
Ilam	1	850	–	–	0.25–1.41	0.59
Hamedan	1	1000	–	–	0.68–2.10	1.20
Isfahan	3	3846	82.44	0.003	0.25–1.77	0.67
Kerman	3	1834	12.27	0.32	1.44–2.92	2.05
Lorestan	1	827	–	–	0.31–1.57	0.70
Western Azerbaijan	1	368	–	–	0.26–2.48	0.80
Qazvin	1	323	–	–	1.89–6.04	3.40
Fars	1	236	–	–	0.21–3.33	0.85
East Azarbaijan	3	1327	74.90	< 0.0001	1.79–1.82	2.50
Tehran	4	3768	84.49	< 0.0001	1.64–4.61	2.76
Khorasan Razavi	1	1830	–	–	0.79–1.82	1.20
Yazd	1	1904	–	–	0.52–1.37	0.84
Sistan and Baluchestan	1	200	–	–	0.381–100	6.50
Zanjan	2	1917	57.80	0.124	0.26–1.57	0.64
Seven Provinces	1	5261	–	–	0.95–1.54	1.21
Test for subgroup differences: $Q = 0.291$, $df(Q) = 3$, $p = 0.96$						
Place of residence						
Urban	9	12322	96.41	< 0.0001	0.06–4.30	1.60
Rural	10	4309	82.42	< 0.0001	0.09–3.2	1.70
Rate ratio of urban to rural: 1.21(95% CI 0.53–2.76, $p = 0.65$)						
Occupation						
Housewives	8	12014	98.93	< 0.0001	1.4–12.5	4.3
Working	8	1923	70.87	0.001	0.02–5.8	1.2
Rate ratio of housewives to working: 2.31 (95% CI 0.36–14.49, $p = 0.37$)						

[a]Number

[b]Confidence interval

significantly decreasing trend, and the p-value was less than 0.0001 for the study year.

Publication bias

Figure 7 shows a funnel plot of HBV prevalence. The Egger and Begg's tests results were $p = 0.09$ and $p = 0.06$, suggesting the absence of a publication bias

Discussion

The present meta-analysis investigated the prevalence of HBV among pregnant Iranian women based on geographical region, province, occupation, place of residence, and study year. We also estimated the odds ratio of HBV risk factors.

The results showed that the prevalence of HBV according to 37 studies with a total sample size of 71,550 pregnant Iranian women was 1.18%. The reported prevalence

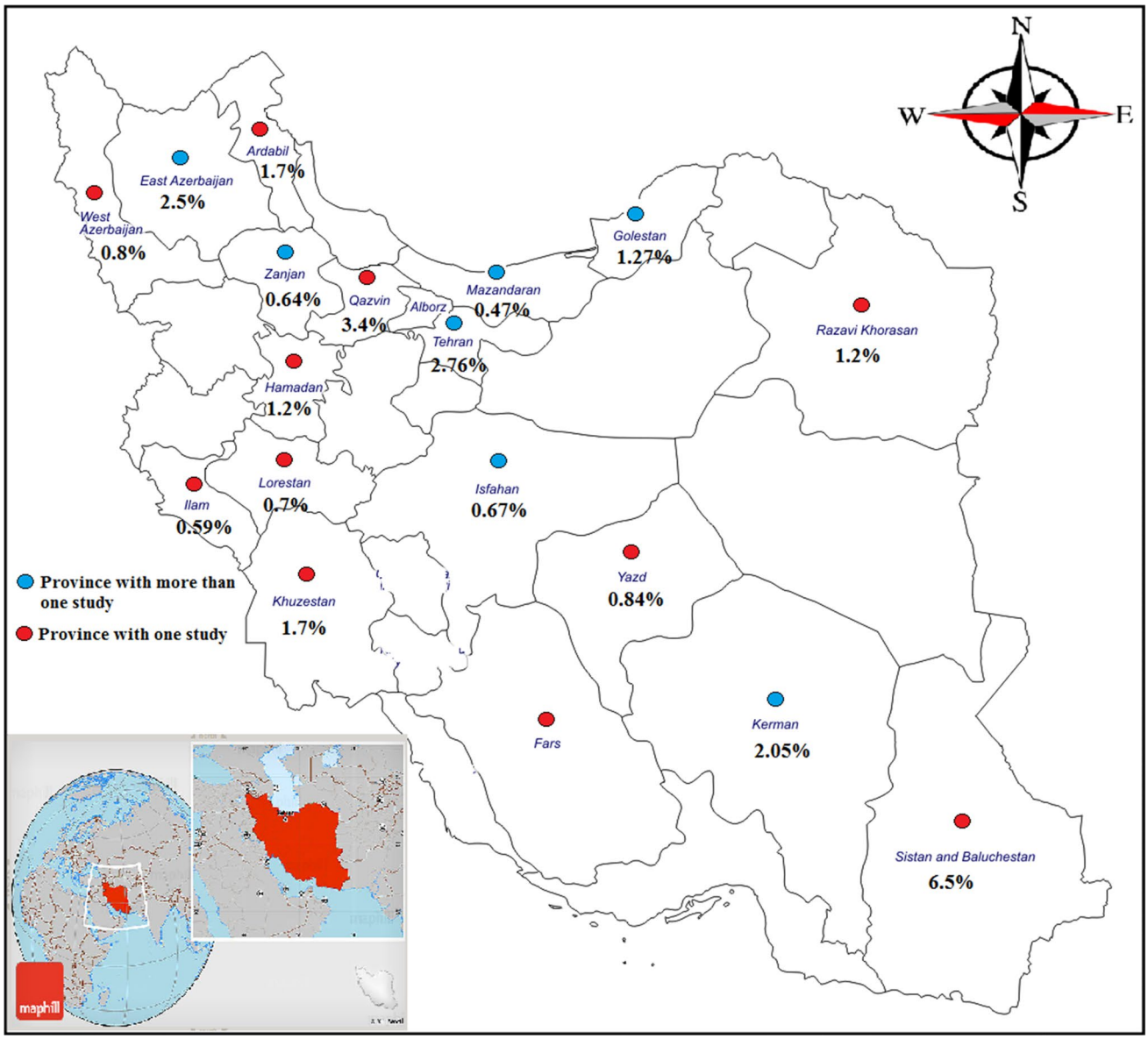

Fig. 4 Geographical distribution of prevalence of HBV infection in pregnant Iranian women

of HBV in different countries varies from less than 1% to 13.1% [51–56].

Previous systematic reviews have reported that the prevalence of HBV was 3.2% among opioid-addicted individuals, 0.08% among blood donors, 0.6% among health personnel and 3% among the total Iranian population [57–59]. These results might possibly be attributed to religious and cultural beliefs, having a single sexual partner, and the low number of opioid-addicted women in Iran [60]. A meta-analysis by Azami et al. [58] revealed that the prevalence of HBV infection among Iranian men was two times higher than in women. One of the most extensive studies that investigated HBV among pregnant Iranian women in seven provinces reported a prevalence of 1.21% [48]. A previous systematic review showed that HBV vaccination coverage among high-risk groups of nurses, physicians, and dentists was 77.2%, 73.1% and 76%, respectively [61–63]. In another systematic review, the efficacy of HBV vaccination in Iranian people was reported to be over 90% [64, 65]. The present results indicate that the HBV vaccination coverage with at least a single-dose injection and $HBsAb^+$ status among pregnant Iranian women was 9.8% and 43.3%, respectively. Therefore, increasing HBV vaccination coverage among pregnant Iranian women is recommended.

The results of assessing the relationship between HBV prevalence and the time of the study revealed a descending pattern in which HBV prevalence decreased over time from 1994 to 2015. This descending triangle pattern might

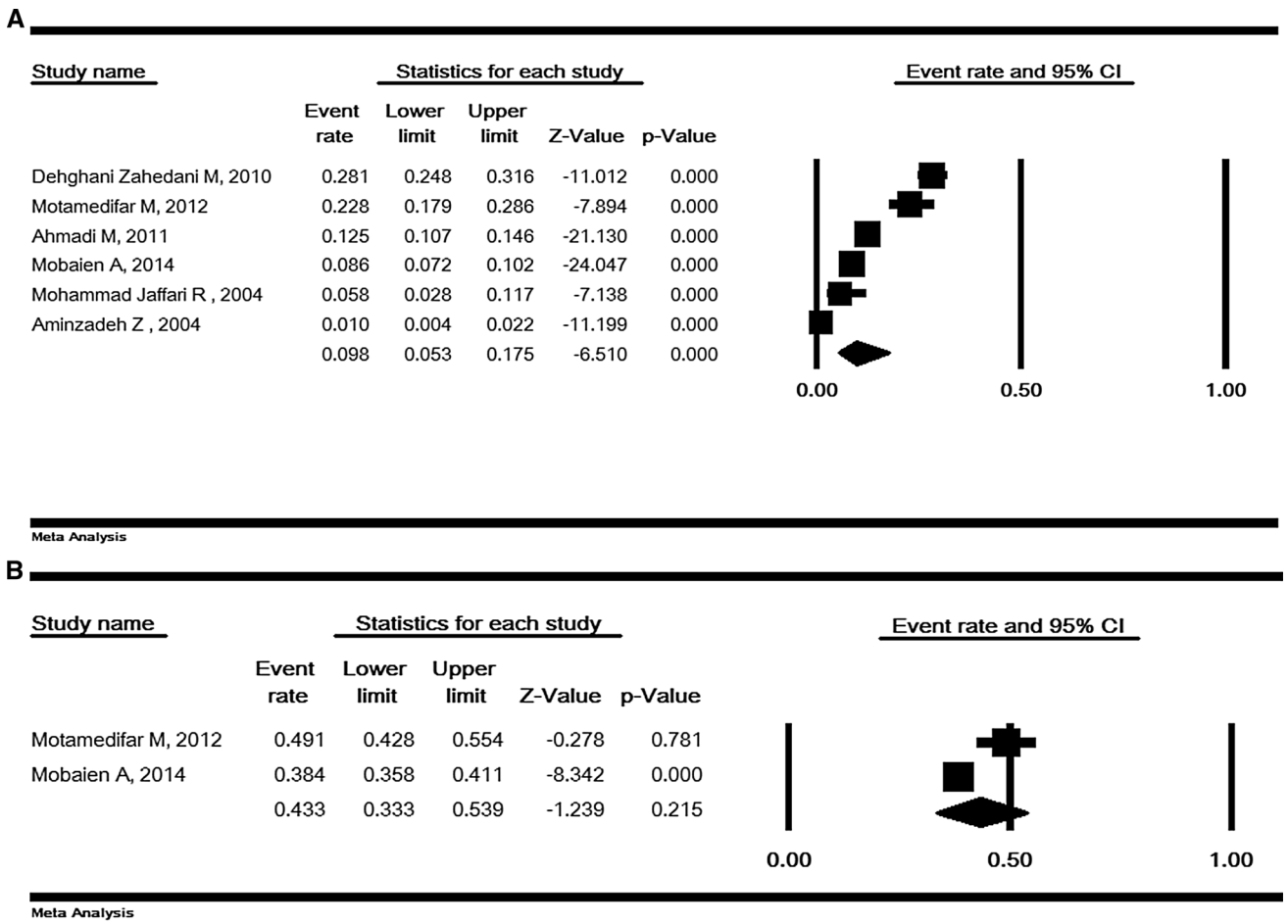

Fig. 5 HBV vaccination coverage with at least a single-dose injection (**a**) and HBsAb$^+$ status (**b**) according to the random-effects model

Table 3 The odds ratio for the risk of developing HBV in pregnant women

Variable	No. of studies (N)	No. of positive cases	No. of cases	Positive control	Control	Heterogeneity		95% CI	Odds ratio (OR)	*p*-value
						p-value	I^2			
Illiteracy	8	24	1377	90	10127	0.010	61.92	1.28-8.79	3.36	0.013
Abortion	6	47	2696	50	5564	0.45	0	1.30-2.95	1.96	0.001
Blood transfusion	7	13	322	71	7677	0.002	71.07	2.32-11.46	5.16	<0.001
Surgery	5	20	1478	42	5402	0.15	40.27	0.69-2.98	1.44	0.32
Tattoo	5	4	172	54	3401	0.024	64.53	0.25-7.69	1.40	0.69
Addicted spouse	2	7	149	18	1534	0.076	68.31	1.03-28.46	5.43	0.045

be due to screening programs for diagnosing HBsAg$^+$ individuals.

The risk of developing an HBV infection was significantly associated with illiteracy, abortion, blood transfusion and having an addicted spouse ($p < 0.05$). However, no significant relationship was observed between HBV infection and urbanization, occupation, history of surgery, or tattooing ($p > 0.05$). Similarly, Ephraim et al. [66] found no significant relationship between HBV and history of surgery or tattooing. Likewise, Akani et al. [67] reported no significant relationship between HBV and history of surgery, tattoos, blood transfusion or circumcision.

There are several limitations in this study that need to be addressed. The first limitation was the lack of enough sensitivity to systematic and combination Search in Iranian databases. Second, there was inadequate data to identify an

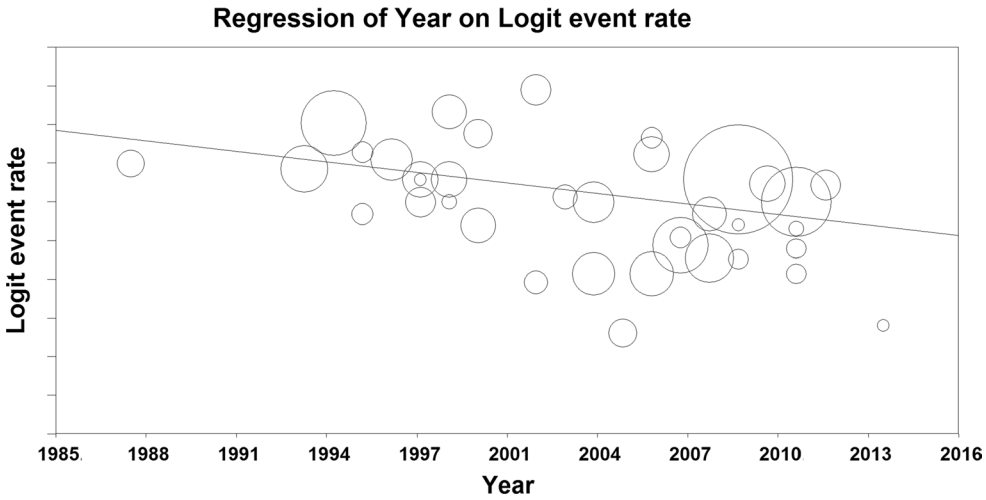

Fig. 6 Meta-regression of HBV prevalence among pregnant women according to time of study. The circles represent overall study weights

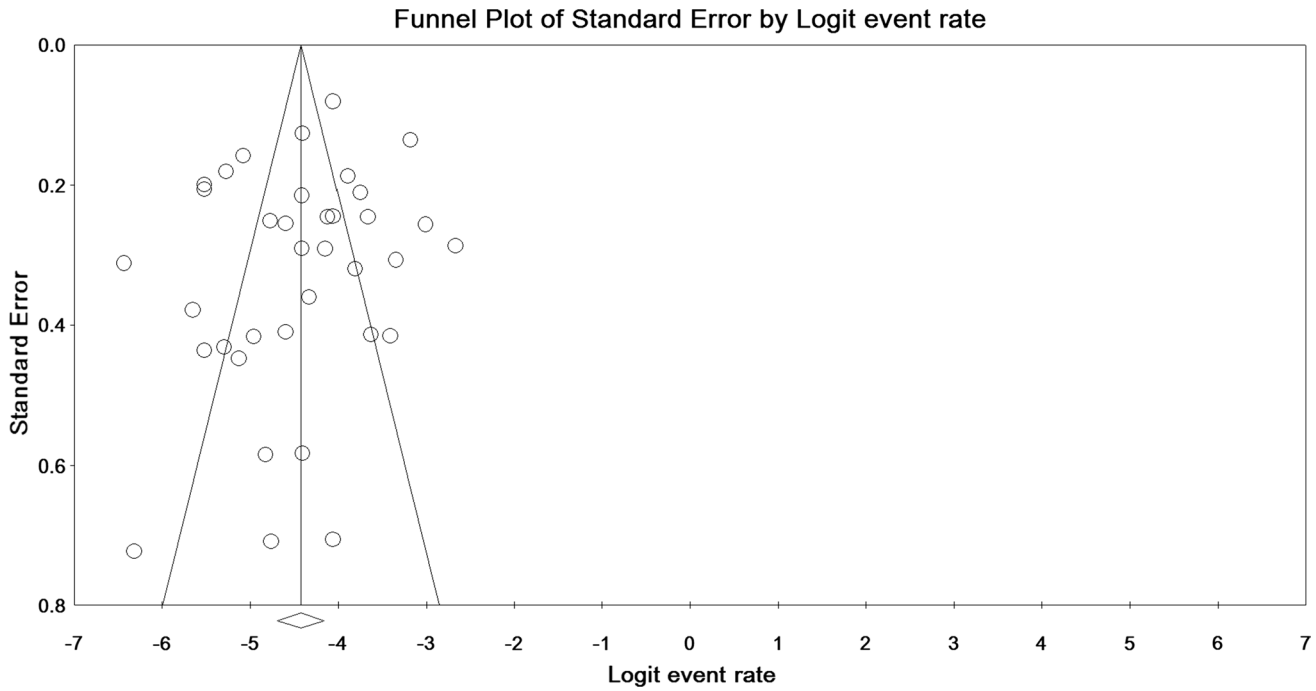

Fig. 7 Funnel plot to assess the publication bias

age pattern of HBV infection in Iranian databases. The third limitation was that majority of studies included in the current meta-analysis did not report the gestational age, which prevented us from assessing the pattern of HBV infection during pregnancy. Finally, we were not able to find information regarding the number of sexual partners or family history of jaundice.

Conclusion

The prevalence of HBV among pregnant women is lower than in the general population of Iran. HBV vaccine coverage is low among pregnant Iranian women. The risk of developing HBV is associated with illiteracy, abortion, blood transfusion and having an addicted spouse.

Author Contributions Gholamreza Badfar and Milad Azami designed the study. All authors performed data collection and data extraction. Milad Azami performed statistical analysis. All authors reviewed and approved the final version of the manuscript.

Compliance with ethical standards

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Conflict of interest All authors declare that there is no conflict of interest.

Ethical approval This article does not contain any studies with human participants performed by any of the authors.

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