Revisiting Sex Differences in Multiple Hereditary Exostoses (MHE): A Comprehensive Retrospective Analysis of Patient Characteristics and Surgical Patterns

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Abstract
Background: Multiple Hereditary Exostoses (MHE) is an autosomal dominant disorder characterized by the development of osteochondromas. These benign tumors can halt bone development, and compress adjacent nerves and muscles, leading to pain, mobility issues, and growth abnormalities. MHE is male-predominant (1.5:1 male-to-female ratio), with males often displaying more acute symptoms. The underlying pathogenesis remains partially elucidated, and treatment primarily involves surgical intervention. There are few retrospective studies that address surgical statistics and challenge the assumed male predominance. This study seeks to provide an encompassing retrospective evaluation of MHE patients, emphasizing patient characteristics, surgical data, and gender discrepancies.
Methods: We examined 103 MHE-diagnosed patients treated at the University of Iowa Hospitals and Clinics (UIHC) from June 2008 to March 2023. Comprehensive chart reviews elucidated surgical data, notably excision locations. Demographic and clinical data were collected through data extraction and chart review. Statistical methods included a one-sample z-test (height percentile differences), a two-sample t-test (age differences in genders), and a two-sample Poisson test (excision rates between genders).
Results: The cohort consisted of 52 males and 51 females, indicating an equal gender distribution. Predominant excision sites included the distal femur (21.01%) and proximal tibia (19.33%). Growth deformities were observed in 50 patients (48.54%), primarily in the knee (37.86%). Significant sex differences were noted in surgical interventions: Males had a higher mean age of excision (23.30 years) than females (15.32 years) (95% CI, 11.48-19.16; p=0.03). Females exhibited a notably higher excision rate (CI 1.17-2.00; p=0.001), with a ratio of 1.53 (female/male). Specifically, females had increased excisions at the foot/ankle (CI 1.3-7.01; p=0.038) and hand/wrist (CI 1.29-4.77; p=0.029).
Conclusion: Our findings challenge the commonly accepted male predominance in MHE, revealing an even male-female distribution. Distal femur and proximal tibia were the chief excision sites, aligning with the most prevalent growth abnormalities. Males exhibited later excisions, potentially due to delayed growth plate closure. Interestingly, females had a higher surgery rate, especially in the foot/ankle and hand/wrist. This contradicts earlier research proposing males have higher lesion counts, suggesting a more intricate gender-specific disease manifestation. This discovery underscores the necessity for continued exploration of sex variances in MHE.
Significance and Clinical Relevance: The unexpected sex-based differences seen in our study differ from previous research and present an intriguing avenue for future research. These findings emphasize the need for a more nuanced understanding of MHE presentation in males and females within Western populations, taking into account psychological, regional, and demographic factors, and ultimately contributing to improved patient care and management strategies.
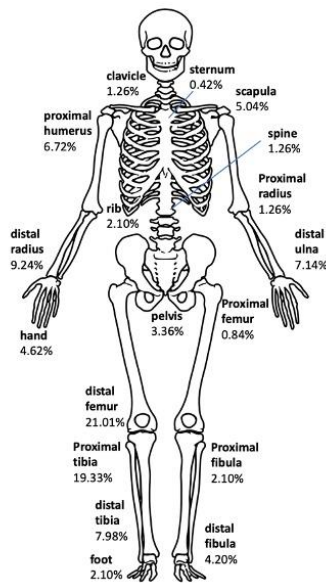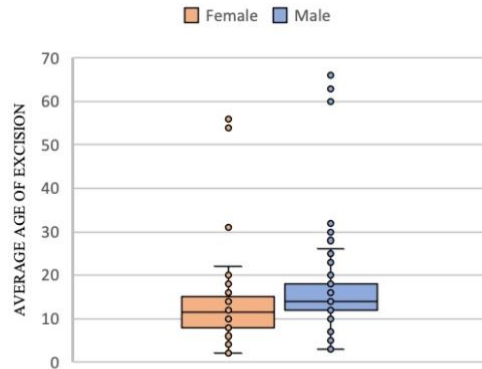
Figure 2. The average age of excision for each female (n=27) who underwent a procedure (left) and to the average age of excision for each male (n=28) who underwent a procedure (right).

Figure 1. Proportion of excision procedures by location.
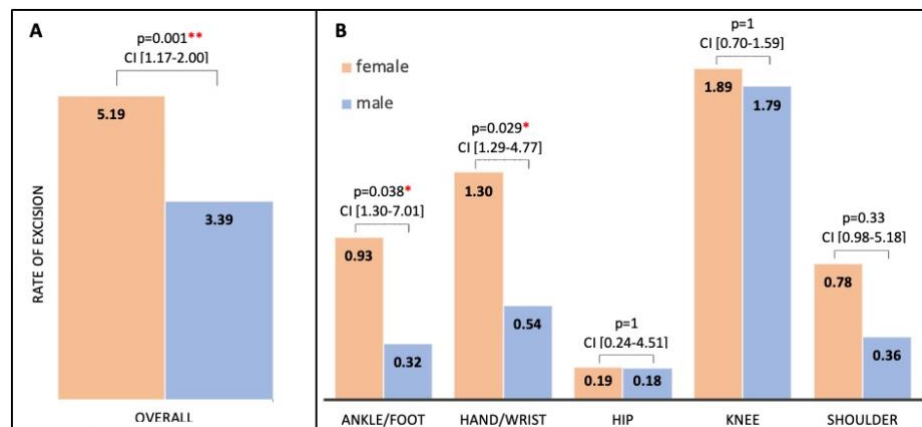

Figure 3. 5A shows the difference in the overall rate of excision between females (left) and males (right). 5B shows the difference in rates of excisions between females (left) and males (right) in different regions. P-values show the significance of the difference between the rate ratio of females/males to a rate ratio of 1. The overall rates of excisions in the two groups were compared using a two-sided exact Poisson test on the rate ratio between sexes. The Poisson test was then repeated for seven excision regions to compare excision rates at each location, and a Bonferroni adjustment was applied to the results of these tests. In all statistical tests, the alpha level was set at the standard 0.05 level.