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Original Article

Family history of diabetes and the risk of gestational diabetes mellitus in Iran: A systematic review and meta-analysis

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ABSTRACT

Objective: Gestational diabetes is the most prevalent metabolic disorder being firstly diagnosed during pregnancy. The relationship between the family history of diabetes and the gestational diabetes mellitus (GDM) has been investigated in several primary studies with a number of contradictions in the results. Hence, the purpose of the present study is to determine the relationship between the GDM and the family history of diabetes using the meta-analysis method.
Method: All published papers in main national and international databases were systematically searched with some specific keywords to find the related studies between 2000 and 2016. We calculated the odds ratio (OR) with 95% confidence interval (CI) in analysis for each study using a random-effect and Mantel-Haenzel method. We also determined heterogeneity among these 33 articles and their publication bias.
Results: We entered 33 relevant studies of 2516 articles into the meta-analysis process including 2697 women with family history of diabetes mellitus as well as 29134 women without. Of them, 954 and 4372 subjects developed GDM respectively. Combining the results of the primary studies using the meta-analysis method, the overall odds ratio of family history for developing GDM was estimated as of 3.46 (95% CI: 2.80–4.27).
Conclusion: This meta-analysis study revealed that the family history of diabetes is an important risk factor for the gestational diabetes mellitus.

1. Introduction

Gestational diabetes mellitus (GDM) is defined as glucose intolerance identified during pregnancy [1]. The prevalence of GDM ranges between 2.4 and 22.3% worldwide [2]. Moreover, the global rate of women with GDM is increasing [3].

It has been reported that many maternal and fetal morbidities are associated with GDM [4,5]. Without appropriate control of GDM, a considerable proportion of them will develop type 2 diabetes during lifetime [6].

According to the available guidelines, several factors increase the risk of GDM: such as, older maternal age, familial history of diabetes (particularly in a first-degree relatives), previous history of GDM, previous history of a macrosomic birth, maternal body mass index more than 30 kg/m^2, genetic factors, and ethnicity particularly in Middle Eastern women [3,7–10].

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Screening for GDM among all pregnant women is costly and is not possible in many communities [11]. Therefore these factors should be considered as cost effective predictors of GDM.

Several evidences are reported family history of diabetes mellitus as a risk factor for developing GDM [11–14]. This association among Iranian population has been reported by primary observational studies which might be prone to methodological biases such as limited sample sizes. Therefore, the estimates might be imprecise [14–16].

To understand the strength of association between GDM and FHD appropriate methodology for search and combining the results of these primary studies is needed. the aim of this study is to estimate the total relationship between GDM and FHD among Iranian pregnant women using a systematic review and Meta-analysis method which is considered as a strongest evidence for this purpose [15].

2. Methods

2.1. Search process

In this study, to find the electronically published articles from 2000 to April 30th 2016, the evidences published in the national and international databases such as Scientific Information Database (SID), Iranmedex, Magiran, Irandoc, PubMed, Google scholar, Scopus, and Web of Science were searched. The search strategy was performed using the following keywords “gestational diabetes mellitus”; “GDM”; “pregnancy induced diabetes”; “risk factor”; “family history of diabetes”; “Iran” and their Persian equivalents. Searching was carried out between May 14th and 27th; 2016. Moreover; the list of references of the published studies was investigated to increase sensitivity and identify a large number of studies. The searching process was independently performed by two researchers. The agreement coefficient of the search results between these two was 79%. The disagreements were studied by a third person. In addition; the research centers and experts in the field of gynecology and endocrinology were interviewed to find unpublished studies.

2.2. Study selection

The full text or abstracts of all papers, documents, and reports were extracted from the advanced search. After removing the duplicates, the irrelevant evidences were removed and the remained papers were investigated in detail reviewing the titles, abstracts and full texts. We selected all studies that Cases (with GDM) had been diagnosed during GDM screening in pregnancy based on the national guidelines [17]. Controls (without GDM) were pregnant women who were considered healthy based on the gestational diabetes screening tests records. It should be noted that

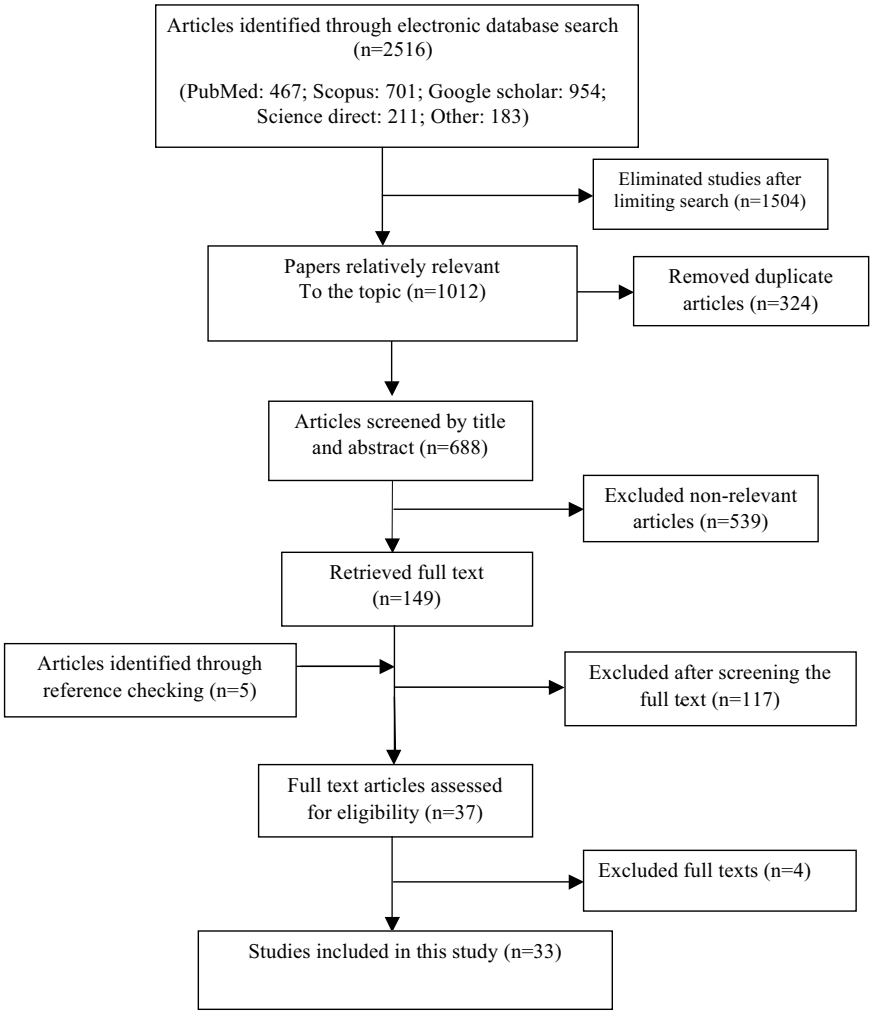

Fig. 1. Literature search and review flowchart for selection of primary studies.

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to prevent bias caused by re-publishing (publication transverse and longitudinal biases), the researchers tried to investigate the results of papers to identify and remove any repeated results.

2.3. Quality assessment

After determining the relevant studies in terms of title and content, the STROBE (ELM) checklist was used to assess the quality of documentation. This checklist includes questions that cover various methodological aspects including the sample size, sampling methods, study population, the data collection method, defining the variables and the way the samples are studied, the data collection tools, statistical tests, research objectives, appropriate presentation of the data and presenting the results based on the objectives. The studies have obtained at least 15 scores, were considered eligible for meta-analysis.

2.4. Inclusion criteria

All English and Persian studies which have achieved the minimum score of quality assessment, Cross-sectional, case-control and cohort studies reporting the sample size of the study and prevalence/incidence of exposure/outcome according to cases/controls or exposed/unexposed groups were included in the meta-analysis.

2.5. Exclusion criteria

Case reports or cases series, papers in which the number of the sample size and the frequency of the outcome/exposure in terms of the case control groups or exposed/unexposed groups were not mentioned, abstracts submitted to the conferences without full text and the studies did not achieve the minimum quality assessment score, were excluded from the study.

2.6. Data extraction

The data were extracted according to the title, the name of the first author, the year of the study, the type of the study, sample size in the case and control group, the number of outcome in terms of the case and control group, and publication language. Data input was done in Excel spreadsheet.

2.7. Data synthesis

The Stata software was used to analyze the data. The heterogeneity index between the studies was determined using the Cochran's test (Q) and I square. The Mantel-Haenzel method and the random effect model were used to estimate the total odds ratio of family history for developing GDM. The point estimates with the 95% confidence intervals were illustrated in forest plots. In this curve, the box size and the lines on both sides represented the weight of each study and the 95% confidence interval, respectively. Moreover, the egger test was used to assess the publication bias and the significance level of below 0.01 has been the judgment criterion. Also, meta-regression and subgroup analysis were conducted to assess the factors for heterogeneity.

3. Results

Totally, 2516 articles were found during the primary search. After restricting the search strategy and removing the duplicates

Table 1
The characteristics of the primary studies having the meta-analysis inclusion criteria of the relationship between the family history of diabetes and the gestational diabetes mellitus.

Id	First Author	Publication year	Type of study	With Family history of diabetes (number)		Without Family history of diabetes (number)	
				With GDM	Without GDM	With GDM	Without GDM
1	Keshavarz [26]	2005	cohort	27	36	174	1073
2	Hossein-Nezhad [23]	2007	cross-sectional	38	76	192	1670
3	Garshasbi [27]	2008	cross-sectional	53	71	284	1520
4	Goli [28]	2012	cross-sectional	23	54	199	1738
5	Mohamad beigi [29]	2007	case-control	21	27	42	308
6	Larijani [30]	2004	cross-sectional	38	76	237	2065
7	Mirfazi [31]	2010	cross-sectional	40	84	91	453
8	Atashzadeh [32]	2006	cross-sectional	30	77	231	1883
9	Karimi [33]	2002	cohort	20	44	195	651
10	Zokaie [34]	2014	case-control	74	146	24	196
11	Hossein-Nezhad [35]	2009	cohort	57	57	900	1402
12	Rahimi [36]	2010	cross-sectional	22	56	111	1550
13	Dehaki [37]	2015	cross-sectional	5	12	33	313
14	Akhlaghi [38]	2012	cross-sectional	15	15	9	21
15	Fekrat [39]	2004	cross-sectional	35	27	10	70
16	Mohamad beigi [40]	2009	cross-sectional	37	33	42	308
17	Navaei [41]	2002	cross-sectional	6	13	120	594
18	Mohamadzadeh [42]	2012	cross-sectional	22	40	205	1009
19	Bozari [43]	2013	cross-sectional	38	47	66	853
20	Ghabi [44]	2002	cross-sectional	32	138	6	244
21	Shiraziyan [25]	2009	Cohort	9	59	203	653
22	Sharifi [45]	2010	case-control	30	34	3	61
23	Khooshideh [46]	2008	Cohort	14	53	28	305
24	Maghboli [47]	2005	Cohort	38	76	258	2044
25	Eslamian [48]	2013	Cohort	23	89	9	150
26	Vakili [49]	2014	cross-sectional	20	28	63	289
27	Karajibani [50]	2015	cross-sectional	26	44	18	122
28	Hadaegh [51]	2005	cross-sectional	8	54	59	579
29	Tabatabaei [52]	2007	cross-sectional	17	56	134	878
30	Kariman [53]	2006	case-control	28	32	19	41
31	Soheilykhah [54]	2010	Cohort	74	36	230	654
32	Heidary [55]	2008	case-control	28	32	19	41
33	Larijani [56]	2002	cross-sectional	6	21	158	1024

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because of the overlap of the databases, 688 documents were removed. Then, 539 irrelevant cases were detected by screening the title and the abstract. The full texts of 149 remaining articles were investigated where 117 cases were irrelevant. Five articles were also introduced into the study by evaluating the references. Then, four documents were removed and 33 remaining articles were introduced into the meta-analysis process by evaluating the quality of the articles and inclusion/exclusion criteria (Fig. 1).

The relationship between the family history of diabetes and the GDM was studied in 33 papers. The articles introduced into the meta-analysis had been published between 2002 and 2015. The type of the studies were Cohort (eight studies), case-control (five studies), and cross-sectional (20 studies) (Table 1).

According to the results of the cohort studies, among 712 pregnant women reported familial history of diabetes, 262 women developed GDM. Of 8929 pregnant women without familial history of diabetes, 1997 developed GDM. Combining the results of the eight cohort studies using the meta-analysis method, the overall estimate of the odds ratio of being diagnosed with the GDM was estimated at 2.54(95% CI: 1.50–4.29).

The total sample size of cases and controls in five case-control studies were 452 (181 of which had familial history of diabetes) and 754 (107 reported familial history of diabetes) respectively. The overall estimate of the odds ratio of being diagnosed with the GDM for these five studies was 3.91 (95% CI: 2.11–7.23).

According to the results of cross-sectional studies, frequencies of GDM pregnant women among those with and without familial history of diabetes mellitus were 511/1533 and 2268/19451 respectively. Combining the results of the 20 cross-sectional studies using the meta-analysis method, the overall estimate of the odds ratio of being diagnosed with the GDM was 3.86 (95% CI: 3.07–4.84).

It is worth mentioning that the confidence interval of the estimated odds ratio separately obtained by the Cohort, case-control, and cross-sectional studies would overlap, this means that the differences are not statistically significant. Thus, the combination of the results of 33 studies is possible using the meta-analysis. Moreover, the temporal priority of exposure (family history of diabetes) over the outcome (GDM), which is one of the Hill's casual relations, has been proved in all studies introduced into the meta-analysis. The total sample size of women with positive familial history in all 33 studies was 2697, 954 of which were diagnosed as GDM. The corresponding size for women without family history was 29134. Of them, 4372 women developed GDM. Combining the results of these 33 studies using meta-analysis method, the overall estimate of the odds ratio of being diagnosed with the GDM in was 3.46 (95% CI: 2.80–427) (Fig. 2).

According to the results of the statistical Egger test, no publication bias was observed ($\beta = -0.21$, $P = 0.9$).Also, the type of the study was investigated as a factor being suspicious for

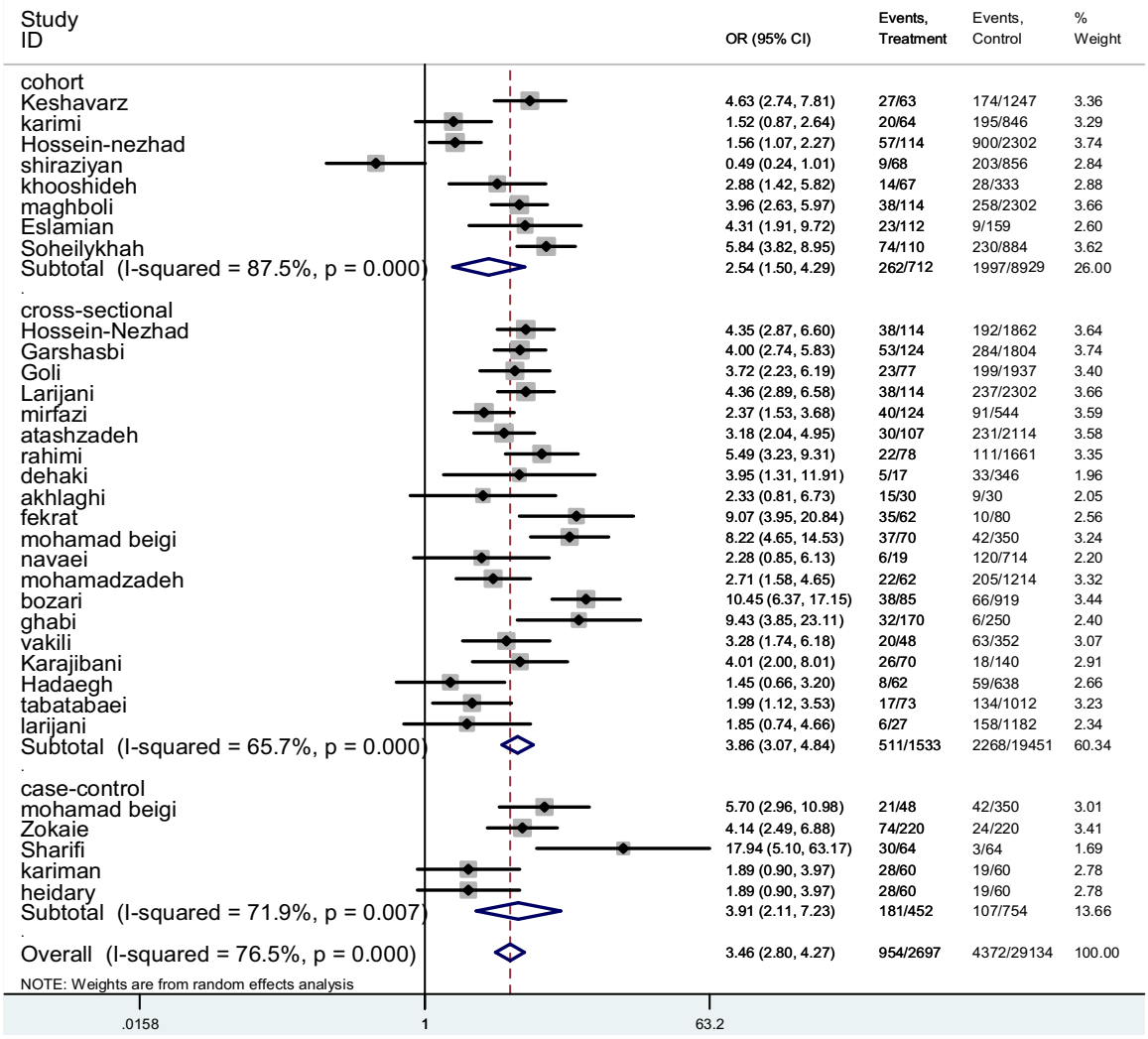

Fig. 2. Estimation of the odds ratio of the association between family history of diabetes and gestational diabetes mellitus by using the random effect model.

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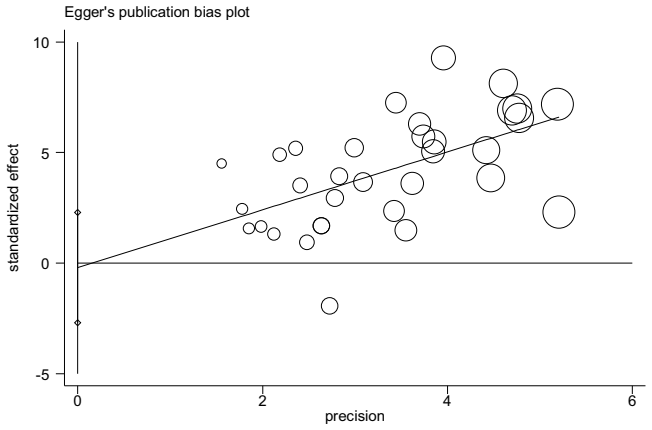

Fig. 3. The Egger graph of studying the publishing bias of the results by using the meta-bias order associated with the effect of the family history of diabetes on the gestational diabetes mellitus.

heterogeneity using the meta-regression method (Fig. 3). The test results revealed that the type of study has not significant impact on heterogeneity between the results of the primary studies ($\beta = 0.19$, $P = 0.2$).

4. Discussion

4.1. Summary of findings

The present study revealed that the odd Ratio (OR) of GDM appears to be mainly associated by the positive family history of diabetes. In a way that, the odds of GDM in women with positive familial history was 3.46 folds greater than that in those without. This systematic review showed that FHD is a strong predictor of GDM in pregnant women. Therefore, evaluating pregnant women with FHD can allow more aimed screening for GDM and can help improve primarily health care measures.

4.2. Strengths and limitations

Present study is the first meta-analysis investigating the relationship between FHD and the future onset of GDM in pregnant women. This study was done by a comprehensive search in the published observational articles performed among Iranian population without any language restriction. Our meta-analysis has estimated a quantitative indicator (OR) for in GDM screening programs. Results of meta regression analysis did not show any heterogeneity due to the study design. Our meta-analysis assessed relationship between FHD and GDM controlling for the effects of potential confounding variables including maternal age, BMI before gestation, number of delivery, previous infant or fetus abnormalities by using matched technique in the primary studies included. Therefore, we could present precise estimates for this association.

4.3. Comparison with existing evidences

Our results were consisted with previous studies around the world [12,18–21]. Similarly, the several prospective and cross-sectional studies have concluded that FHD was one of the strongest risk factors for developing GDM [22–25]. Cianni et al. demonstrated that GDM was more prevalent in pregnant women with FHD (14.5% vs. 7.3%) [7]. Yang et al. have mentioned that women with a positive FHD had about 2 times increased risk of GDM compared to those without [10]. Also, Erem et al. showed that the odds of GDM in Turkish women with FHD was 4.5 fold greater than in women without FHD [20]. Compared two studies conducted by Leng et al. between 1999 and 2012 found that had decreased the odds ratio of GDM for FHD (from 3.46 to1.61), which may be due to increasing in the prevalence of other risk factors [21]. However, even previous studies have found a significant association between FHD and the risk of type 2 diabetes in the general population [14].

4.4. Implications for clinical practice

Since GDM is an important asymptomatic factor for maternal and fetal morbidity designing and implementing a screening program among high-risk women (such as pregnant women with positive FHD) is a critical and cost-effective action in developing countries [11]. Therefore, determining FDH among Iranian pregnant women should be done by health providers in order to prevent developing of GDM.

4.5. Research recommendations

There is a need for systematic review and meta-analysis study to prove the association among FHD and GDM in studies conducted all over the world. Especially, if it is performed using individual participant data (IPD) meta-analysis, many limitations of this study could be managed. On the other hand, several risk factors among pregnant women are also increased the risk of developing GDM, which are a good issue for investigating by systematic reviews.

4.6. Conclusion

Evaluating pregnant women with FHD by health providers can be an effective strategy for prevention of GDM.

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