

Prevalence of joint hypermobility in children and adolescents: A systematic review and meta-analysis

Amir Sobhani-Eraghi¹, Mohsen Motalebi², Siavash Sarreshtehdari¹, Borzooyeh Molazem-Sanandaji¹, Zahra Hasanlu¹

¹Department of Orthopaedics Surgery, Rasoul Akram Hospital, Iran University of Medical Sciences, Tehran, Iran, ²Department of Medicine, Trauma Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran

Background: The inconsistent results of different studies regarding the prevalence of joint hypermobility (JH) or joint laxity in children and adolescents made us conduct a meta-analysis on the prevalence of JH in this age group. **Materials and Methods:** We searched electronic databases including Trip, Scopus, Medline, Embase, PubMed, and Google Scholar; some Iranian databases including Iran Medex and Magiran; and Scientific Information Database to find studies in which the prevalence of JH in children and adolescents had been reported since January 1990 to April 2017. In this process, two researchers evaluated the articles separately while they were not aware of each other's method, and they extracted and matched the information. **Results:** Necessary data of twenty studies (15,097 boys and 6048 girls) were entered into this meta-analysis. The age range in these studies was 3–19 years. According to the meta-analysis conducted on the twenty studies, it was determined that the total prevalence of JH among children and adolescents was 34.1% (95% confidence interval [CI]: 33.3%–34.8%). Based on the results obtained from the studies, a significant heterogeneity (I_2 index equals to 99,415 and $P \leq 0.001$) was shown, so we used random-effects model; moreover, the overall assessment of studies showed a statistically significant publication bias ($P = 0.02$). In total, the prevalence in girls was equal to 32.5% (95% CI: 31.4%–33.7%), and in boys, it was equal to 18.1% (95% CI: 17.2%–19.1%). **Conclusion:** According to this meta-analysis, studies showed high heterogeneity, and the prevalence of JH in children and adolescents around the world was equal to 34.1% (95% CI: 33.3%–34.8%) in total, whereas it was higher in girls and lower in older ages. Level of evidence: 1.

Key words: Child, joint laxity, meta-analysis

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INTRODUCTION

Excessive mobility of joints was first described by Hippocrates in members of a tribe living in the south of Russia, but the term “hypermobility” was first used in the 19th century to explain Marfan and Ehlers–Danlos syndromes.^[1]

Hypermobility refers to excessive joint movement and can be symptomatic or asymptomatic. Hypermobility syndrome in fact refers to the excessive movement of joints (without accompanying other syndromes) with

symptoms such as pain and instability.^[2] Headache, back pain, joint pain, and intervertebral disc prolapse are the hallmarks of hypermobility syndrome.^[3] Despite the high prevalence of this syndrome among children and adolescents, final results are not very comprehensive and reliable due to performing studies on little samples, different methods for evaluation of joint hypermobility (JH), and different methods for pain evaluation. Nevertheless, the studies conducted on children, especially at school level, show that JH range from 30% to 50%.^[4,5] This high prevalence leads ligamentous laxity to be referred to as the variation among the general population in different reviews.

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Address for correspondence: Dr. Mohsen Motalebi, Department of Medicine, Baqiyatallah University of Medical Sciences, Baqiyatallah Hospital, Vanaq Square, Tehran, Iran. E-mail: dr.motalebi@gmail.com

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The report about JH in children between 6 and 15 years old ranged from 8.8% to 64.6%,^[6,7] which is very high. It seems that the reason for the above-mentioned range is that these studies have been carried out among different societies and races with different age groups. Moreover, the sample size has been extremely wide ranging so that the sample size varies from 364^[8] to 2432 cases.^[6] In addition, there is no consensus on whether the incidence of JH is the same or different in joints of both sides so that there are some reports confirming the differences and some emphasizing on the similarity of the involvement of both sides.^[9,10] There is a controversy about the relationship between JH and body weight.^[11,12] Although there is agreement that younger children are more likely to show JH than teens and young people,^[13] there is little evidence in this regard. For example, a study on 1845 Swedish children and adolescents^[14] showed that in all age groups, girls experience higher levels of JH than boys. In addition to that, JH in boys decreases with age, whereas this trend is quite the opposite in girls. On the contrary, in some studies, there was no relationship between age and severity of JH.^[15] Overall, it seems that there are significant gender- and age-related differences in the incidence of JH in children and adolescents, and these statistics are strongly influenced by the characteristics of the population under evaluation, race, geographical area, sample size and method of study design, JH evaluation methods, and genetic tendencies. Considering the high prevalence of JH, and its association with osteoarthritis, and the above-mentioned symptoms on the one hand and these different and widespread statistics about it on the other hand, it is essential to determine a global statistics for the management of this condition, hence we decided to gather all information about JH from all around the world and reanalyzed them to determine its actual prevalence and associations to do better management of this population and develop better health policies.

MATERIALS AND METHODS

We searched electronic databases including Trip, Scopus, Medline, Embase, PubMed, and Google Scholar; some Iranian databases including Iran Medex and Magiran; and Scientific Information Database to find studies which have reported the prevalence of JH and ligamentous laxity in children and adolescents since January 1990 to April 2017. We also made a separate search in Cochrane library and all relating references, in order to decrease the publication bias. We used the following keywords and their synonyms in title and abstract: child, hypermobility, joint laxity, and ligamentous laxity. All searching stages were carried out by two researchers, and any disagreement between them was solved by a third researcher. All final articles were evaluated qualitatively by STROBE questionnaire.^[16] The questionnaire evaluates 22 questions about the quality of descriptive articles, with each item having 1 score and a

total of 22 scores. A score <12 indicates that the article lacks quality. We limited our search to human studies and did not consider the limitations of the language of studies.

Eligible studies

Studies had to have the following conditions to enter this meta-analysis: (1) reviewing the prevalence of hypermobility in children and adolescents under 20 years old; (2) using Beighton score^[17,18] to diagnose hypermobility; (3) having score 12 or higher in STROBE analysis; and (4) having article formats in cross-section, case-control, clinical trial, and cohort. Articles with these conditions were entered into this meta-analysis regardless of the country and the language in which they were done. On the contrary, articles studying on people with musculoskeletal disorders, those who had pain or lesion at the reviewed site of the Beighton score, and people with known syndromic diseases were discarded.

Data extraction

We extracted the following information from the eligible articles entered into the meta-analysis: original writer, publication year, country in which the study was carried out, number of sample volume, boy-to-girl ratio, age range, prevalence of hypermobility, and differences in genders and age ranges. In this meta-analysis, we first analyzed the prevalence of hypermobility in total population, and then we did it in boys and girls separately because of significant differences of hypermobility in both genders according to the meta-regression test.

Definitions

Hypermobility is defined as excessive movement of joints beyond the normal range. All studies in this analysis were based on the criteria of Beighton *et al.*, which were conducted on 1083 children and adults in South Africa,^[17] with all those being almost identical to the Carter and Wilkinson scoring system in 1960.^[19] Based on the Beighton scoring system, a person gets 1 score for doing each of these moves (the first four moves will be performed on both sides and will score 1 for each side): (1) passive extension of the fifth metacarpo-phalangeal joint past 90°, (2) passive opposition of the thumb to the forearm, (3) hyperextension of the elbow joint past 10°, (4) hyperextension of the knee joint past 10°, and (5) trunk flexion allowing the palms to be placed flat on the floor. The maximum score in this system will be 9 and the score ≥ 4 is known as hypermobility.

Data analysis

We used STATA ver. 13.2 (StataCorp Inc., Cary, NC, USA) to conduct this analysis. The heterogeneity level of the study was determined based on I_2 and P value by Q test ($P \leq 0.05$ and high I_2 was considered significant) in evaluating the odds pooled ratio; a random-effects model (based on significant heterogeneity of the study) was used from

various studies. Moreover, publication bias was determined according to funnel plot diagram and Egger test.

RESULTS

Search results

In total, 3874 studies were found from different databases, of which there were 1031 repetitive studies that were deleted. By reviewing the title of 2843 remaining articles, 1796 unrelated studies were identified and removed. Abstract of the 1047 remaining articles were studied, of which 936 were unrelated to our analysis and were omitted. Full text of the 111 remaining studies was evaluated and 91 articles were excluded because of our inclusion criteria. The final twenty studies that were entered into this analysis were evaluated by the STROBE questionnaire. No items were identified as poor-quality articles. Eventually, all the twenty studies^[4,5,7,8,15,20-34] were entered into this analysis [Figure 1].

Characteristics of studies

The total number of patients evaluated in these twenty studies was 21,145 cases (including 15,097 boys and 6048 girls), which included a wide range of children aged between 3 and 19. Studies were carried out in different countries including Asian countries (40%) (Iran, India, Turkey, Pakistan, and Hong Kong), European countries (45%) (England, Denmark, Sweden, Italy, Poland, Spain, Iceland, and the Netherlands), Africa (5%) (Egypt), South America (5%) (Brazil), and Australia (5%). In some studies, the incidence of JH was reported in total population, and, in others, separately in boys and girls. Complete data based on the extracted ones from articles including age range, overall and gender prevalence, and the prevalence regarding age and total sample size of each study are specified in Table 1.

Meta-analysis

Based on the meta-analysis performed on the twenty studies, it was found that the overall prevalence of JH

in children and adolescents was 34.1% (95% confidence interval [CI]: 33.3%–34.8%) [Figure 2]. Based on the analysis done with respect to the I_2 index of 99.415 and $P < 0.001$, the results of the studies have had a significant heterogeneity. In addition, according to $P = 0.02$ in the Egger regression test and Funnel plot, there was a significant publication bias in this analysis [Figure 3].

According to the meta-regression test about gender ($P = 0.01$), only 12 of the 20 studies reported the prevalence of JH based on boys and girls. By assessing these studies, it was found that the prevalence of JH among boys was 18.1% (95% CI: 17.2%–19.1%) [Figure 4]. According to I_2 index of 976/806 and $P < 0.001$, the results of these 12 studies have had a significant heterogeneity. Furthermore, the overall evaluation of the publication bias was statistically significant in these 12 studies ($P = 0.01$) [Figure 5]. Moreover, the prevalence of JH among females, children, and adolescents was 32.5% (95% CI: 31.4%–33.7%) [Figure 6]. Accordingly, the results of the studies showed a statistically significant heterogeneity (I_2 index: 988/405, $P < 0.001$). There was a statistically significant publication bias in these 12 studies ($P = 0.01$) [Figure 7].

DISCUSSION

As we have already mentioned, various studies have been published with different outcomes regarding the prevalence of JH, as well as the gender and age differences in this disorder in different parts of the world, which have reached a different prevalence. Obviously, due to the different prevalence in this regard, there will be significant heterogeneity among different communities. This significant difference is resulted by two categories of factors, including community- and the study environment-related factors and factors associated with the type and design of the study. Regarding the first category, race, geographic location, and genetic tendencies will all be effective in the occurrence of this difference in JH. In contrast, the second category which are related to the study itself include sample size, different criteria and cutting points in the definition of JH, criteria for entering and leaving the study, selection process of the samples, and, most importantly, the different age ranges entered in the study. Considering all these factors and also the need for developing health policies to prevent the occurrence of disease in this group and reduce the cost of treatment, designing and conducting a systematic review and meta-analytic study aimed to achieving a pooled prevalence and determining the factors associated with it was absolutely necessary. In this study, we included all articles regardless of their language for reduction of publication bias and the most generalizability of the result and also searched Cochrane library especially for Clinical Trials Registry to ensure minimum publication bias. In

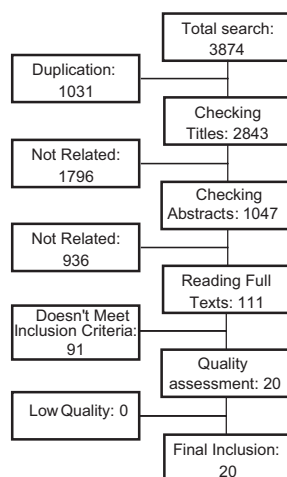


Figure 1: Results of searching strategy

Table 1: Details of evaluative studies in systemic review and meta-analysis

| Author, published year | Research population | Number of sample volume | Girls/boys | Age range | Prevalence (n) | Sexuality | Age difference |
|--|---------------------|-------------------------|------------|-----------|-----------------------------------|---|--|
| Cheng <i>et al.</i> , 1991 ^[20] | Hong Kong | 2360 | 1180/1180 | 3-13 | 65% (1534) | More prevalence in girls than boys | As age increases, score decreases |
| Lamari <i>et al.</i> , 2005 ^[7] | Brazil | 1120 | 586/534 | 4-7 | 64.6% (723) | More prevalence in girls than boys | As age increases, score decreases |
| Subramanyam and Janaki, 1996 ^[21] | India | 1000 | 500/500 | 6-10 | 65% boys, 35% girls (175-325) | More prevalence in boys. Under 10 years old: more prevalence in girls. Higher than 10 years old | As age increases, score decreases in boys |
| Seçkin <i>et al.</i> , 2005 ^[22] | Turkey | 861 | 431/428 | 13-19 | 7.2% boys, 16.2% girls (31-70) | More prevalence in girls | As age increases, the score decreases |
| Gyldenkerne <i>et al.</i> , 2007 ^[8] | Denmark | 364 | 164/200 | 12-13 | 3.3% boys, 16.6% girls (6-27) | More prevalence in girls | As age increases, the score decreases |
| Remvig <i>et al.</i> , 2013 ^[23] | Denmark | 315 | 159/156 | - | 21.2% (67) | - | - |
| Romeo <i>et al.</i> , 2016 ^[24] | Italy | 284 | 138/146 | - | 7% (20) | There is no sexual difference | There is no age difference |
| El-Garf <i>et al.</i> , 1998 ^[4] | Egypt | 997 | 497/500 | - | 14.4% boys, 18% girls (72-89) | There is no sexual difference | As age increases, the score decreases |
| Butt <i>et al.</i> , 2014 ^[25] | Pakistan | 500 | 200/300 | 8-17 | 29.0% boys, 33.5% girls (87-67) | There is no sexual difference | As age increases, the score decreases in girls |
| Morris <i>et al.</i> , 2017 ^[26] | Australia | 1584 | 769/815 | 14 | 36.7% boys, 60.6% girls (300-466) | More prevalence in girls | - |
| Gocentas <i>et al.</i> , 2016 ^[27] | Poland | 778 | 378/400 | 7-12 | 19.2% (149) | - | - |
| Öhman <i>et al.</i> , 2014 ^[28] | Sweden | 138 | 58/80 | 5-8 | 12% (16) | More prevalence in girls | As age increases, the score decreases |
| Clinch <i>et al.</i> , 2011 ^[29] | The UK | 6022 | 3061/2961 | 7-18 | 10.6% boys, 27.5% girls (314-841) | More prevalence in girls | There is no age difference |
| Viswanathan and Khubchandani, 2008 ^[30] | India | 433 | 214/219 | 3-9 | 40.8% (177) | There is no sexual difference | There is no age difference |
| Hasija <i>et al.</i> , 2008 ^[31] | India | 829 | 309/520 | 3-19 | 58.7% (487) | There is no sexual difference | As age increases, the score decreases |
| Qvindesland and Jónsson, 1999 ^[5] | Iceland | 267 | 167/100 | 12 | 12.9% boys, 40.5% girls (13-68) | More prevalence in girls | - |
| Rikken <i>et al.</i> , 1997 ^[15] | The Netherlands | 910 | 449/461 | 4-17 | 10.2% boys, 18.7% girls (47-84) | More prevalence in girls | There is no age difference |
| Verd, <i>et al.</i> , 1991 ^[32] | Spain | 1136 | 444/692 | 11-14 | 13.0% boys, 21.0% girls (90-94) | More prevalence in girls | There is no age difference |
| Ziaee and Moradinejad, 2008 ^[33] | Iran | 252 | 132/120 | 6-16 | 10.0% boys, 13.6% girls (12-18) | More prevalence in girls | As age increases, the score decreases |
| Jamshidi <i>et al.</i> , 2004 ^[34] | Iran | 1005 | 501/504 | 6-19 | 14.1% boys, 33.7% girls (71-169) | More prevalence in girls | As age increases, the score decreases |

addition, all of the references of relevant review studies were checked to find further investigations not found previously in primary electronic search. Two investigators separately did all of the searches and quality assessment procedures and any disagreements between them were

resolved by the third author. Among all the studies that referred to JH among children and adolescents, twenty studies fulfilled the inclusion criteria and based on them, it was found that the overall prevalence of JH was 34.1%, which is estimated to be 32.5% in girls and 18.1% in boys,

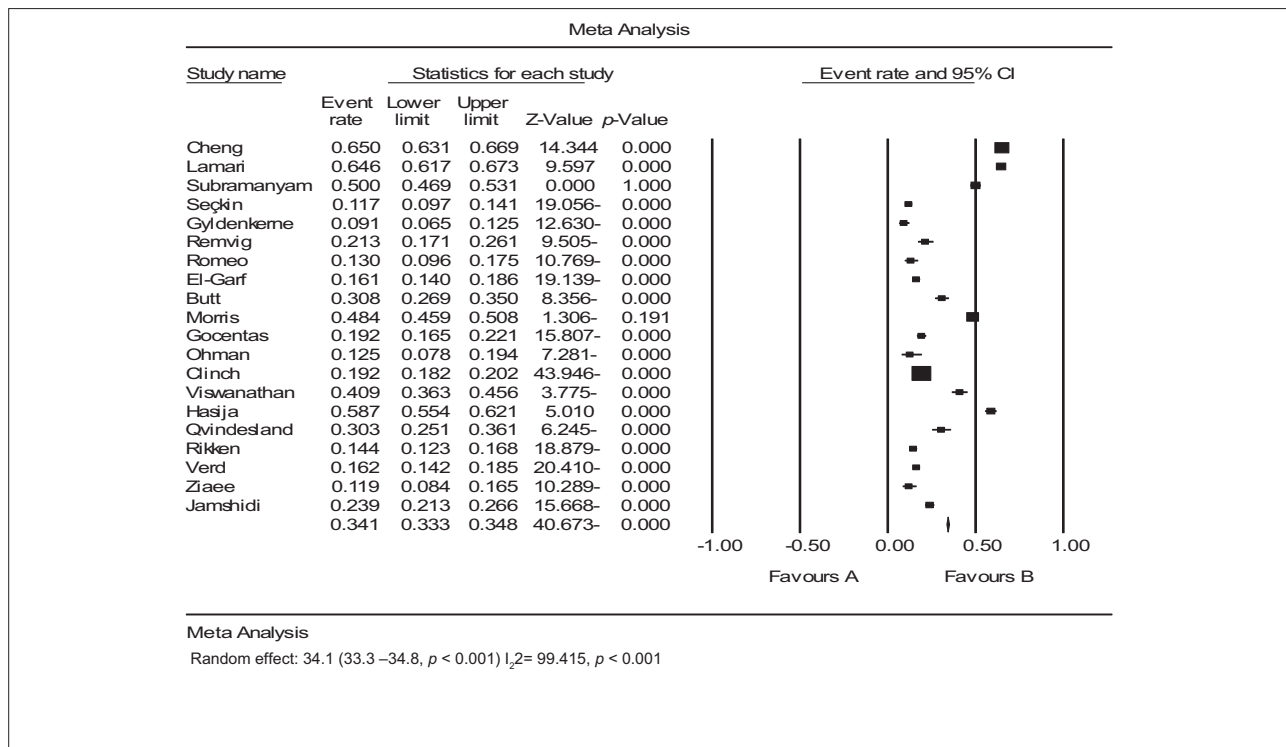


Figure 2: Prevalence of joint hypermobility in the twenty evaluated studies

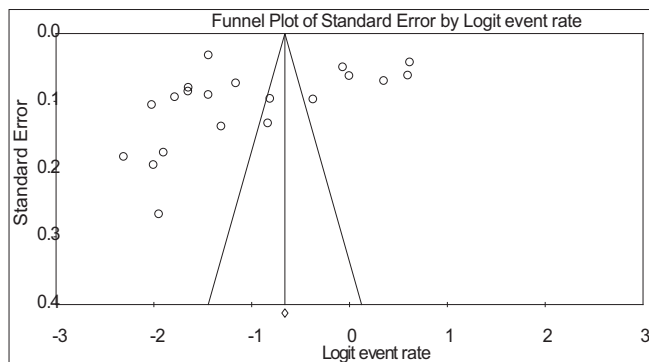


Figure 3: Publication bias in the twenty evaluated studies

which, in general, indicates a higher prevalence of this disorder in girls.

Regarding the prevalence of JH in different genders, in 12 out of the 20 studies,^[5,7,8,15,20,22,26,28,29,32-34] the prevalence of this disorder in girls was significantly higher than that of boys. In one study in India, <10 years old, the prevalence was higher in boys than girls, whereas over the age of 10 this prevalence was *vice versa*.^[21] In the remaining seven studies, there was no statistically significant difference between boys and girls regarding the incidence of JH.^[4,23-25,27,30,31]

Concerning the prevalence of JH in different ages, it was also found that in nine studies,^[4,7,8,20,22,28,31,33,34] the increasing age was associated with a decrease in the prevalence of JH, and this prevalence was independent of sex, but in one

study, the inverse relationship between age and prevalence of the disorder was only in boys.^[21] In another study, this inverse relationship was observed only in girls.^[25] On the contrary, in five studies, there was no relationship between the prevalence of JH and age^[15,24,29,30,32] and in four studies, there was no mention of age differences.^[5,23,26,27] As a result, in the majority of studies, it was found that with increasing age of the patients, the prevalence of JH had significantly reduced. This is due to the tendency of collagen fibers to bind together more as a result of more tissue stiffness with increasing age.^[17,35,36]

There are a few important points in relation to this meta-analysis: first, the number obtained for total prevalence or gender-related prevalence is basically not reliable due to the high heterogeneity among studies. This heterogeneity was due to the difference in the sample size of the studies, the different cut scores for diagnosis of the JH, as well as the demographic and racial differences between the studies. In general, it could be mentioned that, first, the sample size of the study varied widely between 128 and 6022, which was very broad. Second, there was a high geographic dispersion between studies, but in a review of studies, it can be concluded that the highest prevalence was observed in Southeast Asian countries (China and Hong Kong) and South Asian (India) as well as South America (Brazil), whereas in the European countries, we have encountered the lowest prevalence of JH. This conclusion can be an emphasis on a favorable life pattern in European countries,

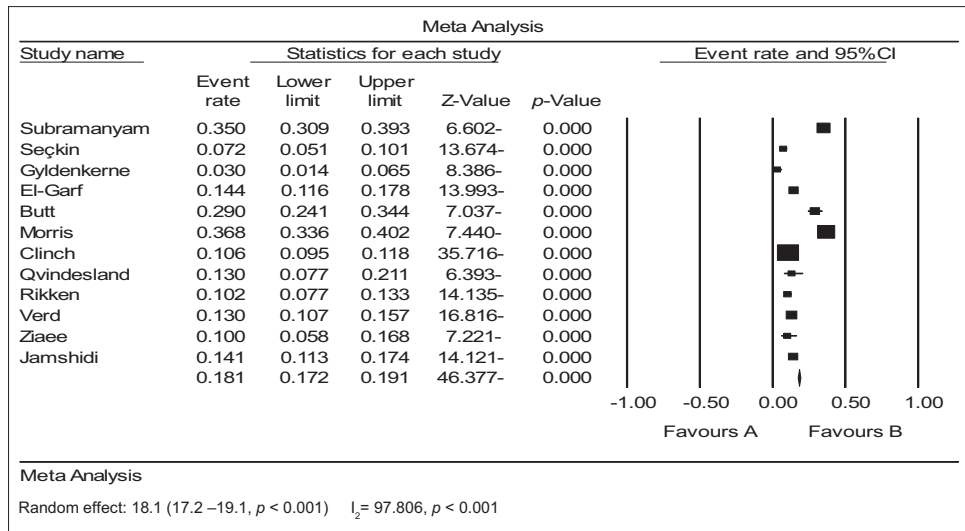


Figure 4: Prevalence of joint hypermobility in boys in the 12 evaluated studies

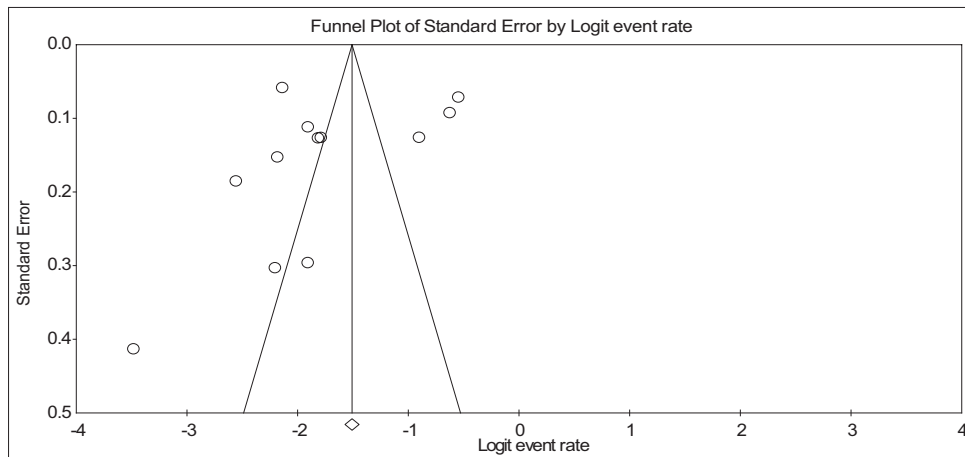


Figure 5: Publication bias in the 12 evaluated studies about prevalence in boys

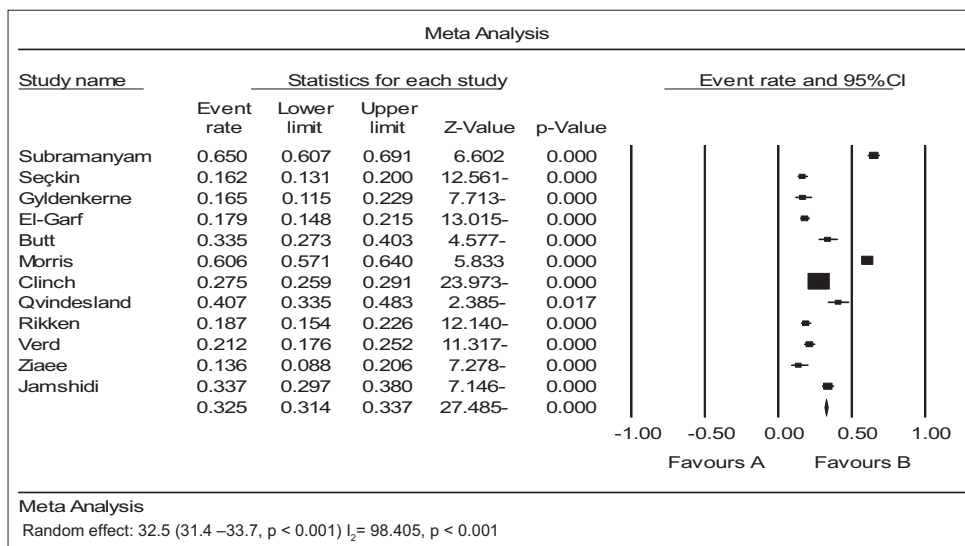


Figure 6: Prevalence of joint hypermobility in girls in the 12 evaluated studies

as well as a more consistent implementation of screening and preventive programs for encountering connective

tissue disorders as well as musculoskeletal disorders in these communities.

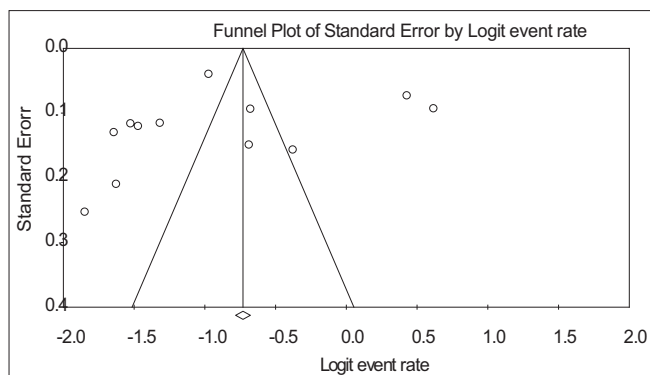


Figure 7: Publication bias in the 12 evaluated studies about prevalence in girls

Higher prevalence of JH in girls than boys can be attributed to the difference of their body structure, as well as hormonal effects before and during puberty in both sexes. On the other hand, decreasing incidence of JH with aging may be due to the physical growth and development of individuals following getting older, especially when they reach adulthood. Finally, the important point to mention is that only two comprehensive studies have been published in Iran that are inadequate for systemic analysis in our society, especially considering racial and geographical diversity in our country.^[33,34] Nevertheless, findings related to JH in Iranian studies (prevalence in the study of Ziaee was 10% in boys and 13.6% in girls, and in the study of Jamshidi was 14.1% in boys and 33.7% in girls) showed that the prevalence in girls was higher than that in boys, and, as the age increases, the disease's prevalence decreases.^[33,34] In both studies, the prevalence in girls was higher than that in boys, and, as the age increases, the disease's prevalence decreases, which is closer to the findings of European studies, which indicates that screening and management of this problem is desirable in our country, but there is still a long way to go in comparison to the developed countries.

Limitation

Our limitations in this analysis were as follows: First, many studies used scores other than the Beighton score to diagnose JH so that we could not include these studies in our work. Second, there are many unreliable reports about the prevalence of JH all around the world, of which none are valid. Third, there was a significant publication bias in our study, indicating that some studies have not been published by researchers for unknown reasons, and these studies are out of reach. However, it seems that in this situation, the results of this meta-analysis would be countable.

CONCLUSION

Regarding this analysis, it can be concluded that, first, the global prevalence of JH was estimated to be 34.1%, which

was more prevalent in girls than in boys and lower in younger ages. Second, the results of studies have had a high heterogeneity. Third, the results of limited studies in Iran show a prevalence of 10%–14.1% in boys and 13.6%–33.7% in girls.

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Conflicts of interest

There are no conflicts of interest.

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