Systematic Review

Prevalence of Preeclampsia and Eclampsia in Iran

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Abstract

Background: Several studies have been conducted to investigate the prevalence of preeclampsia and eclampsia in Iran. These studies have yielded different results. This meta-analysis was aimed to estimate the prevalence of preeclampsia and eclampsia in Iran.

Methods: International and national electronic databases were searched up to August 2014 including PubMed, Science Direct, Scopus, Science Information Database, MagIran, and IranMedex as well as conference databases. All studies, in which the prevalence or cumulative incidence of preeclampsia in Iran was reported, were included in this meta-analysis. Thirty-six separate studies were assessed involving overall 132,737 participants, of which 4360 had preeclampsia and 49 had eclampsia.

Results: Overall prevalence of preeclampsia and eclampsia was 0.05 (95% CI: 0.05, 0.06) and 0.23% (95% CI: 0.12%, 0.33%) respectively. The prevalence of preeclampsia, increased from 0.04 (95% CI: 0.03, 0.05) during 1996 to 2005 to 0.07 (95% CI: 0.04, 0.09) during 2010 to 2013, while the prevalence of eclampsia decreased from 0.30% (95% CI: 0.15%, 0.45%) to 0.01% (95% CI: 0.01%, 0.01%), during the same period.

Conclusions: The preeclampsia prevalence had an increasing growth and the eclampsia prevalence had declining growth in recent years. In addition, despite many studies aimed the prevalence of preeclampsia and eclampsia in Iran, there is a significant variation between the results. So, it is difficult to give an exact estimation of the preeclampsia and eclampsia prevalence in Iran.

Keywords: Eclampsia, incidence, Iran, meta-analysis, preeclampsia, prevalence

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Introduction

Hypertensive disorders of pregnancy are among the most frequent and adverse outcomes of pregnancy worldwide.[1] Hypertensive disorders of pregnancy include chronic hypertension, chronic hypertension with superimposed preeclampsia, gestational hypertension, as well as two main important forms of Hypertensive disorders, including: preeclampsia and eclampsia.[2] Preeclampsia and eclampsia are associated with higher rates of maternal, fetal and infant mortality and morbidity.[3]

The World Health Organization (WHO) estimates that preeclampsia is directly responsible for 10% of direct maternal mortality in Asia.[4] Asian women with preeclampsia have worse pregnancy outcomes than others.[5]

Preeclampsia is related to adverse physical and emotional pregnancy outcomes such as, renal necrosis, pulmonary edema, hepatic rupture, Hemolysis, Elevated Liver Enzymes and Lowered Platelets syndrome, stroke, anxiety and depression.[3,6,7] Changes in maternal characteristics, such as maternal age and pre-pregnancy obesity have increased the prevalence of preeclampsia.[8] Ethnicity could be a risk factor for developing preeclampsia.[9] The prevalence of preeclampsia appeared to have a strong variation in different countries.[10] The prevalence of preeclampsia was reported as 3.4% in the United States,[11] 8.9% in Brazil,[12] 3.3% in Australia,[13] 12% in Bangladesh,[14] 3.2% in India,[15] and 4.7% in Thailand.[16]

Prediction methods and treatments of preeclampsia have declined the prevalence of eclampsia.[8] Nowadays eclampsia is rare in developed countries, however, it is still happening in developing countries and its mortality in these countries has been reached to 15%.[17] Maternal deaths of preeclampsia mainly result from eclampsia. Compared to women with preeclampsia, women with eclampsia have more stillbirths, cesarean section and ICU admissions. Also, neonates have more respiratory distress syndrome and lower birth weights.[18,19] Eclampsia prevalence was reported 0.08% in the United States,[18] 0.02% in the United kingdom,[19] 0.03% in Qatar,[20] and 1.03% in the India.[15]

Several studies have investigated the prevalence of preeclampsia and eclampsia in different parts of Iran, which have indicated different results. Therefore, this meta-analysis was conducted to estimate the overall prevalence of preeclampsia and eclampsia among the Iranian pregnant population.

Methods

Review Registration

This study has been registered in the international prospective register of systematic reviews (PROSPERO) as number CRD42013005973, available online from: URL: http://www.crd.york.ac.uk/PROSPERO_REBRANDING/display_record.asp?ID=CRD42013005973.

Definitions

Preeclampsia defined as a pregnancy-specific disease diagnosed by ongoing development of hypertension and proteinuria after 20 weeks of pregnancy. Eclampsia defined as the occurrence of convulsions superimposed on the preeclampsia.[3,21]

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Searching

Major electronic databases were searched using the mesh terms of Prevalence, incidence, preeclampsia, and Iran. The international databases searched as follows: PubMed (January 1950 to August 2014); Scopus (January 1973 to August 2014); and Science Direct (January 1823 to August 2014). In addition, the following national databases were searched: Science Information Database (up to August 2014); MagIran (up to August 2014); and IranMedex (up to August 2014).

In order to obtain additional literatures, the reference lists of all included studies were scanned. The authors of the included studies were contacted as needed. The following conference databases were searched for unpublished data until August 2014:

- The International *Society* for the Study of Hypertension in Pregnancy; available from: *isshp.org/pageguidelines*
- The Preeclampsia Foundation; available from: URL: www.preeclampsia.org/the-news/events
- Pre eclampsia-International Conferences; available from: URL: www.*conferenceseries.com/pre-eclampsia.php*
- The 2014 Pregnancy Summit; available from: URL: https://www.regonline.co.uk/builder/site/Default.aspx?Event

Inclusion and exclusion criteria

All descriptive, cross-sectional, prospective or retrospective cohort studies, in which the prevalence or cumulative incidence of preeclampsia in the hospitals of Iran was reported, were retrieved regardless of publication date and language. Due to the short duration of pregnancy, the "prevalence or cumulative incidence" of preeclampsia was considered as the "prevalence" of preeclampsia. However, based on the design of the included studies, the prevalence and cumulative incidence of preeclampsia and eclampsia were reported separately. Cross-sectional studies were used to determine preeclampsia and eclampsia prevalence and prospective or retrospective cohort studies to preeclampsia and eclampsia cumulative incidence. The Iranian pregnant population was considered as the study population, regardless of age. The primary, secondary, and tertiary outcomes of interest were the prevalence of preeclampsia, eclampsia, and the cumulative incidence of preeclampsia and eclampsia, respectively. Case-control, randomized clinical trial and quasi-experimental studies were excluded.

Data collection and validity assessment

Two authors (RKh and BO) independently screened the title and abstract of the retrieved studies and reviewed the full texts to extract studies that met the inclusion criteria of this meta-analysis. The authors were not blinded to the names of the studies' authors and journals. Any disagreements were resolved by judgment with a third author (ZCh). The percent agreement of the two authors was 97% and the Kappa statistics for checking reliability was 78.3%. The variables that were extracted for data analysis included publication author, year, province, study design, parity, total number of participants, number of outcomes, age and gestational age.

Seven selected items from the recommended checklist of STROBE[22] were used for assessing the quality of studies. These items included: 1) present key elements of the study design; 2) clearly define the outcome, i.e., preeclampsia and eclampsia; 3) give the eligibility criteria; 4) explain how the study sample was arrived at; 5) describe the setting, locations, and relevant dates; 6) give sources of data and details of methods of assessment (measurement); 7) and describe all statistical methods. The studies were classified as high quality if they achieved all criteria, as intermediate quality if they did not achieve one criterion, and as low quality if they did not achieve more than one criterion.

Heterogeneity and publication bias

Statistical heterogeneity was assessed with Chi-square test, inconsistency through studies results with *I*-square statistic, and between-study variance with tau-square statistic.[23,24] Also, Begg and Egger statistical tests were used to assess publication bias measurably.[25,26] The sources of heterogeneity were found using meta-regression based on our prior knowledge of effective factors on preeclampsia prevalence. The significance level was set at 0.2.

Review manager 5,[27] and Statistical software Stata 11 (Stata Corp, College Station, TX, USA) were used for data analysis. Meta-analysis was performed to obtain summary measures of "prevalence" or "cumulative incidence" of preeclampsia and eclampsia in the Iranian pregnant population. Data were analyzed and the results were reported using a random-effects model with 95% confidence interval (CI) by inverse variance weight.[28]

Results

Description of the studies

We retrieved 1118 studies up to August 2014, including 726 references through searching international electronic databases, 380 references through searching national electronic databases, 10 references through checking reference lists, and two references through personal contact with the study authors. Of 1118 retrieved references, 92 references were excluded because of duplication, 962 references did not relate to the objective of this review, and 28 references did not meet the eligibility criteria (Figure 1). Eventually, we included 36 studies, which reported the prevalence of preeclampsia in the meta-analysis[29–64] that involved 132,737 participants with the mean age of 25.83 years. Among 132,737 participants, 4360 had preeclampsia. Also, six studies of these studies reported the prevalence of eclampsia,[29,32,52,56,59,60] which involved 47,833 participants with a mean age of 26.38 years of which 49 had eclampsia (Table 1).

Estimated prevalence of preeclampsia and eclampsia

The total prevalence of Preeclampsia among Iranian pregnant women was 0.05 (95% CI: 0.05, 0.06). The prevalence of preeclampsia was 0.04 (95% CI: 0.03, 0.05) during 1996 to 2005. However, it increased during subsequent years and reached to 0.05 (95% CI: 0.04, 0.06) during 2005 to 2010 and to 0.07 (95% CI: 0.04, 0.09) during 2010 to 2013. The prevalence of preeclampsia in cross-sectional studies was 0.04 (95% CI: 0.03, 0.05) and in prospective or retrospective cohort studies was 0.07 (95% CI: 0.05, 0.08) (cumulative incidence of preeclampsia in Iran) (Figures 2 and 3).

The overall prevalence of eclampsia among Iranian women was 0.23% (95% CI: 0.12%, 0.33%) or 2.3 cases in 1000 women. The prevalence of eclampsia was 0.30% (95% CI: 0.15%, 0.45%) during 1996 to 2005. Contrary to the preeclampsia prevalence, the eclampsia prevalence decreased during subsequent years and reached to 0.14% (95% CI: 0.13%, 0.15%) during 2005 to 2010 and to 0.01% (95% CI: 0.01%, 0.01%) during 2010 to 2013. The prevalence of eclampsia was evaluated just in cross-sectional studies and in the mixed population of multipar and nullipar women (Table 2).

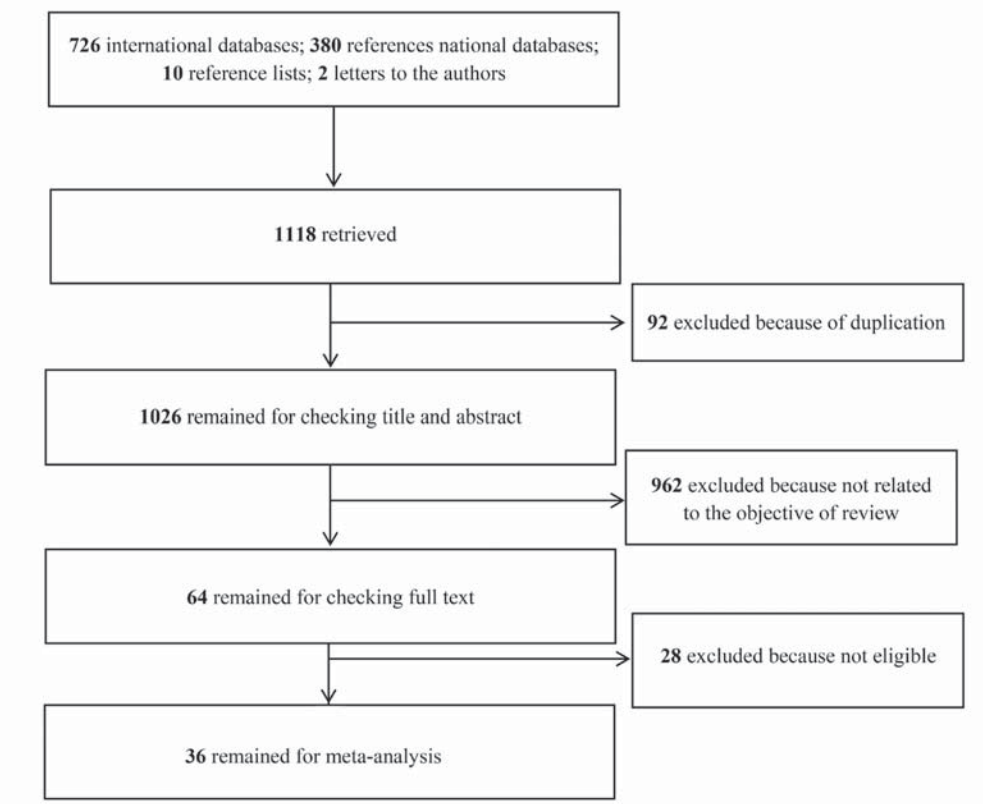

Figure 1. A flow diagram showing the phases of development through the meta-analysis

Quality of the studies

The studies were divided into three categories based on the quality of reporting using the STROBE checklist as follows: 13 studies (36.11%) had high quality; 13 studies (36.11%) had intermediate quality, and 10 studies (27.78%) had low quality. The prevalence of preeclampsia was estimated based on the different qualities of the studies. However, the prevalence of preeclampsia was not differed based on these quality categories; the 95% confidence interval of prevalence was narrower in high quality studies. The prevalence of eclampsia was overestimated by the studies with low quality (Table 2).

Heterogeneity and publication bias

There was considerable heterogeneity among the included studies, so that the result of the Chi-square test for heterogeneity was highly significant ($P < 0.001$). In addition, the *I*-square statistic was 98% to 99% (Figures 2 and 3). Despite the significant heterogeneity, tau-square statistic was very small ($tau^2 = 0.0004$ for preeclampsia and 0.0177 for eclampsia). In order to decrease the heterogeneity, studies were divided into subgroups by province and year. However, heterogeneity was not reduced.

The results of statistical tests for publication bias, including Begg and Egger tests, for preeclampsia were statistically significant (Ps < 0.001). In addition, the results of these tests for eclampsia were statistically significant (Ps = 0.004). These results proved the presence of publication bias.

Discussion

The result of this review showed that the prevalence of preeclampsia in pregnant women was 5% and had increasing growth in recent years. Also, the prevalence of eclampsia was 0.23% and had declining growth in recent years. Therefore, this study supports the prevalence of preeclampsia increase and the prevalence of eclampsia decrease in the world.[8] The increasing prevalence of preeclampsia should be considered as a serious warning that threat maternal, fetal and infant's health in the near future and should be focused by special attention particularly by policy makers and health planners who plan preventive and controlling programs.

Based on the design of the studies in meta-analysis, the cumulative incidence and prevalence of preeclampsia was reported as 7% and 4% respectively. Consistent with results of this study, WHO estimates that 7 to 8 percent of women aged 14 to 59 years develop preeclampsia in the East Mediterranean Region Organization (EMRO), the region where Iran is located in.[65] The prevalence rate of preeclampsia in this study was lower than the cumulative incidence, which may be shown the effective management of preeclampsia without prevention of it. Another reason could be the short duration of pregnancy and the disease. The overall prevalence of preeclampsia was 5%. Consistent with this study, the global prevalence of preeclampsia is reported 4.6%.[66] This prevalence rate was based on the earlier definition of preeclampsia, hypertension with proteinuria. If we consider the new definition of preeclampsia, hypertension with either proteinuria or one or more severe feature, the prevalence of preeclampsia would be estimated higher.[67] The overall prevalence of eclampsia was 0.23%. Women in the industrial countries have a 0.02% – 0.08% chance of developing eclampsia compared with a 0.16% – 0.69% for women in less industrial countries.[8] Therefore, the prevalence (0.23%) is higher than industrial countries and is similar to less industrial countries.

Table 1. Characteristics of the included studies in meta-analysis

Author (Year)	Province	Parity	Age (mean)	Study design	Sample size	Preeclampsia number (%)	Eclampsia number (%)
Aali and Janghorbani (1996)	Kerman	Multipar & nullipar	27.1	Cross-sectional	3339	153 (4.6)	14 (0.41)
Alipour Dizaji, et al. (2007)	Tabriz	Nullipar	23.4	Prospective	696	30 (4.3)	NR
Allahyari, et al. (2009)	Tehran	Nullipar	24.7	Prospective	466	30 (6.4)	NR
Amir Ali Akbari, et al. (2004)	Tehran	Multipar & nullipar	25.9	Cross-sectional	4856	143 (2.9)	8 (0.16)
Bahasadri, et al. (2011)	Tehran	Nullipar	24.8	Prospective cohort	490	58 (12)	NR
Beygi, et al. (2008)	Tehran	Multipar & nullipar	NR	Prospective cohort	170	17 (10)	NR
Dadkhah, et al. (2010)	Tehran	Multipar & nullipar	25.5	Prospective cohort	1000	54 (5.4)	NR
Davari Tanha, et al. (2008)	Tehran	Multipar & nullipar	26.2	Prospective cohort	549	50 (9.1)	NR
Dehghani Firoozabadi, et al. (2007)	Yazd	Nullipar	21	Prospective cohort	120	8 (6.7)	NR
Direkvand-Moghadam, et al. (2012)	Ilam	Multipar & nullipar	28.8	Cross-sectional	610	58 (9.5)	NR
Eslami, et al. (2013)	Kh, R, Ke,M,S, B,Ko, L*	Multipar & nullipar	27.5	Cross-sectional	2993	194 (6.5)	NR
Ghazizadeh, et al. (2000)	Tehran	Nullipar	23.0	Prospective cohort	300	15 (5)	NR
Goshtasbi, et al. (2012)	Tehran	Multipar & nullipar	NR	Retrospective cohort	1513	85 (5.6)	NR
Goudarzi, et al. (2008)	Esfahan	Multipar & nullipar	NR	Prospective cohort	266	42 (16)	NR
Kashanian, et al. (2012)	Tehran	Multipar & nullipar	26.9	Prospective cohort	304	35 (12)	NR
kazemi (2008)	Esfahan	Nullipar	22.6	Prospective cohort	393	35 (8.9)	NR
Kazerooni and Hamze-Nejadi (2003)	Shiraz	Multipar & nullipar	22.8	Prospective cohort	102	8 (7.8)	NR
Keshavarz and Babaee (2003)	Shahroud	Multipar & nullipar	26.1	Prospective cohort	1310	49 (3.7)	NR
Keshavarz, et al. (2008)	Shahroud	Multipar & nullipar	25.0	Prospective coh	1194	162 (3.8)	NR
Keshtkar, et al. (2006)	Tehran-Rasht	Multipar & nullipar	NR	Cross-sectional	1643	85 (3.2)	NR
Khooshideh and Shahriari (2008)	Zahedan	Nullipar	22.4	Retrospective cohort	10352	160 (1.5)	NR
Moghadam, et al. (2008)	Tehran	Multipar & nullipar	NR	Prospective cohort	1800	60 (3.3)	NR
Moghadam, et al. (2013)	Tehran	Multipar & nullipar	26.7	Prospective cohort	1033	20 (1.9)	NR
Moghadamei, et al. (2001)	Tehran	Multipar & nullipar	26.1	Prospective cohort	260	17 (6.5)	NR
Mohaddesi and Nanbakhsh (2012)	Urmia	Multipar & nullipar	31.3	Cross-sectional	2824	166 (5.9)	NR
Mohammadi, et al. (2010)	Noor city	Multipar & nullipar	26.2	Prospective cohort	400	34 (8.5)	NR
Nanbakhsh, et al. (2006)	Urmia	Multipar & nullipar	31.7	Cross-sectional	738	13 (1.8)	NR
Safari and Yazdanpanah (2001)	Yasuj	Multipar & nullipar	NR	Cross-sectional	1000	54 (5.4)	5 (0.5)
Safavi Arbedili, et al. (2011)	Tehran	Multipar & nullipar	27.2	Prospective cohort	600	40 (6.7)	NR
Seyed Aghamiri, et al. (2008)	Tehran	Multipar & nullipar	25.9	Cross-sectional	4490	91 (2)	NR
Sohrabi, et al. (2009)	Tehran	Multipar & nullipar	27.2	Cross-sectional	46628	1811 (3.9)	NR
Taghi Zadeh, et al. (2009)	Tehran	Multipar & nullipar	25.7	Prospective cohort	660	58 (8.8)	NR
Yazdani, et al. (2012)	Babol	Nullipar	NR	Retrospective cohort	1000	69 (6.9)	NR
Zahiri Soroori, et al. (2007)	Gilan	Multipar & nullipar	NR	Cross-sectional	12142	397 (3.3)	17 (0.14)
Zareian, (2004)	Jahrom	Multipar & nullipar	NR	Cross-sectional	2300	28 (1.2)	3 (0.13)
Zibaeenezhad, et al. (2010)	Shiraz	Multipar & nullipar	NR	Cross-sectional	24196	148 (0.6)	2 (0.008)

**Khorassan-e-Razavi, Kerman, Mazandaran, Sistan Bluchestan, Kordestan, and Lorestan; NR: not reported.

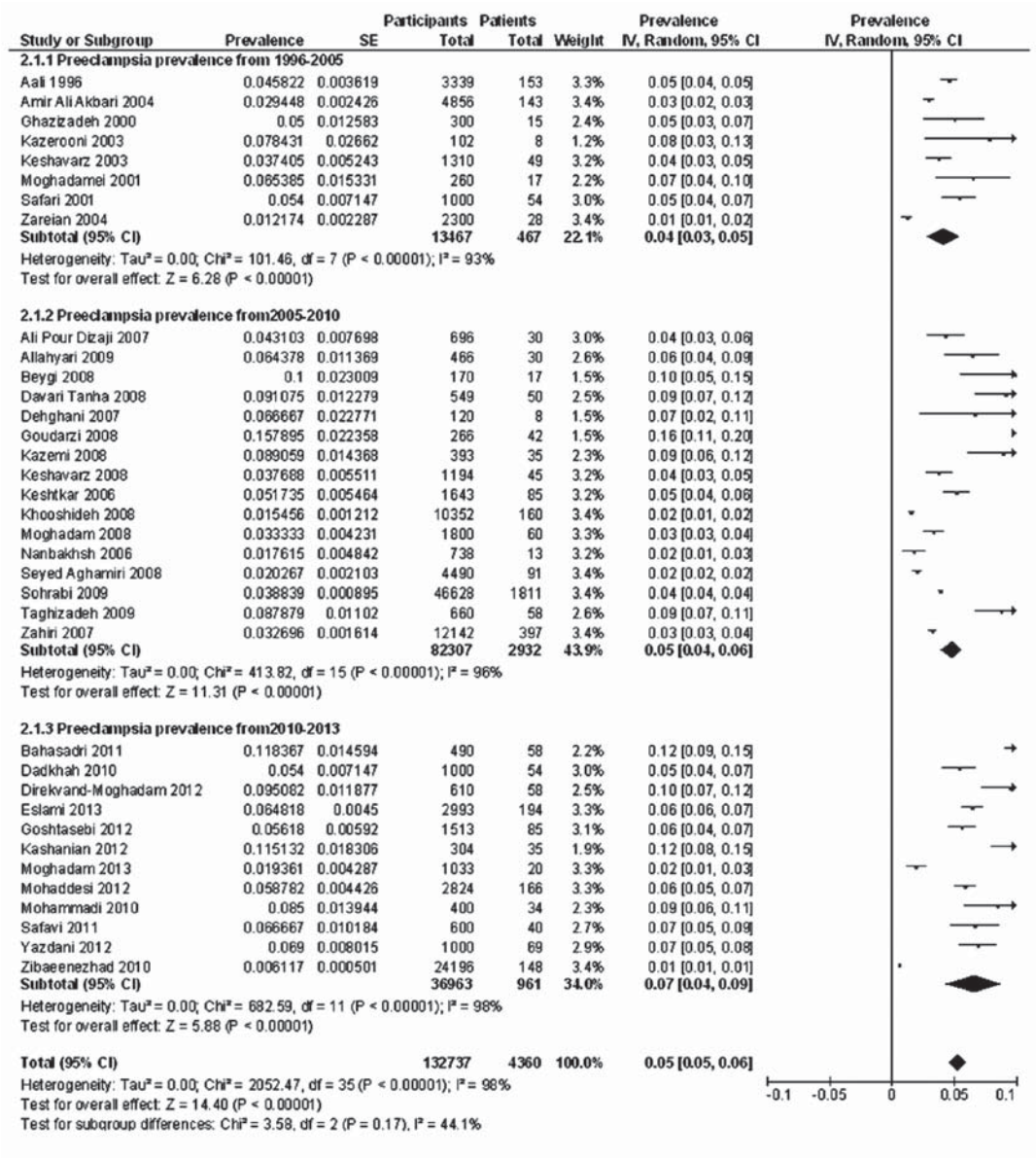

Figure 2. Forest plot of preeclampsia prevalence by year among Iranian pregnant women

There was strong evidence of heterogeneity among the results of the included studies based on the *P*-value of Chi-square test and large *I*-square statistic. Some of the observed heterogeneity could be attributed to the large number of the studies (36 studies) and large sample sizes (132,737 participants) included in the meta-analysis. Because when the sample size is small, the power of the Chi-square test is low. In contrast, when the sample size is high like this study, the test has high power for detecting a small measure of heterogeneity that may be clinically unimportant.[24] Another reason could be the existence of the significant differences between the results of the studies. Also, high quality studies had a lower *I*-square statistic than low or intermediate quality studies (91% vs. 97%) that could be shown the effect of the quality on the homogeneity of the study results. The prevalence of eclampsia in low quality studies was overestimated as well. Despite the significant observed heterogeneity, the tau-square statistic was very small. The reason may be that between-studies variance was low and within-studies variance was high.[68]

Limitations

There were several limitations in this study. First, only 36% of the included studies had high quality; which may increase the possibility of the information bias. Second, no study had been used the new definition of preeclampsia, which may raise the prevalence rate of it.[67] Third, a considerable proportion of the studies was conducted in Tehran (17/36), which may raise the possibility of selection bias.

In conclusion, the preeclampsia prevalence has been increasing in recent years, while the eclampsia prevalence has been decreasing during the same years. It seems that, in the future, preeclampsia and its associated complications will become a serious public health problem in Iran. This issue should be the focus of special attention of policy makers. In addition, despite many studies had been implemented aiming the prevalence of preeclampsia and eclampsia in Iranian pregnant women, there were a significant heterogeneity between the results. Therefore, it seems that a national survey is needed to estimate the exact prevalence of preeclampsia

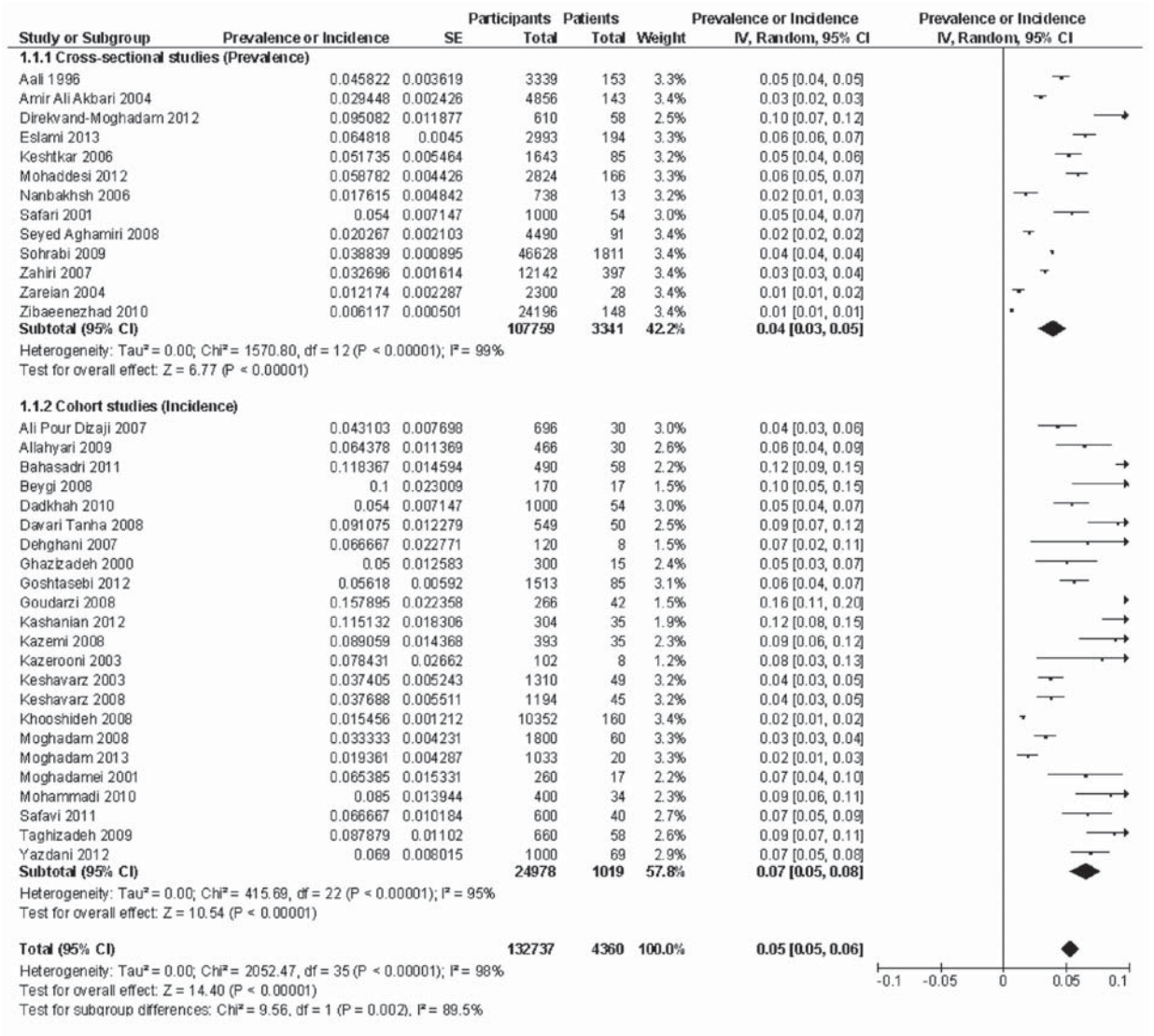

Figure 3. Forest plot of preeclampsia prevalence by design of the studies

Table 2. Subgroup analysis of prevalence of preeclampsia and eclampsia

	Preeclampsia		*P*-Value	Eclampsia		*P*-Value
	Prevalence	95% CI		Prevalence (%)	95% CI	
Quality of the studies						
High	0.05	0.05, 0.06	< 0.001	0.15	0.13, 0.18	< 0.001
Intermediate	0.05	0.04, 0.07	< 0.001	0.21	0.03, 0.40	0.023
Low	0.05	0.04, 0.06	< 0.001	0.42	0.40, 0.44	< 0.001
Year of the studies						
1996–2005	0.04	0.03, 0.05	< 0.001	0.30	0.15, 0.45	< 0.001
2005–2010	0.05	0.04, 0.06	< 0.001	0.14	0.13, 0.15	< 0.001
2010–2013	0.07	0.04, 0.09	< 0.001	0.01	0.01, 0.01	< 0.001
Location of the studies						
Tehran	0.05	0.05, 0.06	< 0.001	0.16	0.15, 0.18	< 0.001
Other cities	0.05	0.04, 0.06	< 0.001	0.24	0.12, 0.36	< 0.001
Design of the studies						< 0.001
Cross-sectional (prevalence)	0.04	0.03, 0.05	< 0.001	0.23	0.12, 0.33	
Prospective or retrospective cohort (cumulative incidence)	0.07	0.05, 0.08	< 0.001	- - -	- - -	- - -
Parity of the mothers						< 0.001
Nullipar	0.06	0.04, 0.09	< 0.001	- - -	- - -	- - -
Multipar and nullipar	0.05	0.04, 0.06	< 0.001	0.23	0.12, 0.33	- - -

and eclampsia in the country. Moreover, the establishment of a surveillance of risk assessment system during pregnancy in Iran could provide valuable estimations on the prevalence of maternal and child health problems such as preeclampsia and eclampsia.[69]

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