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Systematic Review (Pages: 3815-3836)

Prevalence of Macrosomia in Iran: A Systematic Review and Meta-Analysis

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Abstract

***Background*:** Macrosomia is a risk factor for adverse maternal and neonatal outcomes and previous studies have reported different prevalence of macrosomia in Iran. We conducted a meta-analysis to estimate the overall prevalence of macrosomia in Iran.

***Materials and Methods*:** A systematic review and meta-analysis was conducted of all published literature pertaining to prevalence rates of macrosomia using international and national electronic databases ISI Web of Knowledge, PubMed, Scopus, SID, Magiran and Google Scholar from their inception until June 2017 with standard keywords. Egger test and Funnel plot were used to evaluate the publication bias and Cochran test and I^2 statistics were used to examine the statistical heterogeneity. Pooled estimate of the prevalence of macrosomia were calculated using random effects meta-analysis.

***Results*:** A total of 40 studies were included in this meta-analysis. The publication bias assumption was rejected Egger test (P=0.719) and Funnel plot. The results of Cochran test and I^2 statistics revealed substantial heterogeneity (Q=1040.5.00, df = 39, P<0.001 and I^2=96.3%). The overall prevalence of macrosomia using the random effect model in Iran was 5.2% (95% confidence interval [CI]: 4.4-5.9). Moreover, the macrosomia prevalence in Tehran and other cities were 3.9% (95% CI: 3.2-4.7) and 6.0% (95% CI: 5.0-7.1), respectively.

Conclusion: The macrosomia rate in Iran is high. There is a critical need to improve the education and the gestational care and identifying at risk neonates to reduce the macrosomia rate and its adverse outcomes.

Key Words: Iran, Macrosomia, Meta-analysis, Neonate, Prevalence, Systematic review.

*Please cite this article as: Maroufizadeh S, Almasi-Hashiani A, Esmaeilzadeh A, Mohammadi M, Amini P, Omani Samani R. Prevalence of Macrosomia in Iran: A Systematic Review and Meta-Analysis. Int J Pediatr 2017; 5(9): 5617-29. DOI: **10.22038/ijp.2017.24357.2056**

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Received date: Jun.05, 2017; Accepted date: Jun.22, 2017

1- INTRODUCTION

The term macrosomia is used to describe a neonate with a large birth weight (1). Although no absolute consensus has been reached to define this disorder, most previous studies have used a birth weight of more than 4,000g as definition (1, 2). Macrosomia is associated with diverse maternal and neonatal complications. Maternal complications of macrosomia include cesarean delivery, prolonged labor, perineal trauma and postpartum hemorrhage (1, 3). For infant, the immediate complications are shoulder dystocia, infant birth injury and death and later complications include higher risks of diabetes and obesity in adulthood (1, 3-6).

Known risk factors that increase the probability of bearing an infant with macrosomia include maternal diabetes and obesity, excessive weight gain, male fetal sex, prolonged gestation, high maternal age, previous macrosomia and multiparty (2, 7). The prevalence of macrosomia in the USA is 8.0% (8); In developed countries, reported prevalence rate varies from 5% to 20% (1). Furthermore, according to the results obtained from 276,436 births in 363 institutions in 23 developing countries in Asia, Africa, and Latin America, the rate of macrosomia was between 0.5% (India), and 14.9% (Algeria) (2). Numerous studies have been performed to determine the prevalence rate of macrosomia and its associated factors in Iran. However, there is a substantial diversity among the findings.

The prevalence rate of macrosomia in these studies was between 2.00% and 13.75% (9-48). Due to the considerable heterogeneity among the reported prevalence rate of macrosomia and its short- and long-term consequences for neonates and mother, which constitutes a major burden for health care systems, the accurate determination of macrosomia prevalence rate is necessary for strategic plan and health policy. Therefore, we conducted a systematic review and meta-analysis of all published studies to estimate the overall prevalence rate of macrosomia in Iran.

2- MATERIALS AND METHODS

2-1. Search strategy

This meta-analysis was performed according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (49). We conducted a literature search of published papers in June 2017 using international (ISI Web of Knowledge, PubMed, Scopus) and national (SID and Magiran) electronic databases and Google Scholar. Key words included "macrosomia", "prevalence", "Iran". We also checked the reference lists of the included article and review articles for further relevant articles. No language or time restriction was applied to the searches. The grey literature were searched using Google Scholar, as recommended by Haddaway et al. (50), using the abovementioned search strategy. More details about the search strategy are displayed in **Box.1.**

2-2. Inclusion and exclusion criteria

The following inclusion criteria were used to select studies for the meta-analysis: (1) studies with prevalence estimates of macrosomia, (2) studies of any language and time. We excluded the following studies: (1) intervention or treatment studies, (2) repeated or overlapping studies, and (3) no usable data reported.

2-3. Outcome

The outcome variable was macrosomia, defined as "a birth weight > 4,000 grams" (1, 2).

2-4. Data extraction and quality assessment

Two authors (SM and AAH) independently extracted the following data

from the included studies: first author's name, year of publication, location, year of study, sample size, definition of macrosomia, prevalence estimate of macrosomia. Two reviewers (SM and AAH) independently performed the quality assessment based on modified STROBE checklist (http://www.strobe-statement.org/); any Discrepancy, were resolved by third author (PA).

2-5. Statistical analysis

All data analyses were carried out with STATA version 13.0 (StataCorp, College Station, TX, USA). The Cochrane Q test and I^2 statistic were used to test heterogeneity across studies (51). A P-value <0.1, rather than <0.05, was used as evidence of heterogeneity for the Cochrane Q test, as suggested by the Cochrane Collaboration. The I^2 statistic expresses the percentage of total variation across studies due to heterogeneity. I^2 values of 25%, 50% and 75% correspond to low, moderate and high heterogeneity, respectively (51). Considering the remarkable heterogeneity among studies, we used a random effects model for all analyses. Meta regression was used to explore the sources of between-study heterogeneity, including year of study, sample size and place of study. We conducted sensitivity analyses by excluding each study at a time from the meta-analysis. The Funnel plot and Egger's weighted regression test were used to assess publication bias (52, 53).

3- RESULTS

3-1. Study Selection

Figure.1 shows a flow chart of the search studies and selection process for inclusion in the meta-analysis. We identified 195 articles from the database search. After removing duplicates, 134 articles remained. We excluded 85 articles by screening titles and abstracts, and retrieved the full texts of 49 remaining articles. Finally, we identified 40 articles in the present meta-analysis (**Figure.1**).

Box 1. Search strategy for PubMed (MeSH, Medical Subject Heading)

1- "Fetal Macrosomia"[Mesh]
2- "Fetal Macrosomia"[Text Word]
3- "Fetal Macrosomias"[Text Word]
4- "Macrosomia"[Text Word]
5- "Macrosomias"[Text Word]
6- OR 2 OR 3 OR 4 OR 5
7- "Prevalence"[Mesh]
8- "Prevalence"[Text Word]
9- OR 8
10- "Iran"[Mesh]
11- "Iran"[Text Word]
12- 10 OR 11
13- 6 AND 9 AND 12

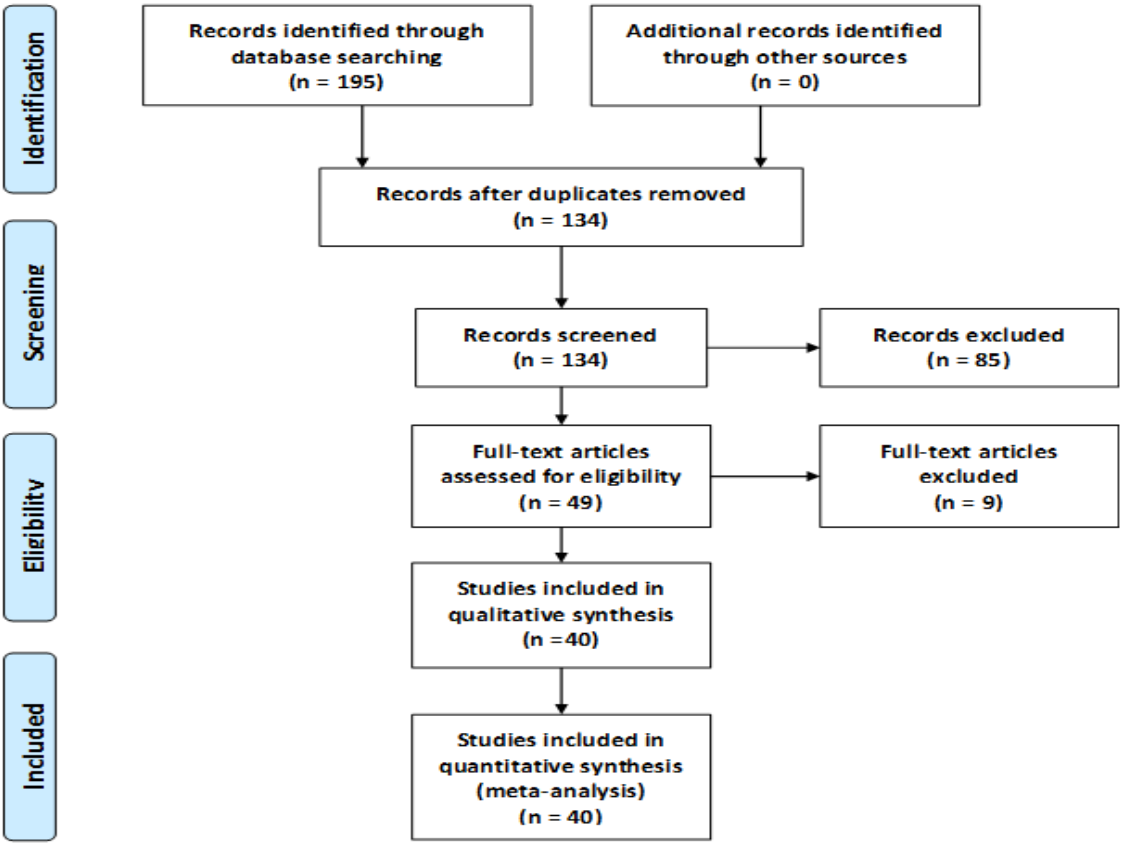

Fig.1: Flow diagram of study process.

3-2. Study Characteristics

The characteristics of included studies are presented in **Table.1**. These studies were published between 1999 (9) and 2016 (48). Fifteen studies were conducted in Tehran, the capital of Iran. The sample size of included articles varied from 100 (17) to 20,000 (35), with a total of 106,665 cases (*Please see the end of paper*).

3-3. Evaluation of Heterogeneity and Meta-Analysis

The results of Cochran's Q test and I^2 statistics showed high heterogeneity among the included studies (Q=1040.5, df = 39, P<0.001 and I^2=96.3%), and thus random effects model was used for meta-analysis. The overall, pooled prevalence of macrosomia was 5.2% (95% CI: 4.4-5.9). As shown in **Figure.2**, the lowest and highest prevalence of macrosomia was reported by Forouzmehr et al. in Isfahan (2.00%, 95% CI: 0.4-3.6) (12), and Yazdani et al. in Babol (13.75%, 95% CI: 8.4-19.1) (45) (*Please see the end of paper*).

3-4. Publication Bias

The funnel plot showed symmetry, suggesting the absence of publication bias among the included studies (**Figure.3**). Similarly, the Egger's test indicated no evidence of publication bias among the

included studies (P=0.719) (*Please see the end of paper*).

3-5. Meta Regression

Meta regression was used to explore the sources of between-study heterogeneity, including year of study, sample size and place of the study. It was found by meta-regression that the place of the study (Tehran- Other cities) might be the source of heterogeneity (P=0.017), but not the year of study (P=0.472) or the sample size (P=0.278). Therefore, a sub group analysis based on place of the study was done. According to the results, prevalence of macrosomia in Tehran (3.9%, 95% CI: 3.2-4.7) was lower than other cities (6.0%, 95% CI: 5.0-7.1) (**Figure.4**) (*Please see the end of paper*).

3-6. Sensitivity Analysis

We conducted sensitivity analyses by excluding one study at a time and recalculating the prevalence rate to evaluate whether the summary prevalence was significantly influenced by any Individual Study. Based on the sensitivity analysis, no study had a notable influence on the overall estimate, the pooled prevalence varying between 4.98% [when excluding Najafian et al. (35)] and 5.24% [when excluding Forouzmehr et al. (12)].

4- DISCUSSION

Macrosomia is associated with increased risks of adverse delivery outcomes. Several studies have been conducted to determine the prevalence of macrosomia in Iran, but the results were inconsistent. As individual studies may have insufficient sample size, our meta-analysis of ten studies involving a relatively large number of births and provided more reliable estimates of prevalence of macrosomia. To the best of our knowledge, this is the first systematic review and meta-analysis study that focuses on prevalence rate of macrosomia in Iran. Forty studies with a total of 106,665 births were identified. In the present study, the overall prevalence of macrosomia using the random effect model was 5.2%, which is lower than what was reported in USA (8.0%) (8) and Nordic countries (1), but higher than what was reported in some developing countries in Africa such as Niger (2.5%), DRC (2.8%), Angola (2.8%) and Kenya (3.6%) and South and Southeast Asia such as India (0.5%), Philippines (1.1%), Sri Lanka (1.3), Nepal (1.5%), Thailand (2.2%), Cambodia (2.3%) and Vietnam (3.4%) (2). This difference may be due to geographic and ethnic diversity and different type of nutrition. The results of meta-regression showed that the prevalence rate of macrosomia was not associated with year of study and sample size, but was associated with location of the study. Since the year of study and sample size were not significantly associated to the prevalence of macrosomia, we cannot consider the sample size and the year of the study as the cause of heterogeneity, so this heterogeneity can be due to other factors.

However, over the past few decades the rate of this disorder has increased worldwide which it could be due to increased prevalence of diabetes and obesity in women of reproductive age. In this study, the location of the study was significantly associated with the prevalence of macrosomia, as it was observed that the prevalence of macrosomia in Tehran was lower than other cities in the country. This difference could be due to racial, geographical, and nutrition differences, body mass index of the mother, order of birth and prenatal care. The present study has several strengths that should be mentioned. The major strengths of our study were the large sample size of birth, which enabled us to estimate the overall prevalence of macrosomia from different prevalence

studies. Second, the funnel plot and the Begg and Egger's tests did not support the presence of publication bias, providing further indication of the robustness of our results. Third, the definition of macrosomia was not varied among the included articles. Nevertheless, the meta-analysis has some limitations that should be considered when interpreting the results. First, substantial heterogeneity was detected among studies. Therefore, even if we used random effects model to take heterogeneity into account, our overall estimates should be interpreted with caution. Second, we could not perform meta-regression for other sources of between-study heterogeneity—maternal age, maternal obesity, gestational diabetes and excessive weight gain—since we did not have data on these factors. These variables have been found to be associated with macrosomia. Third, the generalizability of the findings should be interpreted with caution. The 37.5% of the articles included in this study were conducted in Tehran, the capital of Iran; and finally, we did not search some other database such as Embase, CINAHL and DOAJ.

5- CONCLUSIONS

Macrosomia has multiple complications for mother and its infant and it has a considerable socio-economic burden and needs to be diminished. According to the results, the prevalence of macrosomia in Iran, particularly outside Tehran, was relatively high, so implementing activities such as identification of mothers at risk, providing necessary training for them, and improving prenatal care can reduce rates of Macrosomic births.

6- CONFLICT OF INTEREST: None.

7- ACKNOWLEDGMENTS

This study was founded by Reproductive Epidemiology Research Center, Royan Institute for Reproductive Biomedicine, ACECR, Tehran, Iran.

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Table 1 Description of the studies included in the meta-analysis

	Authors	Publication year	Location	Year	Sample Size
1	Eftekhari (9)	1999	Kerman	1999	2000
2	Fakhri (10)	2000	Sari	1997	5440
3	Ghaemmaghami (11)	2002	Tehran	2000	450
4	Forouzmehr (12)	2004	Isfahan	2002-2003	300
5	Barouti (13)	2004	Tehran	2003-2004	300
6	Keshavarz (14)	2005	Shahrood	2001	1,310
7	Kahnamoiee (15)	2005	Ardabil	1999-2000	1,000
8	Gharibzadeh (16)	2005	Tehran	2002	3,377
9	Behnamfar (17)	2005	Kashan	2004	100
10	Haji Ebrahim Tehrani (18)	2007	Tehran	2004	17,236
11	Hossein-Nezhad (19)	2007	Tehran	2007*	2,416
12	Khalili Matinzade (20)	2007	Tehran	2004-2005	2,226
13	Tabandeh (21)	2007	Gorgan	2003-2004	350
14	Mortazavi (22)	2008	Sabzevar	2003	795
15	Garshasebi (23)	2008	Tehran	2005-2006	1,805
16	Mosavat (24)	2008	Rafsanjan	2005	3,340
17	Ghanbari (25)	2008	Tehran	2008	2,000
18	Mohammadbeigi (26)	2009	Shiraz	2006	414
19	Panahandeh (27)	2009	Rasht	2005-2006	918
20	Khoshniat Nikoo (28)	2010	Tehran	2005	1,801
21	Hematyar (29)	2010	Tehran	2006	1,000

22	Faraji (30)	2010	Rasht	2007	555
23	Hematyar (31)	2011	Tehran	2009	200
24	Sekhavat (32)	2011	Yazd	2002-2004	940
25	Tabatabaei (33)	2011	Kazerun	2010	5,172
26	Marsoosi (34)	2011	Tehran	2008-2010	2,219
27	Najafian (35)	2012	Ahwaz	2011	20,000
28	Sharifzadeh (36)	2012	Tehran	2008-2009	396
29	Salimi (37)	2012	Ardabil	2009	6,685
30	Pakniat (38)	2012	Qazvin	2010-2011	1,376
31	Yazdani (39)	2012	Babol	2008-2009	1,000
32	Alijahan (40)	2013	Ardabil	2009-2010	8270
33	Esmaili (41)	2014	Mashhad	2010	800
34	Mardani (42)	2014	Khorramabad	2010	500
35	Bahrami (43)	2014	Qazvin	2010	3,076
36	Akbari (44)	2014	Khorramabad	2013	600
37	Yazdani (45)	2014	Babol	2012	160
38	Mossayebi (46)	2014	Tehran	2010-211	154
39	(47)Bahrami Taghanaki	2016	Mashhad	2013	1,642
40	Maroufizadeh (48)	2016	Tehran	2015	4,342

* Year of publication.

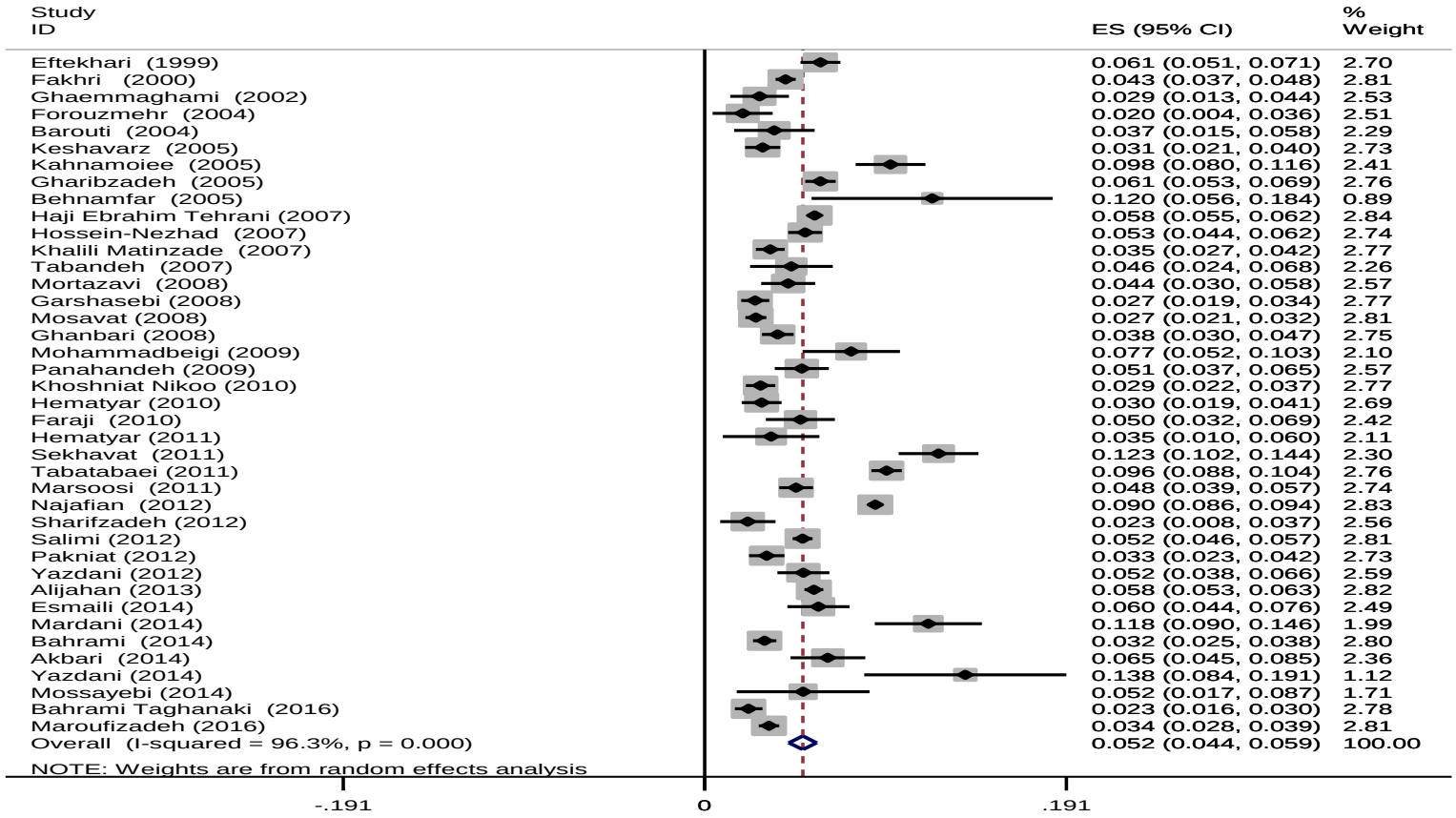

Fig.2: Forest plot showing prevalence of macrosomia in Iran.

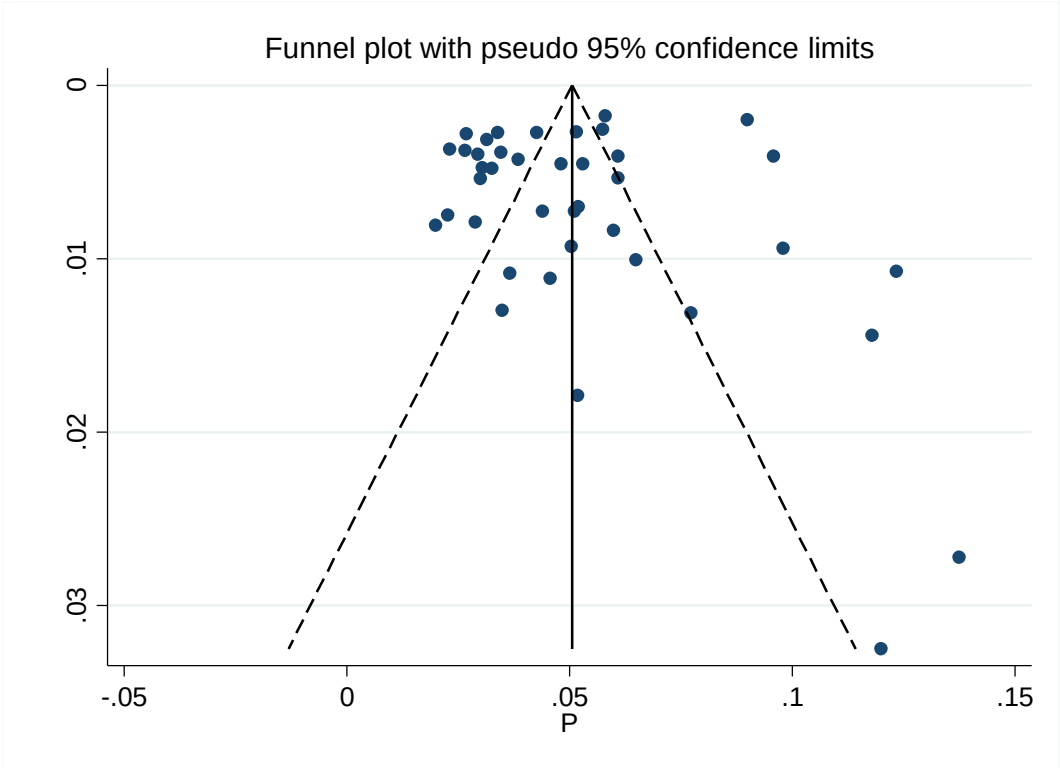

Fig.3: Funnel plot for assessing publication bias in meta-analysis.

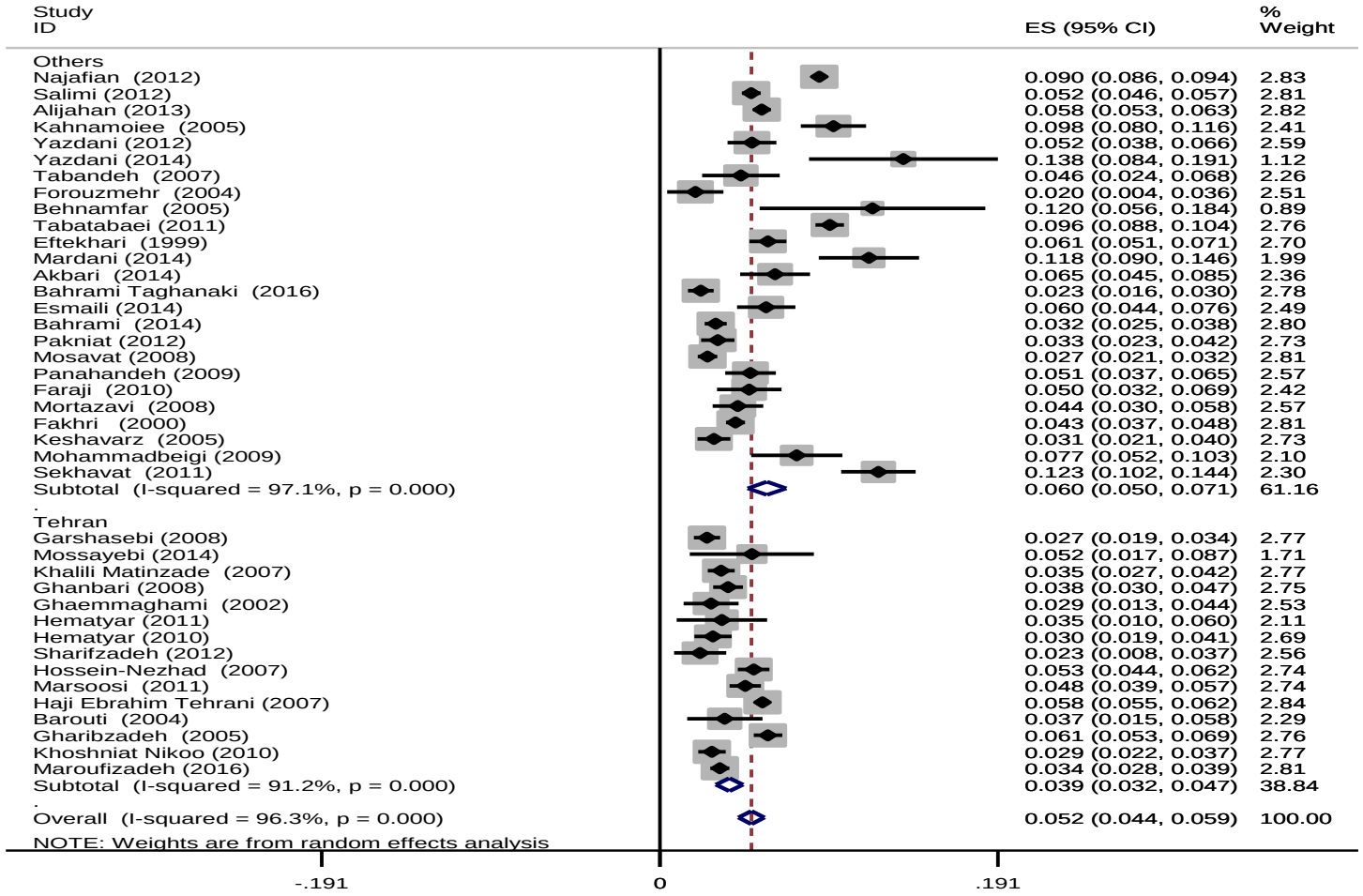

Fig.4: Forest plot showing prevalence of macrosomia according to location of the study (Tehran, Other cities) in Iran.