INCIDENCE OF HIP FRACTURE IN THE EASTERN MEDITERRANEAN REGION- A SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT

BACKGROUND

Hip fracture is a major health concern with high rates of mortality and disability. The purpose of this study was to conduct a systematic review and meta-analysis on the incidence of hip fracture in the Eastern Mediterranean Region (EMR).

METHODS

We searched the databases of PubMed, Scopus, Web of Science and Index Medicus for the EMR for observational studies reporting the incidence of fracture in the EMR countries, which were published from inception to September 2018 with no language restriction. Study selection and data extraction were conducted independently by two reviewers.

RESULTS

After applying inclusion and exclusion criteria, 10 articles were finally included in this study. The overall pooled crude incidence rate of hip fracture in the EMR was estimated to be 107.4 per 100,000 population/year (95% confidence interval [CI]: 83-131.8). Analysis also showed that the overall pooled age-standardized rate was 174.4 per 100,000 population/year (95% CI: 103.9-244.9). Lebanon had the highest crude incidence rate (140.1 per 100,000 population/year), and Kuwait had the lowest rate (21.9 per 100,000 population/year). Age-standardized rate for males was 121.3 per 100,000/year (95% CI: 80.8-161.7) and for females was 227.4 per 100,000/year (95% CI: 129-325.9). The overall crude incidence for traumatic fracture was estimated to be 79.2 per 100,000/year (95% CI: 21.8-136.6).

CONCLUSIONS

A considerable incidence rate was seen for hip fractures. There were also significant variations in the incidence of different countries of the EMR. Implementing preventive measures against fractures is needed in the region.

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BACKGROUND

Fractures can happen in any bone due to trauma (e.g. accidents) or non-traumatic mechanisms (e.g. medical conditions such as osteoporosis). Fractures can be either displaced or non-displaced based on the type and severity of imported energy, and each one has its own prognosis.[1-4]

Bone fractures occur mostly in young or older people. Its epidemiology varies between different communities, as well as between regions within the same country.[5-7] Hip fracture is a serious health issues, because it is strongly associated with mortality, disability and high medical costs.[8-10] In 1990, 1.6 million hip fractures was estimated in world, expecting to increase to 6.3 million by 2050.[11] Its medical costs were calculated US $153 billion in 1997, increasing to US $446.3 billion by 2050.[12]

The Eastern Mediterranean Region (EMR) consists of 22 developing countries with population of about 583 million people.[13]

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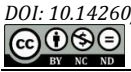

Studies report variable rates of incidence for hip fracture in these countries for example, a study from Kuwait reported an age-standardized rate of 48.4 per 100,000 population/year.[14] On the other hand, a study from Morocco stated that age-standardized rate of hip fracture is 69 per 100,000 population/year.[15] The outcomes of fracture are also important. One investigation reported a mortality rate of 7% for hip fracture in the Lebanese population after one year and 18% after 5 years.[16] Another survey from Iran reported a death rate of 11.2% during 2007-2008.[17] Our recent meta-analysis showed that the prevalence of osteoporosis has increased over the last years in the EMR[18] therefore, osteoporotic fractures will probably become more prevalent and become an even greater concern for this region.

Epidemiological studies on fracture should be helpful for the healthcare providers to better plan for its control and prevention. While the fracture incidence has been evaluated in different studies in the EMR, we believe that a systematic review and meta-analysis will help long-term planning by policy makers.

METHODS

Information Sources and Search Strategy

A literature search was conducted from the bibliographic databases of PubMed, Scopus, Web of Science and Index Medicus for the EMR published from the inception to 31 September 2018 with no language restriction. The related terms were searched in the Medical Subject Headings (MeSH) database, and finally, the keywords included "fracture" OR

"fractures" OR "broken" AND "epidemiology" OR "incidence" AND "Afghanistan" OR "Bahrain" OR "Djibouti" OR "Egypt" OR "Iran" OR "Iraq" OR "Jordan" OR "Kuwait" OR "Lebanon" OR "Libya" OR "Morocco" OR "Oman" OR "Palestinian" OR "Pakistan" OR "Qatar" OR "Saudi Arabia" OR "Somalia" OR "Sudan" OR "Syria" OR "Tunisia" OR "United Arab Emirates" OR "Yemen". The search was limited to Title/Abstract. Name of countries was limited to affiliation as well. Reference lists of the related reviews and the retrieved papers were manually searched for additional materials.

Inclusion and Exclusion Criteria

We included all observational studies reporting the incidence of hip fracture in the general population or a community. We excluded those studies that did not cover all cases of hip fracture in a region. For example, a registry study covering 100% of the patients was considered as a reference and studies using such database were included for further analysis. On the other hand, we excluded any study that was conducted in only one hospital that was not a referral center for fractures. We also excluded those studies that evaluated incidence over a period of less than 1 year. Other exclusion criteria were as follows:

1. Reviews, case reports, editorials, letter to the editors and abstracts from conferences.
2. Duplicate articles or evaluating the same sample.
3. Case-control studies.
4. Studies included subjects with other specific diseases (e.g., cancer, haemophilia, etc.)
5. Surveys without clear methodology or results.
6. Full-texts not being available.

Study Selection and Data Extraction

Two reviewers screened independently the titles and abstracts of all references for potential suitability. Full-texts of the potential articles were obtained for the final assessment of suitability for inclusion. Any discrepancies pertaining to the inclusion of articles were resolved by consensus with a third reviewer. Data were assessed and extracted from the studies and finally included for analysis into a Microsoft Excel spreadsheet. The following data were extracted: author's name, study location, study date, publication date, characteristics of the samples (including gender, age), sample size, overall and sex-specific incidence rate of hip fracture (crude rate and age-standardized rate), and fracture type (traumatic or non-traumatic). We tried to split the studies by fracture type and study date as much as possible, and each was considered as a separate report. The incidence rates were extracted as cases per 100,000 persons/year from each study. Google Translate was used to translate non-English reports. We excluded duplicates and only selected those with the most comprehensive details.

Study Outcomes and Statistical Analysis

The data extracted from the retrieved articles were combined to give the pooled incidence rates. The pooled incidence rates were presented as per 100,000 population/year and 95% confidence interval (CI). The heterogeneity between the studies was evaluated by I^2 statistic. We used fixed- and random-effects models to calculate the pooled estimates when I^2 was <50% and >50%, respectively. Subgroup analyses were performed according to country, gender (male and female), study period (≤2006, >2006), and type of fracture (traumatic). Splitting the study date into ≤2006 and >2006 was mainly based on the distribution of the number of reports in each period category. In order to determine a significant difference between the groups, we relied on coverage of 95% CI. All statistical analyses were done using STATA (Stata Corp, College Station, TX, USA).

RESULTS

Search Results, Study Selection and Characteristics

The initial search in the databases identified a total of 2027 citations and 1252 remained after removing duplicates. After evaluating the title and/or abstract, 1228 articles were excluded because of failure to meet the inclusion criteria. Full-text of the remaining 24 papers were assessed for eligibility; 10 eligible articles were included in the final analyses. The results of search strategy is shown in a flow diagram according to the PRISMA (Preferred reporting items for systematic review and meta-analysis) guideline [19] (Figure 1). The characteristics of the included articles are summarized in Table 1.

Estimated Incidence of Fracture

- **Overall**

  All of 10 articles included to this systematic review reported the crude incidence rate, but age-standardized rate was found in only 4 papers. The overall pooled crude incidence rate of fracture in the EMR was estimated to be 107.4 per 100,000 population/year (95% CI: 83-131.8; I^2=99.9%; p=0.000) (Figure 2). Analysis also showed that the overall pooled age-standardized rate was 174.4 per 100,000 population/year (95% CI: 103.9-244.9; I^2=99.5%; p=0.000) (Figure 3). Analysis of 3 nationwide articles indicated an overall pooled crude incidence rate of 111.4 per 100,000 population/year (95% CI: 52-170.8; I^2=99.9%; p=0.000) in the EMR. The overall pooled age-standardized rate for nationwide studies was also estimated to be 187.4 per 100,000 population/year (95% CI: 59.2-315.5; I^2=99.7%; p=0.000).

- **Country-Based Incidence**

  Iran had the highest number of articles (n=5), and other countries (Kuwait, Lebanon, Morocco, Oman and Saudi Arabia) each only had 1 article. The pooled crude and age-standardized incidence rates analysed for each country are reported in Table 2. Lebanon had the highest crude incidence rate (140.1 per 100,000 population/year), but Kuwait had the lowest rate (21.9 per 100,000 population/year).

- **Gender**

  All of 10 articles reported the crude incidence of hip fracture in males in the EMR and the overall pooled incidence rate was estimated as 97.9 per 100,000 population/year (95% CI: 74.7-121.1; I^2=99.7%; p=0.000). The age-standardized rate in males was reported in 5 articles and the overall pooled incidence was estimated to be 121.3 per 100,000 population/year (95% CI: 80.8-161.7; I^2=98.2%; p=0.000). Regarding females, the same number of articles reported the crude and age-standardized incidence rates for hip fracture in

the EMR. The overall pooled crude incidence rate was 113.8 per 100,000 population/year (95% CI: 87.7-140; I^2=99.7%; p=0.000). In addition, the overall pooled age-standardized rate was estimated to be 227.4 per 100,000 population/year (95% CI: 129-325.9; I^2=99.3%; p=0.000). Figures 4 and 5 show the forest plots of the pooled data related to gender.

- **Study Date**

Six papers were in the ≤2006 group and 5 studies were conducted after 2006. The pooled crude incidence of fracture for the first period was 123.3 per 100,000 population/ year (95% CI: 47.4-199.1; I2=99.8%; p=0.000). In relation to second group (>2006), the overall crude incidence rate was 97.1 per 100,000 population/year (95% CI: 54.5-139.7; I2=100%; p=0.000).

- **Fracture Mechanism**

With respect to the mechanism of fracture, 4 articles reported the fractures to be due to trauma, but 6 articles did not specify the mechanism. After pooling the data related to traumatic fracture, the overall crude incidence was estimated to be 79.2 per 100,000 population/year (95% CI: 21.8-136.6; I^2=99.9%; p=0.000) in the EMR.

Region	First Author	Publication Year	Fracture Type	Study Year	Age	Total (N)	Crude Rate (per 100000 Population/year)	Age-Standardized Rate (Per 100000 Population/Year)	Male (N)	Crude Rate (Per 100000 Population/Year)	Age-Standardized Rate (Per 100000 Population/Year)	Female (N)	Crude Rate (Per 100000 Population/Year)	Age-Standardized Rate (Per 100000 Population/Year)
Iran														
Kermanshah	Beyranvand	2009	Not specified	2007-2008	≥50	114206	141	194	58653	150.4	181.1	55553	131.7	214.6
Nationwide	Ahmadi-Abhari[20]	2007	Accidental injuries	2005	≥50	8845000	115.4	-	4361000	115.2	-	4484000	115.6	-
Nine provinces	Abolhassani[21]	2006	Fall-related	2003	≥20	5074178	30.4	-	2581714	31.8	-	2492464	29	-
Tabriz	Aliasgarzadeh[22]	2009	Not specified	2006	>50	234142	175.1	-	121647	175.9	-	112495	174.2	-
Zanjan	Valizadeh	2008	Not specified	2006-2007	≥50	139109	175.4	210.2	68627	190.9	206.5	70482	160.3	214.8
Kuwait														
Nationwide	Azizieh	2017	Not specified	2009-2012	0 to >80	14448034	21.9	48.4	8754991	24.8	45.1	5693043	18.9	52.5
Lebanon														
Nationwide	Sibai[23]	2011 (A)	Not specified	2006	≥50	394099	141.1	239.5	183929	88.1	109.7	210170	187.5	370.4
Nationwide	Sibai	2011 (B)	Not specified	2007	≥50	388251	142.7	234.1	181199	106.5	134.1	207052	174.4	335.1
Nationwide	Sibai	2011 (C)	Not specified	2008	≥50	394673	136.6	228.3	184197	105.3	128.7	210476	163.9	329.0
Morocco														
Rabat	Maghraoui	2005	Not specified	2002	≥50	312461	48	69	153178	43.7	58.5	159283	52.1	80.7
Oman														
South Sharqiya	Shukla	2008	Falling	2002-2007	≥40	120787	121.7	-	60978	114.8	-	59809	128.7	-
Saudi Arabia														
Riyadh	AI-Nuaim[24]	1995	Traumatic	1990-1991	>40	204424	50.4	-	92848	54.9	-	111576	46.6	-

Table 1. Characteristics of Studies Included in the Systematic Review on Incidence of Hip Fracture in The Eastern Mediterranean Region

Country	Crude Rate (Per 100,000 Population/Year)	95% Confidence Interval	Age-Standardized Rate (Per 100,000/Year)	95% Confidence Interval
Iran	126.9	72.5-181	203.1	183.3-222.9
Kuwait	21.9	21.1-22.7	48.4	46.7-50.1
Lebanon	140.1	133.3-146.8	233.8	222.6-245.1
Morocco	48	40.3-55.7	69	58-80
Oman	121.7	121.6-121.8	-	-
Saudi Arabia	50.4	40.7-60.1	-	-
Eastern Mediterranean Region	107.4	83-131.8	174.4	103.9-244.9

Table 2. Incidence of Hip Fracture by Countries in Eastern Mediterranean Region

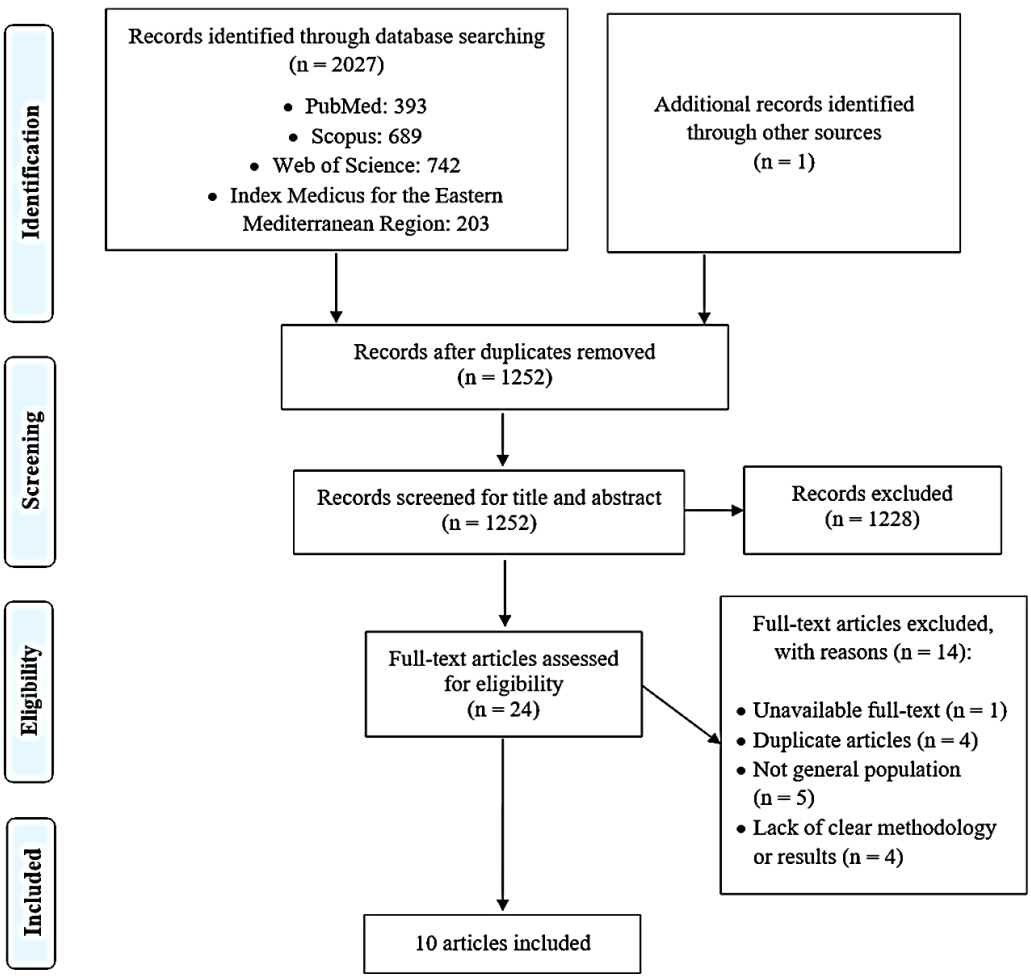

Figure 1. Prisma Flowchart

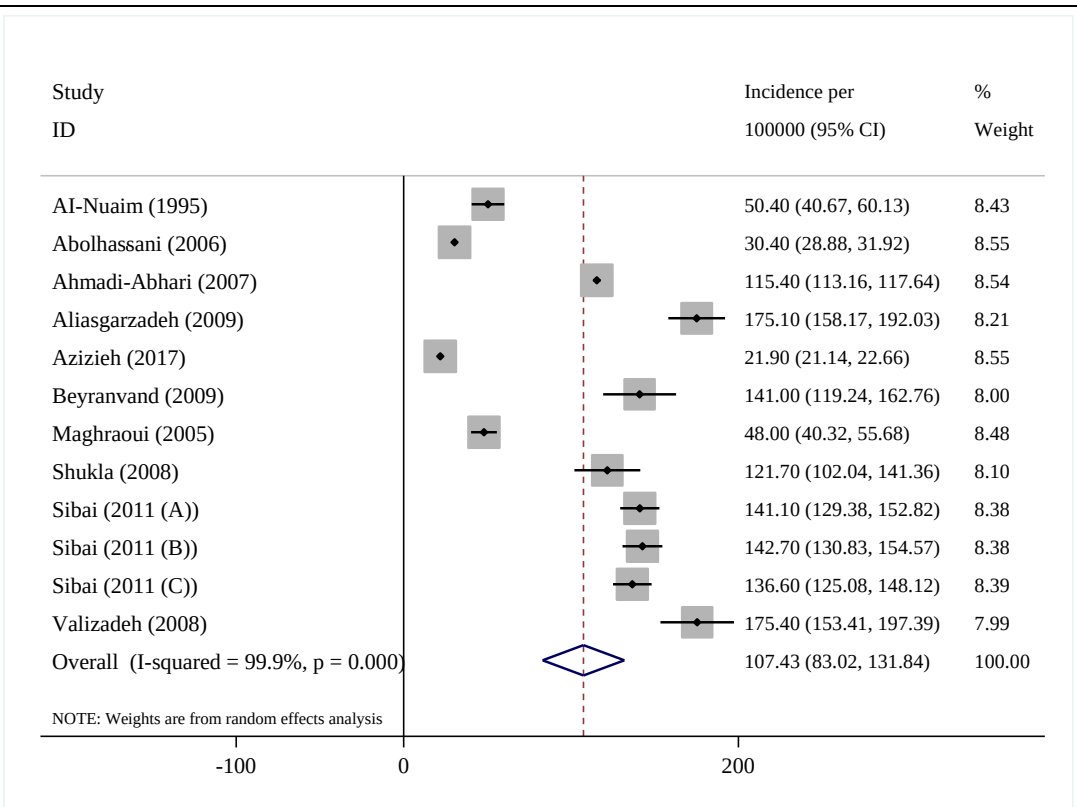

Figure 2. Forest Plot of Pooled Crude Incidence of HIP Fracture in Eastern Mediterranean Region

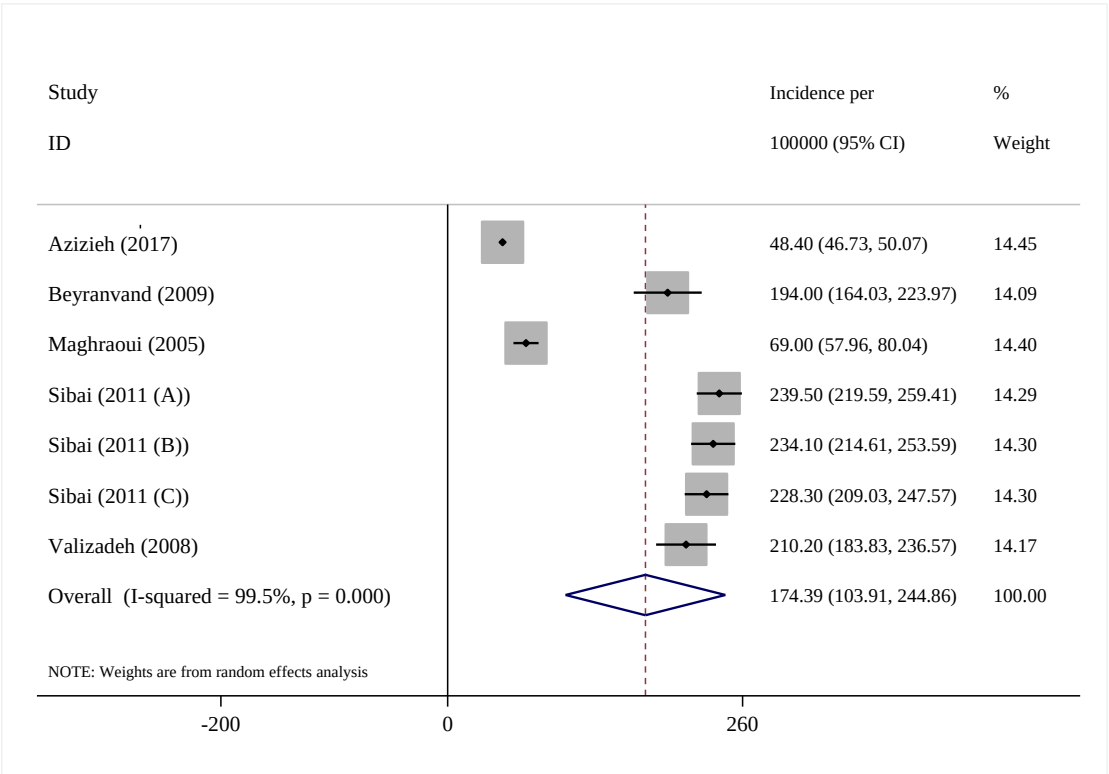

Figure 3. Forest Plot of the Pooled Age-Standardized Incidence of Hip Fracture in Eastern Mediterranean Region

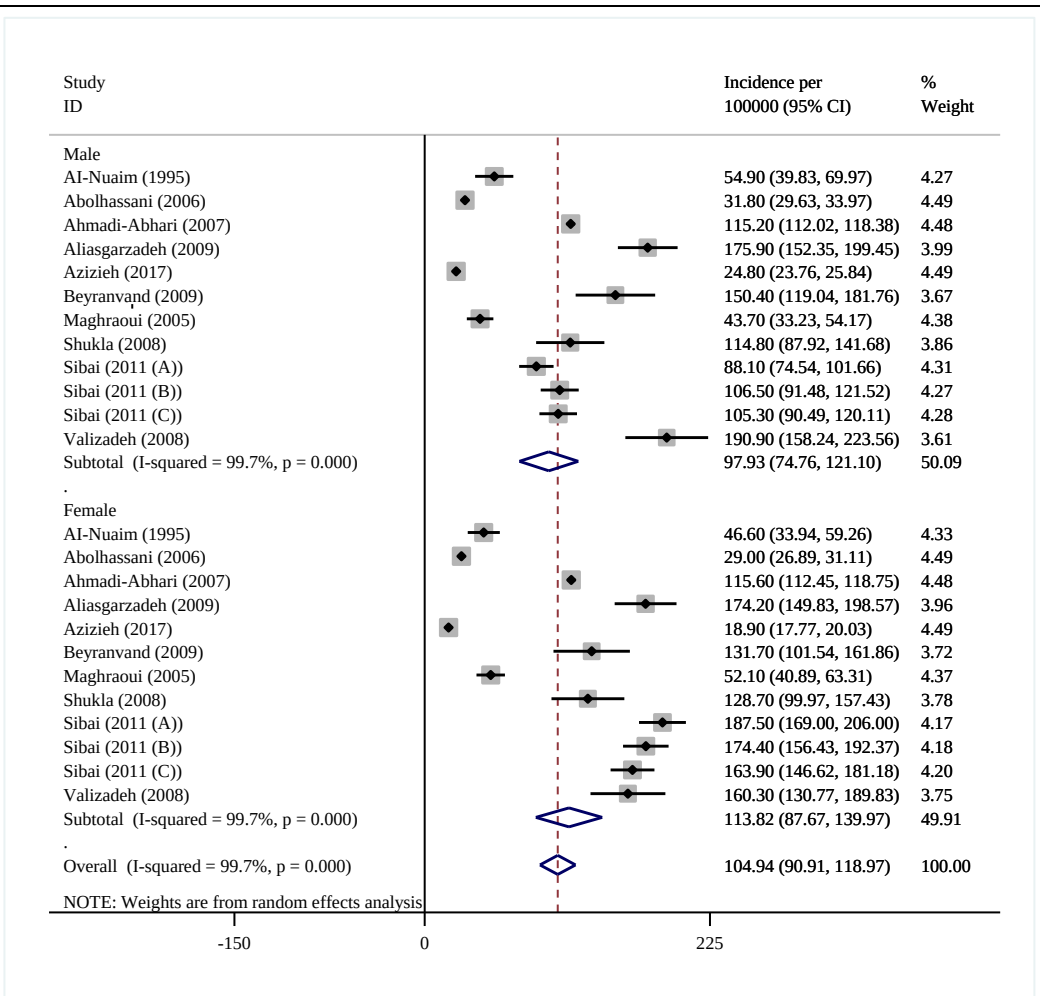

Table 4. Forest Plot of Pooled Crude Incidence of Hip Fracture by Gender in Eastern Mediterranean Region

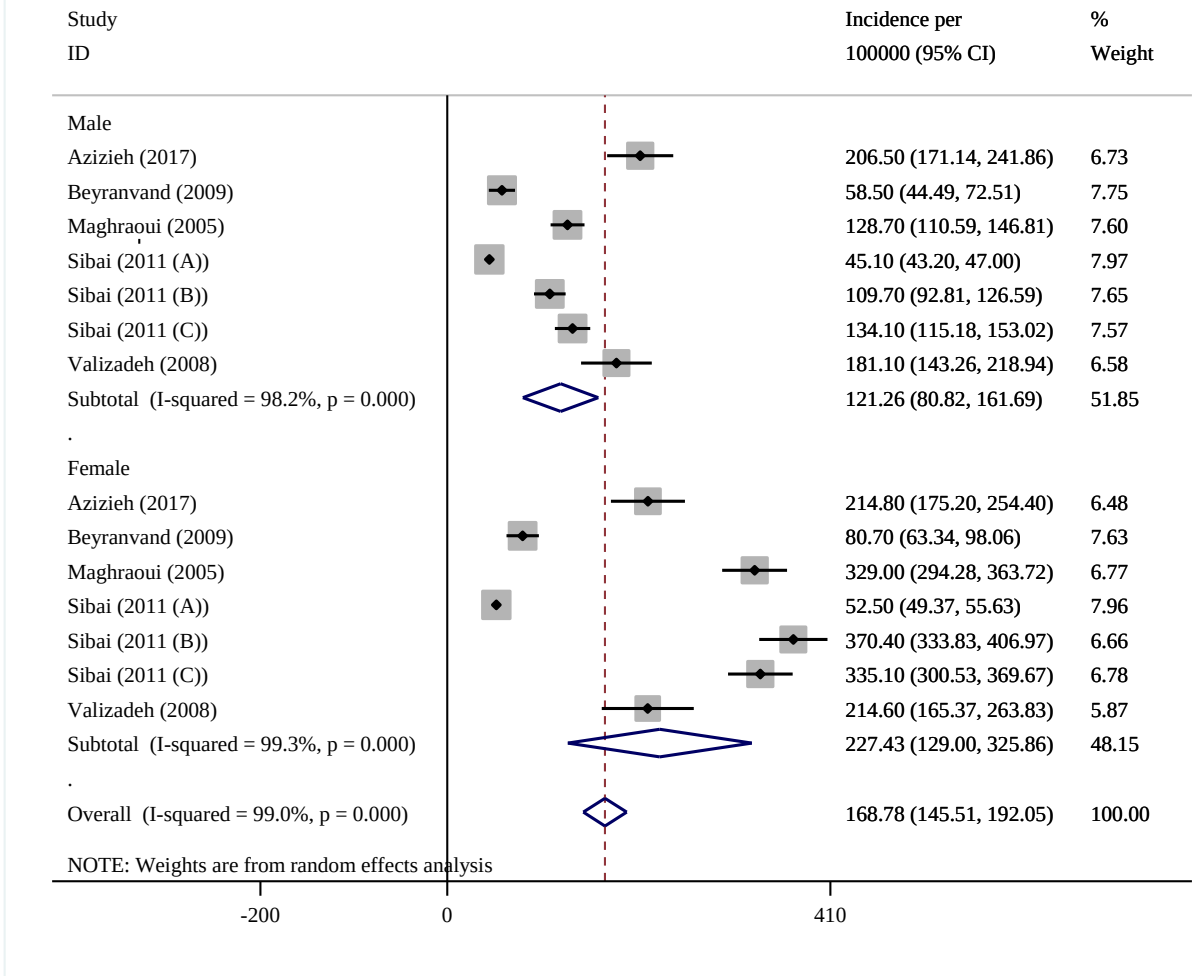

Figure 4. Forest Plot of Pooled Age-Standardized Incidence of Hip Fracture by Gender in Eastern Mediterranean Region

DISCUSSION

According to the results of this systematic review, the overall pooled crude incidence rate of hip fracture was 107 per 100,000 population/year in the EMR. The age-standardized rate was estimated to be 174 per 100,000 population/year. This rate was highest in Lebanon (crude rate of 140 per 100,000 population/year), and lowest in Kuwait (crude rate of 29 per 100,000 population/year). Analyses also showed that the overall age-standardized rates in males and females in the EMR were 121 and 227 per 100,000 population/year, respectively. The incidences of hip fracture in the EMR was lower in than most Western and European communities. For instance, a study by Amin et al.[25] In the US, stated that the incidence of hip fracture was 294 per 100,000 population/year. A study on 14 European countries indicated the predicted maximum hip fracture incidence rate from 376 per 100,000 population in Portugal to 1390 per 100,000 population in Sweden among females, and from 157 per 100,000 population/year in Portugal to 742 per 100,000 population/year in Sweden among males.[26] The results of this study, however, should be interpreted with caution because of differences in number of studies, being nationwide or local scale, and lack of reporting the age-standardized rate in some studies.

Following subgroup analysis, we did not find a significant difference between studies conducted before and after 2006. In the study by Azizieh.[14] From Kuwait, an increase of 3.9% in annual incidence rates for all fractures was seen over 2009-2012. Shukla and Khandekar.[27] reported that incidence of hip fracture increased four-fold from 2002 to 2007. There have been differences in trends of hip fracture incidence worldwide. In most of the western countries and Oceania, there was initially a rise in the annual age-standardized rate, then followed by a decrease in recent years. An article from the United States, for example, reported that age-standardized annual incidence of hip fractures in females increased from 964 per 100,000 in 1986 to 1051 per 100,000 in 1995, then decreased to 794 per 100,000 in 2005.[28] This trend was also seen in males, as the annual age-standardized rate increased from 392 per 100,000 to 457 per 100,000 from 1986 to 1995, and decreased to 369 per 100,000 in 2005.[28] Another article reported this decline by 2015 as well.[29] On the other hand, it was found that in most of the Asian countries, the annual incidence of hip fracture has steadily increased 2- to 3-fold over the past three decades.[30] It should be noted, however, that changes in the pattern of fracture incidence depend on region, fracture type, and population characteristics.

Two main causes are responsible for hip fracture are low bone mineral density (related to osteoporotic fracture) and falling (related to traumatic fracture)[31,32] Hip fracture is the most devastating type of osteoporotic fracture.[33] The

relation between bone mineral density and fracture is understudied in the EMR.[16] The World Health Organization developed a fracture risk assessment tool (FRAX) to predict 10-year major osteoporotic and hip fracture probabilities, which has been reported in the EMR as well.[6,34,35] Studies have demonstrated that osteoporosis management in subjects at high risk of hip fracture based on FRAX can be associated with a subsequent decrease in the rate of fracture.[36,37] Therefore, FRAX system is helpful for clinicians to prevent hip fracture. Of course, we should consider the fact that rate of fracture increases with age too.[38,39]) therefore, it is necessary to pay more attention to the older patients.

About gender difference in fracture, it is stated that the risk of fracture is higher in females than in males, especially in postmenopausal females due to lower bone mineral density. Other reasons also exist, such as differences in bone size and bone strength between males and females.[40] Although fracture incidence is higher in females, males are prone to have worse outcomes and poorer treatment rates, and it is reported that mortality in males is as much as twice that of females.[41,42] However, it has been also expressed that because of more social and recreational activities, falling and traumatic fracture possibilities are higher in males than in females in some regions.[17,43]

A limitation of this study was that there were no data from 16 countries of the EMR, including Afghanistan, Bahrain, Djibouti, Egypt, Iraq, Jordan, Libya, Palestine, Pakistan, Qatar, Somalia, Sudan, Syria, Tunisia, United Arab Emirates and Yemen. Some countries, like Iran, have a fracture registry and it needs to be established in all countries of the EMR. Another limitation was lack of data related to age-standardized incidence rates in every included papers, therefore, we sometimes had to rely on crude data. We also witnessed high heterogeneity between the studies. This can be explained by differences in study date, the status of fracture registration in each country, population age and gender. We tried to decrease the heterogeneity by inclusion of studies which were population-based and representative of community. However, such heterogeneity is usually seen in the epidemiological studies and is not unexpected.[18,43]

CONCLUSIONS

According to results of this study, there are significant variations in the annual incidence of hip fracture between the different countries of the EMR. However, lack of information was observed from most of the countries. It is suggested that preventive measures need to be implemented against traumatic and non-traumatic fractures in these countries by the relevant authorities. We also encourage all countries of the EMR to establish a national fracture registry.

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