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Systematic Review

Epidemiology and Heterogeneity of Hypertension in Iran: A Systematic Review

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There are many descriptive studies on hypertension in Iran, mostly assessing the prevalence of the disease and its associations with various risk factors. In order to gain a better insight into the epidemiology of hypertension in Iran and its heterogeneity around the country, we systematically reviewed all available studies and analyzed their findings using meta-analysis methods.

All published papers in Iranian and international journals, final reports of research projects, papers presented in relevant congresses, and also all dissertations of medical students were reviewed using standard keywords. Studies published during 1996 – 2004, which met the eligibility criteria were entered into meta-analysis.

We found 38 studies, of which 29 were eligible with a total sample size of 93,661 subjects. Also, we accessed the results of a very large national survey, which reported the prevalence of hypertension in 27 provinces. Our estimation for the overall prevalence of hypertension in 30 – 55 and >55-year-old population were around 23% and 50%, respectively. The prevalence in men was 1.3% less than that in women (*P*<0.0001). The mean diastolic blood pressure in men was 0.62 mmHg less than that in women while the mean systolic blood pressure was 0.67 mmHg greater.

We found a sharp increase in the prevalence of hypertension by age, and also greater risk in females. It seems that the overall prevalence of hypertension in Iran is considerable. Iranian health system should pay more attention to control and treatment of hypertension in general population.

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Introduction

There is convincing evidence showing that we are facing an outbreak of hypertension (HTN) around the world. As a consequence of new lifestyle and obesity, the incidence of HTN increased in last three decades mostly in the developed countries.[1–4] HTN affects approximately one billion individuals worldwide and the relationship between blood pressure and the risk of cardiovascular events is continuous, consistent, and independent of other risk factors.[5]

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The prevalence of HTN varies considerably worldwide. It is 11 – 30% in Latin America, 20 – 33% in Africa, 18 – 22% in the USA, 44% in some European countries, and 25 – 30% in China, Korea, and Taiwan.[1, 4,6–8]

Nonetheless, there is strong evidence that in developing countries such as Iran, HTN outbreak has started more recently.[1–3] On top of that, longer life expectancy, better care, and more effective treatment push the HTN prevalence up as well.

Therefore, it seems that nowadays HTN is going to be a major public health problem in most developing countries as well. The accelerated change and adoption of western lifestyles by people and urbanization in developing countries has led to a sharp rise in morbidity and mortality from cardiovascular diseases, particularly those related to HTN.[1,2] It is well established that as populations become obese, physically inactive, with high sodium intake and stressful life, HTN

will become a major public health problem.[2]

Iran is a wide country located in Middle-East, with around 70 million population of different ethnicities (Turkish in north-west, Kurdish in west, Arab in south and south-west, Fars in center, Turkmen in north-east, and Baluch in east). They have quite different cultures, lifestyles, and socio-economic status, which might cause variation in the prevalence of HTN. It is known that the prevalence of HTN is influenced by population characteristics such as age, race, gender, and socioeconomic status. [9]

In addition, Iran experiences a profound economic growth after a social revolution and long war with Iraq. This improvement might have an impact on health, and accordingly on the prevalence of common noncommunicable diseases such as HTN. We found many small- to intermediate-scale studies around the country that estimated the prevalence of HTN. Hence, we believe that we can extract valuable information from these studies if we explore their findings deeply.

Even without any statistical analysis, it is reasonable to believe that the prevalence of HTN has a considerable heterogeneity in different studies. Generally, the studies recruited different target groups with quite different age groups, sex distribution, and so on. So, in this study, we will not only check the degree of heterogeneity using statistical test, but also explore the source of heterogeneity.

Meta-analysis is a statistical method, which combines the findings of different studies and explores the possible sources of differences among study findings. Generally, meta-analysis methods combine the findings of analytical studies to generate a combined effect size. However, meta-analysis has other capabilities in combining the findings of descriptive studies and also checking the source of heterogeneity.[10,11]

According to the above explanations, in this study, we aimed to systematically review the findings of all available studies and combine them to estimate the overall prevalence of HTN in Iran. More importantly we aimed to explore the potential sources of heterogeneity.

Materials and Methods

Search strategy

We searched the English-language medical literature published between January 1996 and December 2005 using the Medline database of the National Library of Medicine and their Persian equivalents. Using the medical subject headings (MeSH), we searched for "hypertension", and "cardiovascular diseases" combined with "prevalence" and "Iran" including all subheadings. In addition, all abstracts, conference proceedings, titles of theses, dissertations, and reports in other databases in the Persian (Farsi) language such as IranMedex, IranDoc, Iranian Archive for Scientific Documents Center (IASD), and Iranian National Library (INL) were searched. The Persian keywords were equivalent to their English words and all probable combinations were considered. Moreover, the references of selected citations were hand-searched. All sources were searched with the same strategy and keywords.

Study selection

In the second step, all citations that reported the prevalence of HTN were reviewed. In this stage, we selected all studies that reported the prevalence of HTN according to latest criteria of the seventh annual report of Joint National Committee for HTN, systolic blood pressure (SBP) >140 mmHg and diastolic blood pressure (DBP) >90 mmHg.

We also reviewed a national health survey [Iranian Health Profile Survey (IHPS)], which was carried out in all provinces of Iran by the Ministry of Health in 1999.[12] Because it was a large population-based survey with different methodology (mainly in the sampling method and age group of subjects) compared with other studies, we presented IHPS findings aside from the results of local studies.

Having reviewed full text of citations, studies which estimated the prevalence of HTN in a non-random sample or in a small sample size less than 300 were excluded. Afterward, the quality of studies was assessed according to items related to their objectives, population or sample characteristics, explicity of inclusion/exclusion criteria, usage of the same mode of data collection for all subjects and its validity, clearly described findings, interval estimations, and appropriate data analysis methods. The nonqualified studies were omitted as well. Moreover, duplicated citations and those studies that assessed the prevalence in children and infants were excluded, which resulted in 29 eligible studies out of 38. Most of them were excluded due to lack or incomplete items related to quality assessment.

Data extraction

Having reviewed the age categorizations in the studies, we set cut-offs in a way to maximize the compatibility of our age groups with the age groups reported in the eligible studies. Hence, the age groups were: less than 15, 15 – 29, 30 – 55, and greater than 55 years old. Nonetheless, most of citations were reported the prevalence of HTN in more than one age group; therefore, we entered the age-specific prevalence of these studies in our meta-analysis. In addition, the mean age of subjects, publication date, sample size classified by sex, study location, and type of study entered in our meta-regression analysis to assess the trend of HTN.

Statistical analysis

The variance of HTN prevalence in each study was computed based on the binomial distribution formula. Having used heterogeneity test, we found significant variations between study findings. Hence, we used random effect model to estimate the overall prevalence of HTN. In addition, in order to minimize the random variation between point estimations of studies, we adjusted all findings of the studies using Bayesian analysis. In this adjustment, the overall point estimation based on the random effect model was used as prior prevalence. Having described the findings in forest plots, the point estimations and their 95% confidence intervals (CIs) were computed accordingly.

In the next step we used meta-regression to check the effect of age and sex distribution of the studies, type of study (separated vs. IHPS), living location of subjects (rural vs. urban area), and publication date as possible source of heterogeneity among the study findings and to estimate the stratum-specific prevalence. We estimated tau-square (τ^2), using restricted likelihood method, as the indicator of heterogeneity. All of the analyses were done by Stata software version 8.

Results

The findings of this systematic review are summarized in Table 1. Having excluded non-eligible studies, we recruited the data of IHPS in 27 provinces and findings of 29 separated studies from 20 provinces around the country. Maximum and minimum sample sizes of recruited separated studies were 12,494 (in Isfahan and Markazi Provinces) and 342 (in Illam City), respectively. The maximum and minimum of sample size in IHPS were 11,054 (in Tehran) and 651 (in Semnan), respectively. Maximum and minimum prevalence of HTN in recruited separated studies were in Tehran (47.0%) and Ghazvin (6.9%), respectively; while the maximum and minimum prevalence in IHPS were observed in East-Azerbaijan (24.1%) and Sistan and Baluchestan (8.8%), respectively.

The overall estimation of HTN based on the data of IHPS and separated studies were 12.5% (95%CI: 10.6 – 14.4%) and 22.1% (95%CI: 18.9 – 25.2%), respectively (Table 1). However, the findings of both categories of studies had substantial heterogeneity (P<0.001), and the estimated prevalence in these two categories had a great difference as well (P<0.0001).

Using meta-regression, our results showed that in average the modeled prevalence of HTN decreased by 1.11% per one year increase in publication year (P=0.075), which means that there may be a trend toward decreased prevalence. In addition, the difference between HTN prevalence in rural and urban populations was not significant (difference=0.03%; P=0.99).

Moreover, the results of meta-regression showed that, the big difference in the crude estimations of HTN in IHPS and separated studies categories (12.5% vs. 22.1%) was mainly due to the confounding effect of difference in age distribution of subjects in these two categories. Having adjusted for age, we found only 2% difference between the estimated prevalence between these two categories, which was not statistically significant (P=0.38) (Table 2).

Based on the above findings, the main source of heterogeneity was the mean age of subjects. Overall, we found that by each year increase in the mean age of subjects after age 20, the HTN prevalence increased by 0.54% (P<0.001).

To estimate the age stratum- specific prevalence, we computed weighted means based on the sample size of studies (Figure 1). Based on these findings, it seems that the prevalence of HTN in 30 – 55-year-old subjects were slightly greater than 23%, while it is more than 49.5% in subjects with more than 55 years old.

The combined prevalence of HTN in males was 1.3% less than that in females, which was statistically significant (P=0.026). Nonetheless,

Table 1. The estimated prevalences of hypertension and their 95% confidence intervals, in the local studies and in Iranian Health Profile Survey (IHPS) classified by province. Estimations were adjusted using Bayesian method.

Province	Loacal studies				IHPS*			
	Prevalence	95%CI		Sample size	Prevalence	95%CI		Sample size
Ardabil	—	—	—	—	12.51	7.75	17.27	1075
Boshehr[13 – 15]	22.1	18.47	25.72	2180	9.19	4.03	14.36	897
	22.1	18.18	26.01	1854				
	16.94	11.64	22.24	1036				
Chaharmahal & Bakhtiari	—	—	—	—	10.19	5.02	15.36	880
East- Azarbaijan[16,17]	21.36	17.88	24.84	2400	24.07	21.32	26.82	3441
	16.29	12.71	19.88	2400				
Isfahan[18- 20]	18.79	15.93	21.66	3694	11.52	8.67	14.37	3776
	48.34	44.81	51.87	12494				
	17.29	15.7	18.88	6442				
Fars[21,22]	25.71	23.09	28.34	4045	9.13	6.17	12.08	3600
	22.15	18.75	25.54	2496				
Ghazvin[23,24]	7.21	4.77	9.64	5917	14.87	9.94	19.8	936
	22.37	17.16	27.58	1000				
Golestan	—	—	—	—	9.61	5.29	13.93	1450
Guilan[25]	8.22	3.52	12.92	1500	14.7	11.18	18.21	2236
Hormozgan[26]	23.24	18.58	27.91	1235	11.87	7.86	15.88	1255
Hamedan	—	—	—	—	11.84	7.3	16.38	1692
Illam[27]	38.76	31.46	46.06	342	11.33	6.42	16.24	1003
Kerman[28-30]	25.84	20.74	30.93	1000	21.27	17.67	24.88	1914
	20.65	15.38	25.91	1000				
	8.28	0.83	15.73	537				
Kermanshah	—	—	—	—	17.97	14.16	21.78	1760
Khorasan[31,32]	17.74	10.15	25.33	450	11.29	8.95	13.63	5812
	20.96	16.4	25.53	1359				
Kohkilooyeh[33]	21.31	9.24	33.38	—	11.27	6.32	16.21	986
Kordestan[34]	15.8	11.87	19.72	2000	10.17	5.56	14.78	1214
Khozestan[35]	26.84	23.78	29.9	2900	9.02	6.12	11.92	3740
Lorestan	—	—	—	—	10.9	6.61	15.18	1456
Markazi[36]	10.29	6.24	14.35	2000	17.25	12.73	21.78	1142
Mazandaran	—	—	—	—	11.1	7.43	14.76	2132
Qom	—	—	—	—	9.06	3.71	14.41	810
Semnan	—	—	—	—	10.32	4.63	16.02	651
Sistan & Baluchestan[37]	14.46	9.97	18.95	1530	8.84	4.84	12.85	1173
Tehran[38-44]	19.05	16.94	21.15	6899	13.08	11.37	14.79	11054
	22.46	19.2	25.71	2705				
	33.23	29.66	36.79	1919				
	21.7	19.85	23.56	8647				
	46.06	42.73	49.39	1766				
	22	20.13	23.87	8491				
	30.6	23.46	37.75	423				
West Azarbaijan	—	—	—	—	9.69	6.29	13.09	2586
Yazd[45]	19.68	7.21	32.15	1000	11.63	6.58	16.68	935
Zanjan	—	—	—	—	17.28	12.43	22.14	922
Overall	**22.06**	**18.92**	**25.19**	**93661**	**12.54**	**10.64**	**14.43**	**69489**
Heterogeneity	Q=835.9	*P*<0.0001			Q= 159.9	*P*<0.0001		

* Data were obtained from reference No. 12.

there was a considerable heterogeneity among the findings of the studies (Q=304.7, *P*<0.0001) (Figure 2).

Only 13 local studies reported means for SBP and DBP in males and females. The combined mean for SBP using meta-regression model was

Table 2. The results of meta-regression model; this model assessed the effects of the mean age of subjects, publication year, and the type of studies (SS vs. IHPS).

	Coefficient	SD	*P* value
Age (year)	0.54	0.09	<0.001
Publication date	-1.11	0.62	0.075
Type (IHPS as baseline)	-1.95	2.21	0.38

SS=Separated articles, IHPS=Iranian Health Profile Survey.

0.67 mmHg greater in males compared with that in females (P =0.31) (Figure 3); while the combined DBP was 0.62 mmHg greater in females compared with that in males (P=0.12). This means that the difference of SBP and DBP between males and females was not statistically significant (Figure 4).

Discussion

We found that the prevalence of HTN in Iranian population was strongly age dependent and by each year increase in age, the HTN prevalence increases around 0.54% after the age of 20. Our estimation for the prevalence of HTN in middle age (30 – 55) and old age (more than 55) was around 23% and 49.5%, respectively. However, we did not find any strong evidence to support the idea that the prevalence of HTN varied between 1996 and 2004. Overall, we found a risk of HTN in females.

Compatible with our expectation, we found that the prevalence of HTN varied in a very wide range among studies. Therefore, it would be a point of concern if we simply use meta-analysis methods to combine the findings of studies, even using random effect models. Because age was the main source of heterogeneity, we reported the estimated prevalence of HTN in each age group separately to minimize within age-group heterogeneity.

In the literature there is a great deal of studies that reported a wide range of HTN from around 11% up to more than 40%. Arterial HTN is the most common cardiovascular disease and a major health problem in both developed and developing countries. It affects about 20% of the adult population worldwide.[1,3–8] The prevalence of HTN in Saudi Arabia has been reported 25%, in Taiwan 24%, in China and Korea 25 – 30%, in Lebanon 26%, and in Egypt 30 – 43%.[1, 6,46–48]

Although it seems that the prevalence of HTN in Iran is less than the average these developing countries, we think that the results of these studies are not comparable straightforwardly. Firstly, because most of these studies were collected their samples in a small area or a city and did not cover whole a country. Thus, generalizing the estimated prevalence to a country is a point of concern. Secondly, there are very strong pieces of evidence that show HTN is highly age-dependent.[5] In other words, the estimated prevalence highly depends on the age group of subjects. Therefore, even population-based sampling from communities with different age pyramids could show quite varied prevalences even with comparable risks of HTN. This issue is very important in explaining the differences in the prevalence of HTN in developed and developing countries.

Also, in a country such as Iran that is in a

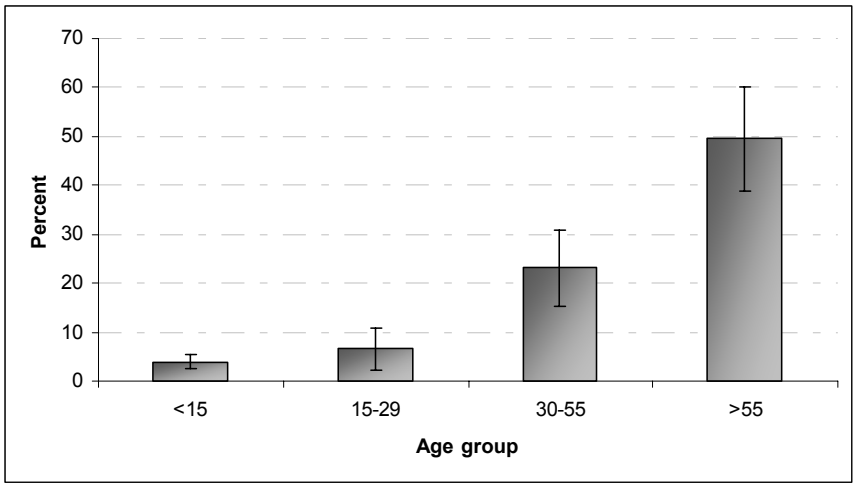

Figure 1. The prevalences of hypertension in different age groups and their 95% confidence intervals; the numbers were weighted based on the sample size of the studies.

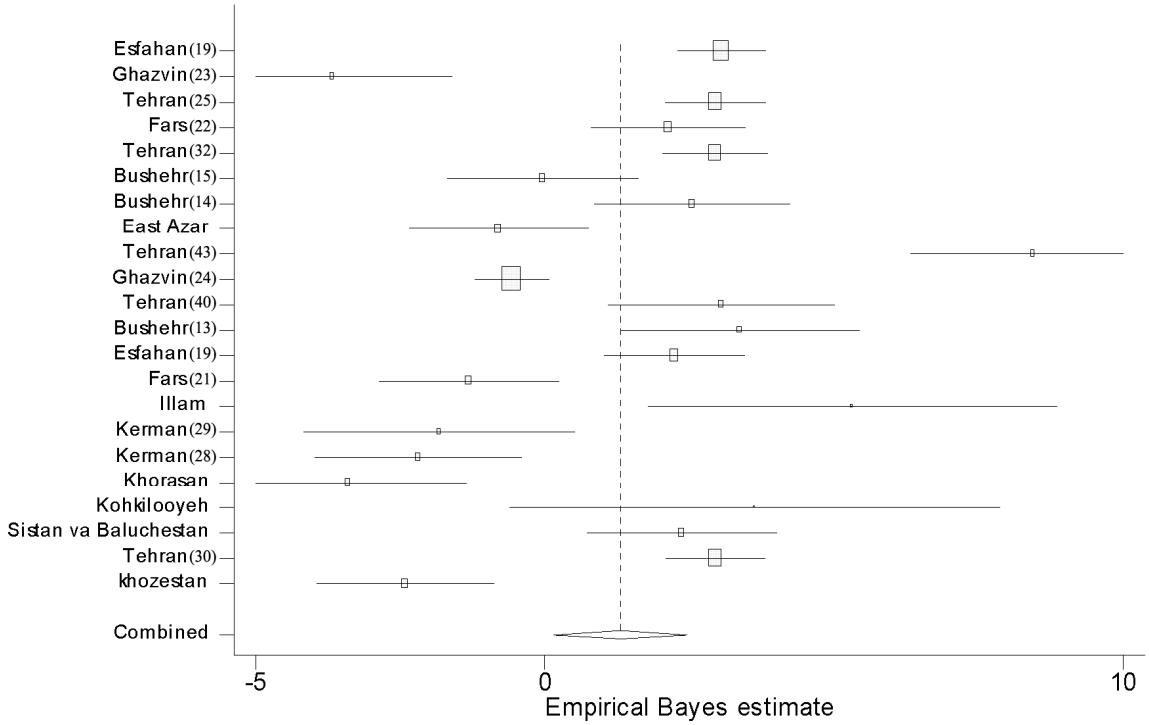

Figure 2. The difference between the estimated prevalence of hypertension in females and males; the overall difference shows that the prevalence in males was less than that in females.

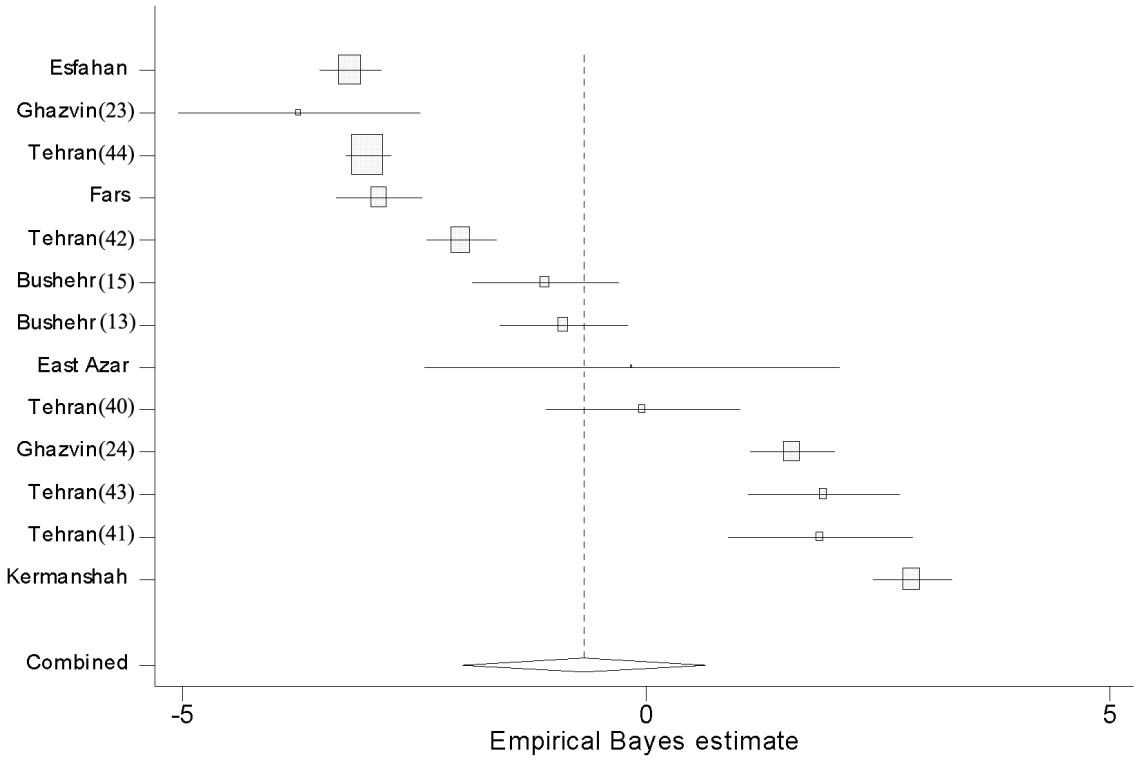

Figure 3. The difference between the estimated mean systolic blood pressure (SBP) in females and males; the overall difference shows that SBP in females was nonsignificantly less than in males.

transitional status, the changes in age pyramid even during a few decades are considerable. Hence, the temporal increase in the prevalence of HTN might be partly due to the aging phenomenon of the population.

Based on the above explanations, we suggest that meta-analysis and meta-regression methods can adjust the data for important confounding factors such as age. They can help us to generate more reliable hypotheses about the time and location variations of HTN among and even within countries.

Moreover, we found that the prevalence of HTN in females was around 1.3% greater than that in males in Iranian population. Greater prevalence of HTN in females has been detected in many other studies as well.[2,6,8,49,50] Because of data limitations and also the risk of ecological fallacy we could not assess the reasons of such a difference. However, greater body mass index (BMI) among females and their lifestyles were counting as possible factors in other studies.[2,49,50] Oral contraceptives may also increase blood pressure and the risk of HT increases with the duration of use. Meanwhile, menopause can be another factor affecting the prevalence of HTN in women.[50,51]

We should acknowledge to the limitations of such a meta-analysis as well. The main limitation is that the estimated prevalence is not adjusted based on the size of target population. In this way, surely the result of a cluster analysis is more reliable. However, from the practical point of view, running a wide study with perfect cluster sampling is very difficult and costly even within a country. For that reason, it seems that meta-analysis could be a feasible and an efficient method to utilize the findings of other studies appropriately. Therefore, from this point of view we used the data of most studies in this issue in Iran and generated a more comprehensive national vision.

Publication bias is one of the other issues in most of the meta-analyses that may distort their findings. In this study, we searched all available data sources to cover grey literature as much as we could. Consequently, as a general comments, we suggest that researchers should not limit their data sources for such a meta-analysis to only published papers in order to minimize the publication bias.

As a conclusion, we showed that how meta-analysis method can be used to aggregate the data of separated descriptive studies to generate a more

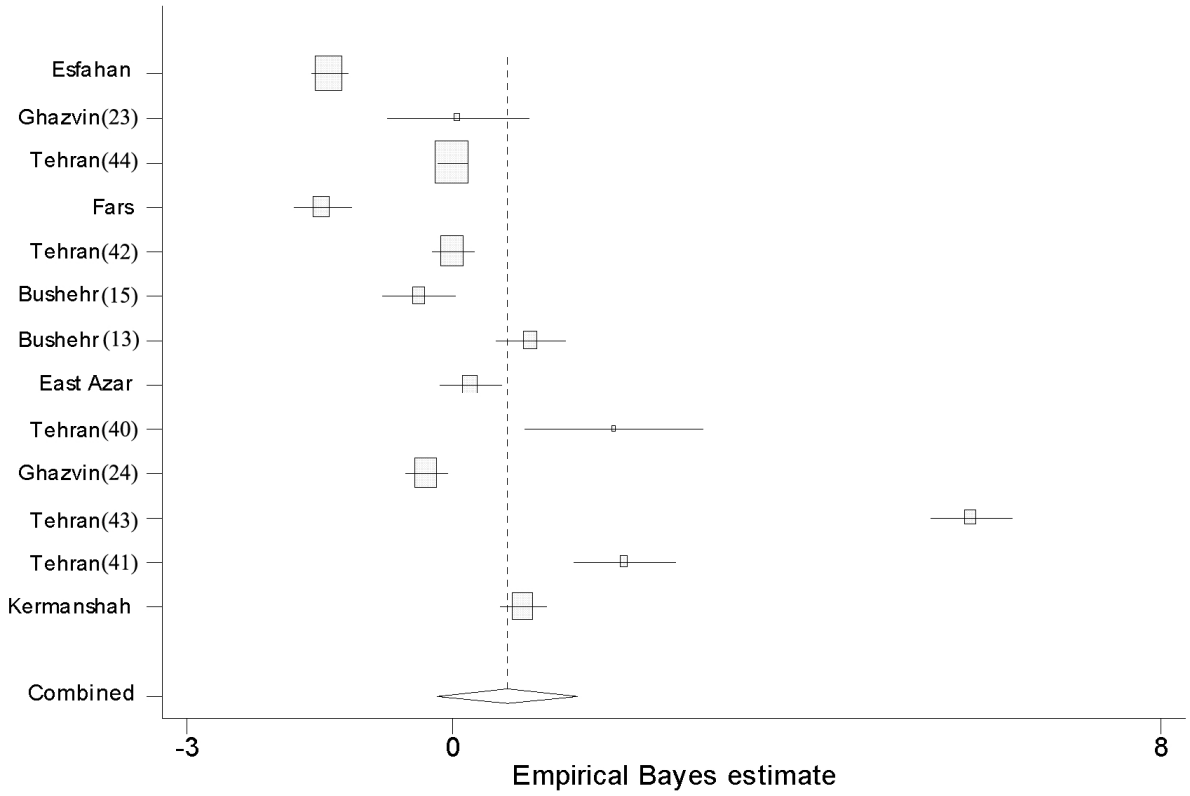

Figure 4. The difference between the estimated mean diastolic blood pressure (DBP) in females and males; the overall difference shows that DBP in males was nonsignificantly less than in females.

comprehensive picture of the variable of interest in national level. In our paper, we showed that age was a very important factor mostly after 20 years old in Iran. It seems that HTN is a public health issue in Iran because of its high prevalence. In addition, we expect an increasing trend in its prevalence because of the changes in the age pyramid of Iranian population in following decades.

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