RESEARCH ARTICLE

Epidemiology of Generalized Ligamentous Laxity in Iran: A National Study Including Different Iranian Ethnic Groups and its Relationship with Musculoskeletal Disorders

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Abstract

Background: Ligamentous laxity is a condition that leads to joints' hypermobility beyond their average and normal range of motion. It can cause musculoskeletal and joint injuries. This national multi-centered study investigated the epidemiology of generalized ligamentous laxity and its relationship with musculoskeletal disorders among Iranian adults with different ethnic backgrounds.

Methods: A total of 1,488 people (age range: 17-40 years) were selected from eight cities and six different ethnicities of Iran and included in this cross-sectional study. The presence of ligamentous laxity with clinical examinations was searched according to Beighton score criteria. They were also examined for any kind of musculoskeletal disorders that might accompany ligamentous laxity. The Chi-square test was used to compare the frequency of ligamentous laxity based on gender and ethnicity; moreover, the t-test was utilized to compare the frequency of ligamentous laxity based on age.

Results: In total, 280 (18.8%) participants had generalized ligamentous laxity, and it was more prevalent in women (22.7%), compared to men (14.4%). Regarding ethnicity, the highest and lowest prevalence rates were in Gilak (37.9%) and Persian-Arab (6%) ethnicities, respectively (*P<0.001*). Ligamentous laxity showed a significant relationship with sports injury, joint complaint, joint dislocation, ligament sprain, sciatica and back pain, Baker's cyst, and varicose veins (*P<0.001*). Most participants with generalized ligamentous laxity (93.6%) had no knowledge of their problem and its importance in choosing an appropriate sports activity.

Conclusion: The prevalence of generalized ligamentous laxity seems to be relatively high among the 17-40-year-old population of Iran, especially in women. It seems to be significantly related to ethnicity. It is strongly recommended that examinations, screening, and information be provided at an early age in schools or at least in areas with a high prevalence as national programs.

Level of evidence: I

Keywords: Ethnicity, Hypermobility, Iran, Joint laxity, Ligamentous laxity

Introduction

Ligamentous laxity is a condition that leads to joints' hypermobility beyond their average and normal range of motion (1). As far as the authors know, it was first described 2,400 years ago by Hippocrates in some soldiers who could not use their weapons properly because of shoulder and elbow instability (2). In 1967,

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Kirk et al. explained this condition as a hypermobility syndrome in a group of patients with ligamentous laxity, joint instability, and musculoskeletal symptoms (3). Generalized joint laxity is a genetically inherited trait that alters the composition and alignment of the collagen matrix within connective tissues, such as ligaments, thereby increasing the range of a joint via enhanced soft-tissue extensibility in a normal population (4). This condition is observed as a known feature in some collagen disorder diseases, such as Ehlers-Danlos syndrome, Marfan, and osteogenesis imperfecta. It has also been observed in many healthy people in the absence of other diseases, which is called generalized benign joint hypermobility (5, 6). Ligamentous laxity with no association with systemic or rheumatologic diseases occurs in 4%-13% of the general population (7, 8). Its prevalence is about five times higher in women than men (9). It is also widely believed that younger children are more flexible than adolescents (10). Therefore, the reported prevalence of generalized joint laxity in 6-15-year-old people has been up to 64.6% (11). Although people with ligamentous laxity may not have a complaint about their condition, they are always at risk of musculoskeletal problems, such as ankle sprain, injury of knee's cruciate ligaments, shoulder instability, and flat foot (12, 13). Ethnic background can influence hypermobility (14, 15). Ligamentous laxity has been more prevalent in African, Asian, and Middle Eastern races (16). The most common way of diagnosing ligamentous laxity is the use of the Beighton scoring system (17). This is a 9-point scale and requires five maneuvers, including four passive bilateral and one active unilateral performance. It was originally introduced for epidemiological studies involving the recognition of hypermobility in populations (2, 10). Iran has more than 81 million people with different ethnicities the same as many other countries. The exact population distribution based on ethnic groups is not known as it is classified as national security information. There has never been a national study on the epidemiology of ligamentous laxity among the adult population of Iran. Therefore, this pilot study was conducted in one province which had four ethnic groups in 2018 (1).

It was decided to do a national study using the results of that research and with the help of eight medical universities in different provinces of Iran, including Fars, Isfahan, East Azerbaijan, Kurdistan, Khuzestan, Guilan, Khorasan Razavi, and Hamadan. This study was a continuation of the pilot study which was published in 2020. It is believed that studying joint laxity and the possible presence of generalized ligamentous laxity can make people aware of this problem. It is hoped that it can lead to implementing pre-screening methods in schools and sports clubs to help people choose an appropriate sports activity, thereby preventing musculoskeletal and sports injuries (1). Since ethnic background can influence hypermobility, it was wondered whether prevalence was different in various ethnic groups (14, 15). Accordingly, the epidemiology of generalized ligamentous laxity and its relationship with musculoskeletal disorders was investigated as a national multi-centered study for the first time among Iranian adults with different ethnic backgrounds.

Materials and Methods

This nationwide cross-sectional study was conducted on different Iranian ethnic groups. Similar to our pilot study, the sampling sites were high schools, universities, and sports clubs including various sports. In total, six sub-groups were selected based on the chosen ethnicities. The participants lived in the capital cities of the selected provinces, and they were from such ethnicities (and cities) as Azeri (from Tabriz), Lur (from Khorramabad), Persian (from Shiraz, Mashhad, and Isfahan), Kurd (from Sanandaj), Persian-Arab (from Ahvaz), and Gilak (from Rasht) [Figure 1]. It should be mentioned that the people who were originally from the aforementioned cities and ethnicities, and cases whose both parents were from those cities and ethnicities were selected and included in this study.

The exact population distribution based on ethnic groups is not known since it is classified as national security information; accordingly, the number of participants was estimated according to the results of our pilot study (1). The participants were clinically examined using a goniometer. The Beighton scoring system was also used to evaluate the ligamentous laxity severity [Table 1]. A score of four or higher was considered a positive result for ligamentous laxity, and a higher score meant a more severe condition. The demographic characteristics were collected using a questionnaire. The inclusion criteria were: 1) age range within 17-40 years; and 2) residency of the participant (him/herself) and parents in the same city from the same ethnicity. On the other hand, the participants with congenital or acquired problems in their upper or lower extremities, spinal cord, vertebral column or trunk, as well as those who refused to complete the questionnaire and undergo

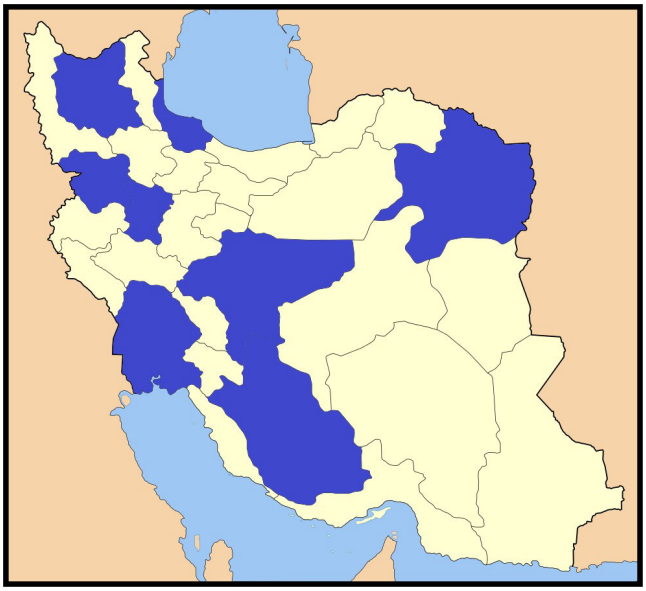

Figure 1. The studied provinces each of which had an Iranian ethnicity as its majority, Are highlighted in blue.

Table 1. Beighton score to assess generalized ligamentous laxity

Joint	Evaluation	Point
Left little (5th) finger	Passive dorsiflexion > 90°	1
Right little (5th) finger	Passive dorsiflexion > 90°	1
Left thumb	Passive dorsiflexion to the flexor aspect of the forearm	1
Right thumb	Passive dorsiflexion to the flexor aspect of the forearm	1
Left elbow	Hyperextension > 10°	1
Right elbow	Hyperextension > 10°	1
Left knee	Hyperextension > 10°	1
Right knee	Hyperextension > 10°	1
Forward flexion of the trunk with knees fully extended	Ability to rest palm and hands flat on the floor	1

all the examinations were excluded from the study. The questionnaires were anonymous, and the information was reported confidentially in the form of tables and charts. All participants older than 18 years of age signed an informed consent form before participating in the study. For those who were between 17 and 18 years of age, the informed consent was signed by their parents. The study protocol was approved by the Ethics Committee of Hamadan University of Medical Sciences, Hamadan, Iran (IR.UMSHA.REC.1395.19).

Statistical analysis

Descriptive information was summarized in the form of tables, charts, as well as measures of central tendency and dispersion. The number of required samples was estimated to be 864 cases according to the results of our pilot study; however, 1,488 cases were examined in this study. The Chi-square test was utilized to compare the frequency of ligamentous laxity based on gender and ethnicity. The frequency of ligamentous laxity based on age was compared using the t-test. The statistical population included the total population aged 17-40 years old in eight different cities (Tabriz, Khorramabad, Isfahan, Shiraz, Ahvaz, Mashhad, Sanandaj, and Rasht) in 2020. The collected data were analyzed using SPSS software (version 25) at the confidence level of 95%.

Results

In total, 1,488 people were included in this study, and the majority of the participants were female (n=777; 52.2%). The mean age of the cases was obtained at 28.44±6.82 years (age range: 17-40 years). The first, second, and third quartiles were estimated at 23, mid-28, and 34 years, respectively. Regarding ethnicity, this study included 469 (31.5%) Persian, 174 (11.7%) Azeri (Persian-Turkish), 171 (11.5%) Kurd, 214 (14.4%) Gilak, 245 (16.5%) Lur, and 215 (14.4%) Persian-Arab participants. A number of 280 (18.8%) participants had ligamentous laxity (Beighton score of 4 and more). Regarding gender, 14.4% and 22.7% of the male and female participants had ligamentous laxity, respectively (*P=0.00*) [Table 2]. Furthermore, the highest and lowest

Table 2. Frequency distribution of ligamentous laxity and its prevalence among study participants by gender and ethnicity

Variable	Category	Ligamentous laxity (%)		*P-value*	Prevalence (95% Confidence interval)
		Positive	Negative		
Gender	Male	103(14.4%)	608	0.00	14.4 (11.9: 17.3)
	Female	177(22.7%)	600		22.7 (19.8: 25.9)
Ethnicity	Persian	90(19.1%)	379	0.00	19.1 (15.7: 23.0)
	Azeri	35(20.1%)	139		20.1 (14.4: 26.8)
	Kurd	23(13.4%)	148		13.4 (8.7: 19.4)
	Gilak	81(37.8%)	133		37.8 (31.3: 44.7)
	Lur	38(15.5%)	207		15.5 (11.2: 20.6)
	Persian-Arab	13(6%)	202		6.0 (3.2: 10.1)
Total		280(18.8%)	1208	NA	18.8 (16.8: 20.9)

prevalence rates of ligamentous laxity were in the Gilak (37.9%) and Persian-Arab ethnicities (6%), respectively (*P=0.00*) [Table 2]. The mean age was obtained at 26.26±6.40 years in those with ligamentous laxity which was significantly lower, compared to those who did not have this condition (mean age: 28.90±6.68 years; *P<0.001*).

The prevalence of conditions that might have had a relationship with ligamentous laxity in the literature was also investigated in this study. The prevalence of some complications was significantly higher in the ligamentous laxity group, such as sports injury, joint complaint, joint dislocation, ligament sprain, sciatica and back pain, Baker's cyst, and varicose veins. However, no significant relationship was found between our ligamentous laxity group and some other complications, such as Raynaud's phenomenon, easy bruising, poor skin healing, and flat foot [Table 3].

Only 6.4% of the participants with ligamentous laxity knew about their problem. Interestingly, 0.6% of the

Table 3. Prevalence of complications in the studied Iranian population

Variables	Negative	Ligamentous laxity	Positive	Total	Significance
Sports injury	No	1131 (82%)	249 (18%)	1380	*P=0.010*
	Yes	77 (71.3%)	31 (28.7%)	108	
Joint complaint	No	1143 (82.1%)	249 (17.9%)	1392	*P=0.001*
	Yes	65 (67.7%)	31 (32.3%)	96	
Joint dislocation	No	1167 (82.2%)	253 (17.8%)	1420	0.00
	Yes	41 (60.3%)	27 (39.7%)	68	
Ligament sprain	No	1156 (82.5%)	245 (17.5%)	1401	0.00
	Yes	52 (59.8%)	35 (40.2%)	87	
Sciatica	No	1157 (82.7%)	242 (17.3%)	1399	0.00
	Yes	51 (57.3%)	38 (42.7%)	89	
Raynaud's phenomenon	No	1200 (81.2%)	277 (18.8%)	1477	*P=0.443*
	Yes	8 (72.7%)	3 (27.3%)	11	
Easy bruising	No	1192 (81.3%)	275 (18.7%)	1467	*P=0.573*
	Yes	16 (76.2%)	5 (23.8%)	21	
Poor skin healing	No	1192 (81.1%)	278 (18.9%)	1470	*P=0552*
	Yes	16 (88.9%)	2 (11.1%)	18	
Baker's cyst	No	1192 (81.6%)	268 (18.4%)	1460	*P=0.030*
	Yes	16 (57.1%)	12 (42.9%)	28	
Varicose veins	No	1184 (81.8%)	263 (18.2%)	1447	*P=0.001*
	Yes	24 (58.5%)	17 (41.5%)	41	
Flat foot	No	1178 (81.2%)	273 (18.8%)	1451	*P=1.00*
	Yes	30 (81.1%)	7 (18.9%)	37	
Total		1208 (81.2%)	280 (18.8%)	1488	

normal healthy people falsely believed that they have ligamentous laxity. In the ligamentous laxity group, 43.9% of the cases did regular exercises. The most common exercises were bodybuilding and fitness (11.8%). On the other hand, in our normal healthy population, only 22% of the cases exercised regularly which was significantly lower than those in the ligamentous laxity group (*P=0.00*). It is worth mentioning that bodybuilding and fitness were the most common exercises in this group.

In addition, 89.2% of all participants and 88.9% of the cases with ligamentous laxity did not know that they had this condition, they should be careful about choosing the type of activities and exercises, to be more prone to sports injuries, or to have a plan to prevent injury.

Discussion

The epidemiology of generalized ligamentous laxity was investigated among adults (17-40 years old) who lived in eight different provinces of Iran. Therefore, 1,488 participants, of whom 280 (18.8%) people had generalized ligamentous laxity (Beighton score of 4 and more) were included in this study. In our pilot study (1), no significant relationship was found between the prevalence of generalized ligamentous laxity and ethnicity (1). However, by adding Gilak and Persian-Arab ethnicities in this study and increasing the number of participants, it was found that the prevalence of generalized ligamentous laxity was significantly related to ethnicity. The highest and lowest prevalence rates were in the Gilak (37.9%) and Persian-Arab ethnicities (6%), respectively. It is believed that although ethnicity is a good indicator of genetic factors, the role of environmental factors cannot be ruled out since many people of the same ethnicity usually live in the same environment in addition to having similarities genetically.

According to the previous studies, the prevalence of ligamentous laxity is 4%-13% in a population with no associated systemic and rheumatologic diseases (7, 8). However, its prevalence was obtained at 18.8% in our study which is a bit higher than that in other studies. The results also reveal that its prevalence is higher among women; moreover, it has a direct and inverse relationship with age. These results are consistent with the finding of other studies (7, 8, 18, 19). To our knowledge, there is only one study about the epidemiology of ligamentous laxity in Iran. Jamshidi et al. investigated the prevalence of joint hypermobility syndrome on 1,005 students aged 6 to 19 years in Tehran, Iran (18). The prevalence of hypermobility syndrome was 23.9%, which was significantly higher in girls (33.7% in girls, compared to 14.1% in boys). Hypermobility was also more prevalent in the younger age groups. They did not consider ethnicity in their study, and they had a higher prevalence probably because they had only studied children and adolescents.

Ligamentous laxity might be an advantage in some sports that require optimal flexibility for aesthetic and performance-enhancing purposes, such as gymnastics (20). However, it may be detrimental in sports where the link between generalized joint laxity and musculoskeletal injury has previously been established.

There are many studies about the relationship of ligamentous laxity with increased risk of sports injury. Ramesh et al. stated that 42.6% of the patients with anterior cruciate ligament injuries had generalized ligamentous laxity, while this value was estimated at 21.5% in the control group. They also showed an internal relationship among proprioception, increasing ligamentous laxity, and joint injuries (10). In another study on this issue, Bin Abd-Razak et al. compared 100 military personnel aged 18 to 25 years old suffering from musculoskeletal injuries with 100 individuals without any musculoskeletal injuries or complaints. The generalized ligamentous laxity was observed in 12% of the first and 4% of the second groups. The results indicated that the presence of generalized ligamentous laxity in people with musculoskeletal injuries was probably a contributing factor to those injuries (21). Saremi et al. showed that athletes with ligamentous laxity suffered significantly more pain in the shoulders and had chronic shoulder injuries and instability, compared to non-affected individuals (22). In addition, Okamura et al. found a significant relationship between low back pain and generalized ligamentous laxity in 192 men who were ice skating athletes in Japan (23).

Tingle et al. did a systematic review on the links between generalized joint laxity and the prevalence/severity of limb injuries related to physical exercises (24). They demonstrated a relationship between generalized joint laxity and lower limb injury incidence in different forms of physical exercise. Still, evidence for potential links between generalized joint laxity and upper limb injury, or injury severity, was inconclusive. They suggested more research on the link between generalized joint laxity and upper limb injury. Their review had focused on "physical exercise", including both doing sports and being physically active while not taking part in a defined sport. The prevalence of musculoskeletal injuries, such as sports injury, joint complaint, joint dislocation, sciatica and back pain, as well as ligament sprain and Baker's cyst, were significantly higher in those who had generalized ligamentous laxity. The results in this study are consistent with the findings of other similar studies. Varicose veins can also be added to this list that is a non-musculoskeletal complication.

In a study on 50 university student girls in Tehran, Iran, Shakeri et al. found a significant correlation between the general hypermobility of the body and lower arched feet. However, the same results were not obtained in the present study since no significant relationship was observed between ligamentous laxity and flat foot (25). However, flat foot, but not its severity was considered in this study. The rate of doing regular exercises in our ligamentous laxity group was twice of that in the normal participants. Although there is no evidence that regular exercise can affect the laxity of ligaments, this could be a subject of research that needs a long-term cohort study. A possible reason might be that people with ligamentous laxity subconsciously feel the need for more exercise. Our hypothesis is based on the finding that most of them do bodybuilding, which is a recommended sport for laxity (26).

Limitations

Although trained researchers did all the examinations, this can still be a possible point of error. Moreover, when a participant was considered within an ethnic group according to the ethnicity of the parents (that is where s/he and his/her parents were born), there may still be a person in his predecessors (grandmother or grandfather) who is from another ethnic group that we are not aware of. Therefore, a person's true ethnicity might not be completely of the ethnic group in which we have grouped him/her. Sample size can be another limitation of our study because, for the time being, it will not be possible to know the exact national statistical population of each ethnic group in the country. Finally, this study was conducted on six major Iranian ethnic groups. However, Iran has other ethnic groups, such as Baloch, Turkmen, Mazandarani (Mazani), Armenian, Assyrian, Jew, Tat, Circassian, and Mandaeans, which were not included in this study. As far as we know, most of them most probably have fewer populations, compared to the six studied ethnicities.

It seems that the prevalence of generalized ligamentous laxity is relatively high among the population aged 17 to 40 years in Iran, especially in women. The history of musculoskeletal disorders is significantly higher in the affected, compared to non-affected individuals. It was found that 93.6% of the participants with ligamentous laxity were not aware of their condition, and almost 90% of them had no idea of its importance in choosing an appropriate activity and exercise. Accordingly, it is strongly recommended to provide examinations, screening, and information at an early age in schools or at least in areas with a high prevalence as national programs. It is also recommended that future studies consider the other Iranian ethnic groups in studying the prevalence of generalized ligamentous laxity.

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