

## Association of Benign Joint Hypermobility Syndrome with Mitral Valve Prolapse in Iranian Children

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### Abstract

**Aim and purpose:** The aim of this study was to determine the association of benign joint hypermobility syndrome (BJHS) with mitral valve prolapse. **Subjects and methods:** This is a case-control study. Sixty-three children with benign joint hypermobility syndrome were included in case group and 63 without any rheumatologic disease were placed in control group. We used Carter-Wilkinson and Beighton criteria for diagnosing of benign joint hypermobility syndrome. Mitral valve prolapse was evaluated by echocardiography in both groups. The mitral leaflet displacement  $>2$  mm considered as cut off for diagnosis of mitral valve prolapse. Cardiologist did not have any information about patients group during echocardiography. Data was analysed using SPSS ver. 13.0. Chi-square used for comparison. **Results:** In this study, 32 girls and 31 boys were included. Mean of age in case group was  $7.1 \pm 2.67$  and for control was  $6.9 \pm 3.25$  years. Mitral valve prolapse was discovered in 54% of cases and 12.7% of control groups ( $P=0.001$ ). Mitral valve prolapse was significantly higher among cases with BJHS aged  $>7$  (58.8%) year compared to 3-7 (41.2%) year of age ( $P=0.027$ ). Heart murmur and palpitation was more common among children with benign joint hypermobility syndrome with mitral valve prolapse compared to children without mitral valve prolapse ( $P<0.05$ ). **Conclusion:** The incidence of mitral valve prolapse among children with benign joint hypermobility was significantly higher than control group.

### Key words

Beighton criteria; Benign joint hypermobility syndrome; Mitral valve prolapse; Rheumatologic disease

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## Introduction and Aim

Benign joint hypermobility syndrome (BJHS) is a clinical condition characterised by an increased distensibility of joint during passive movements and hypermobility in dynamic movements. There are several diagnostic criterion suggested by Rotes-Querol,<sup>1</sup> Carter and Wilkinson,<sup>2</sup> Beighton et al<sup>3,4</sup> and Bulbena et al.<sup>5</sup> Beighton diagnostic criteria is the most famous criteria which is the revised version of Carter and Wilkinsons's. In 1992, the validity and reliability tests are done by Bulbena et al.<sup>6</sup> Beighton score was also validated by van der Giessen et al for Dutch children aged 4-12 years.<sup>7</sup> Prevalence of hypermobility was reported between 5-30% using several criteria.<sup>8-11</sup> The highest prevalence of BJHS was found in Iraq<sup>12</sup> and Nigeria respectively.<sup>13</sup> BJHS may affect many organs such as Cardiovascular system, genitourinary system<sup>14</sup> as a consequence of involvement of connective tissue.

Mitral valve prolapse (MVP) is the most commonly diagnosed cardiac abnormality and affects around 5% of population.<sup>15</sup> Abnormalities of collagen have been found in valves of patients with MVP.<sup>16,17</sup> Similar findings were noted in the skin biopsies of patients with BJHS.<sup>18</sup> As the results, there was suggested common pathogenic mechanism for abnormal production or maturation of collagen in both diseases.<sup>19</sup>

There were limited published papers concerning children with BJHS and MVP. The aim of this study was to determine the association of benign joint hypermobility syndrome with mitral valve prolaps in Iranian population.

## Materials and Methods

This case control study was carried out in Mofid children's hospital as the referral center for pediatric rheumatology in Iran. Sixty-three cases with BJHS and 63 healthy children without rheumatologic disease were studied in two groups of case and control respectively. Both groups were matched in age and sex. Beighton criteria were used to diagnose BJHS.<sup>3</sup> Age, sex, joint pain, muscular pain, joint dislocation, chest pain, and heart murmur was recorded for each individual. The hereditary musculoskeletal disorders as like as, Marfan syndrome, Ehlers-Danlos, and Osteogenesis imperfecta, were considered as Exclusion criteria in our study. Mitral valve prolapse was checked by echocardiography in both of case and control groups.

Diagnosis of mitral valve prolapse was based on modern echocardiographic techniques which can pinpoint abnormal leaflet thickening and other related pathology. The mitral leaflet displacement (MLD) >2 mm considered as cut off for diagnosis of MVP. Data was analysed using SPSS ver 13 (SPSS Inc, Chicago, IL, USA). Chi-square and Mann whitney U-test were used for comparison. The informed Consent application form was signed by parents.

## Results

In this study, 63 (M=31, F=32) subjects were studied in each groups of case and control. Mean of age in case group was  $7.1 \pm 2.67$  (range: 3-13, median=7, mode=5) and for control was  $6.9 \pm 3.25$  (range: 3-16, median=6, mode=3). Mitral valve prolapse was significantly higher in case group compared to control (Chi-Square,  $P < 0.001$ ) (Table 1). MVP was significantly higher among cases with BJHS aged >7 years compared to 3-7 years of age ( $P = 0.027$ ) (Table 2). Heart murmur and palpitation was more common among BJHS cases with MVP compared to cases without MVP ( $P < 0.05$ ) (Table 3). Among the BJHS cases without MVP, tricuspid regurgitation was more frequent than palpitation or heart murmur ( $P < 0.05$ ) (Table 3). Myalgia was more common than arthralgia or dislocated joint ( $P < 0.05$ ). Statistically, we could not find significant relation between myalgia and/or arthralgia with MVP ( $P = 0.406$  &  $0.653$ ) (Table 3).

Distribution of MVP among cases with Beighton score 6-9 has been shown in Table 4. By increasing Beighton score, there was slight increase in the proportion of the cases with MVP. By the age 7, 75% of cases had MVP. It is difficult to drawn a conclusion due to insufficient number of sample.

Among BJHS cases with MVP, there was no statically significant difference between prevalence of myalgia and arthralgia ( $P = 0.2$ ). Among BJHS cases with MVP, there were no statistically significant differences in terms of prevalence of heart murmur, palpitation, and tricuspid regurgitation.

## Discussion

This study showed that there is a significant correlation between BJHS and mitral valve prolapse. In this study we illustrated that by increasing the Beighton score, the possibility of detecting MVP has been increased. Prevalence

**Table 1** Comparison of distribution of MVP among case and control groups

MVP	Case	Control	Total
Positive	34 (54%)	8 (12.7%)	42 (33.3%)
Negative	29 (46%)	55 (87.3%)	84 (66.7%)
P<0.001			

**Table 2** Distribution of MVP among cases with BJHS according to age classification

MVP	3-7	>7
Positive	14 (41.2%)	20 (58.8%)
Negative	20 (69%)	9 (31%)
P=0.027		

**Table 3** Clinical findings among BJHS cases with and without MVP

		MVP (+)	MVP (-)	P-value	Odds ratio
Arthralgia	Yes	12 (35.3%)	8 (27.6%)	0.512	0.698
	No	22 (64.8%)	21 (72.4%)		
Myalgia	Yes	20 (58.8%)	14 (48.3%)*	0.402	0.653
	No	14 (41.2%)	15 (51.7%)		
Dislocated joint	Yes	1 (2.9%)	1 (3.4%)	NA	1.179
	No	33 (97.1%)	28 (96.6%)		
Heart murmur	Yes	14 (41.2%)	4 (13.8%)	0.016	0.229
	No	20 (58.8%)	25 (86.2%)		
Palpitation	Yes	8 (23.5%)	1 (3.4%)	0.023	0.116
	No	26 (76.5%)	28 (96.6%)		
Tricuspid regurgitation	Yes	16 (47.1%)	8 (27.6%)*	0.113	0.429
	No	18 (52.9%)	21 (72.4%)		

\*P<0.05, discussed in the result

**Table 4** Beighton score among cases with and without MVP

Beighton score	MVP (+)	MVP (-)	Total
6	15 (50%)	15 (50%)	30
7	3 (75%)	1 (25%)	4
8	9 (52.9%)	8 (47.1%)	17
9	7 (58.3%)	5 (41.7%)	12

of MVP was also higher in BJHS children who aged more than seven years old compared to younger children.

In our study, about 50.8% of cases were female which is almost similar to report of Adib et al.<sup>20</sup> Male/female ratio in another study was also similar.<sup>21</sup>

In current study, we found higher prevalence of heart murmur and palpitation among BJHS cases with MVP compared to BJHS cases without MVP. It may be supposed that the association of MVP with BJHS may aggravate heart murmur and palpitation in cases.

Mishra et al conducted a research on adults with joint laxity, including 58 cases and 30 controls. MVP was detected in 6 (10%) of cases and 2 (7%) of controls. They

found no significant difference between case and control for MVP. Their study was conducted on cases aged 15-79 years and differed from our study.<sup>22</sup>

In the study by Pitcher and Graham, hypermobility of joints was significantly more common in patients with MVP than controls.<sup>23</sup> They used hypermobility score proposed by Beighton and Horan.<sup>24</sup> In the study by Ondrasik et al on 27 cases with MVP, 14 cases found to have joint hypermobility.<sup>25</sup>

In the study by Yazici et al, 46 adult with MVP compared to healthy subjects. The incidence of hypermobility was significantly higher than control cases using the Beighton criteria.<sup>26</sup>

There was a controversy regarding association of BJHS with MVP. Previous studies have shown an association between MVP and BJHS.<sup>27</sup> By using new stricter criteria for diagnosis of MVP, this association is under question.<sup>22</sup> The prognosis for patients with BJHS is generally good.<sup>28</sup> However, physician should be aware of cases with hypermobility in whom cardiac findings suggest MVP. Further evaluation to rule out more serious cardiac abnormalities and connective tissue disorders may be necessary.<sup>22,27,29</sup>

## Conclusion

Few studies have associated the mitral valve prolapse and BJHS using various methods of assessment. Furthermore, the methods used to evaluate joint mobility in health conditions are considered restricted. Early detection of BJHS and possible association with MVP is important to prevent possible complications. We recommend another study to compare complication of MVP in cases with BJHS compared to non-BJHS subjects.

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