

## INTRODUCTION

Hyperostosis frontalis interna (HFI) is a benign manifestation of thickening of the frontal bone inner lamina of the skull.<sup>1</sup> Diagnosis of HFI is often incidental on x-ray films, computed tomography, or magnetic resonance images of the skull. HFI is generally found on the frontal bone, but those with the diagnosis of HFI, often have nodules of the frontal, parietal, or occipital bones.<sup>2</sup> A higher prevalence in females compared to males with HFI has been reported possibly due to different hormonal imbalances.<sup>3</sup>

Based on past literature, HFI is more prevalent in postmenopausal women. In a recent study, women with HFI were found to have a higher incidence of headache, neurological and psychiatric disorders, as well as a lower incidence of giving birth.<sup>2</sup> In nulliparous postmenopausal women, there is higher estrogen exposure throughout their lifetime, since pregnancy and breastfeeding decrease estrogen exposure.<sup>4</sup>

To expand on this knowledge of HFI, a study was conducted to identify the prevalence of HFI in cadavers at two medical institutions. This case study was designed to determine if there is a predominance of HFI in females compared to males. There were also other parameters identified in the study such as: skull nodules, gonad weight, and liver weight.

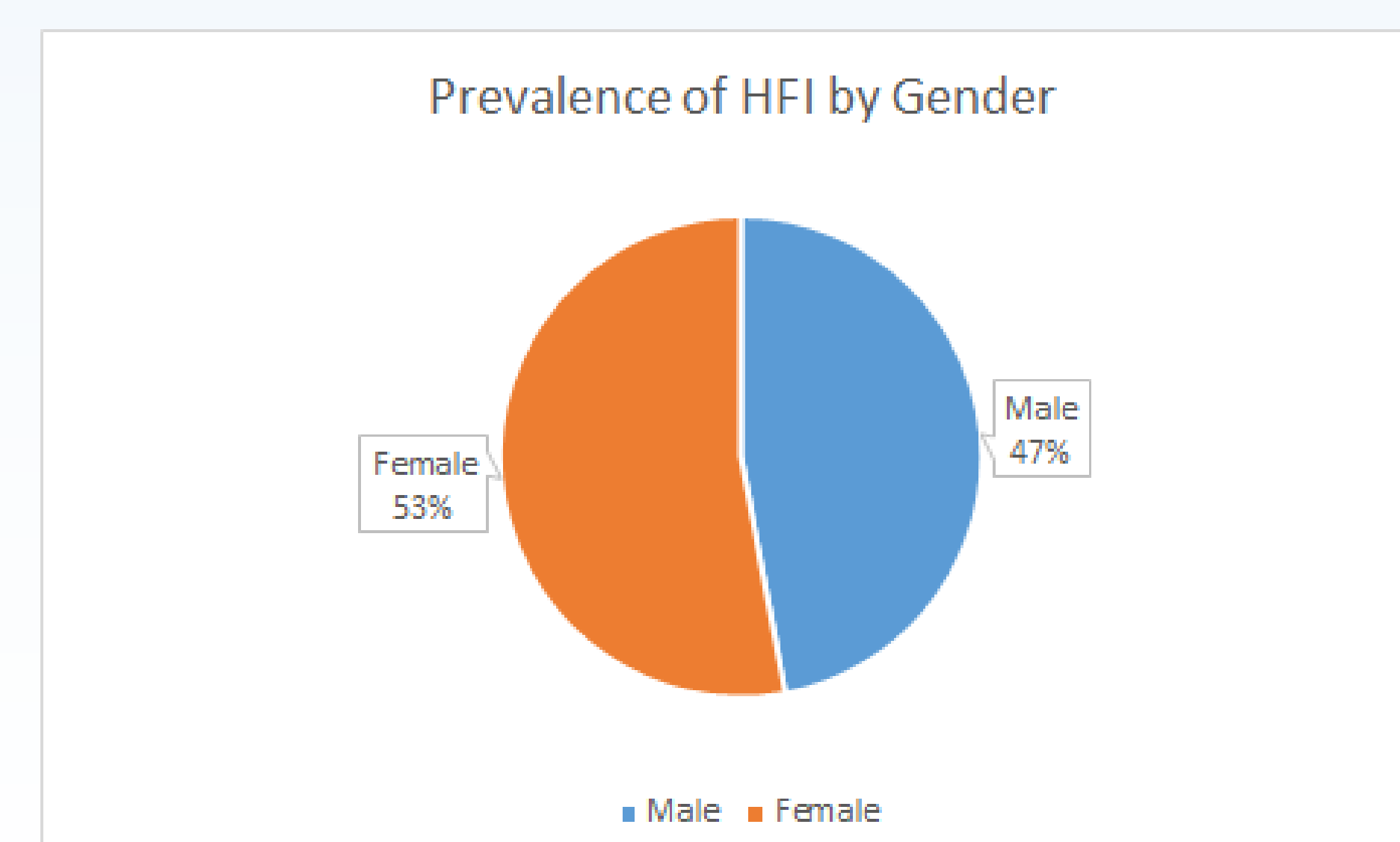
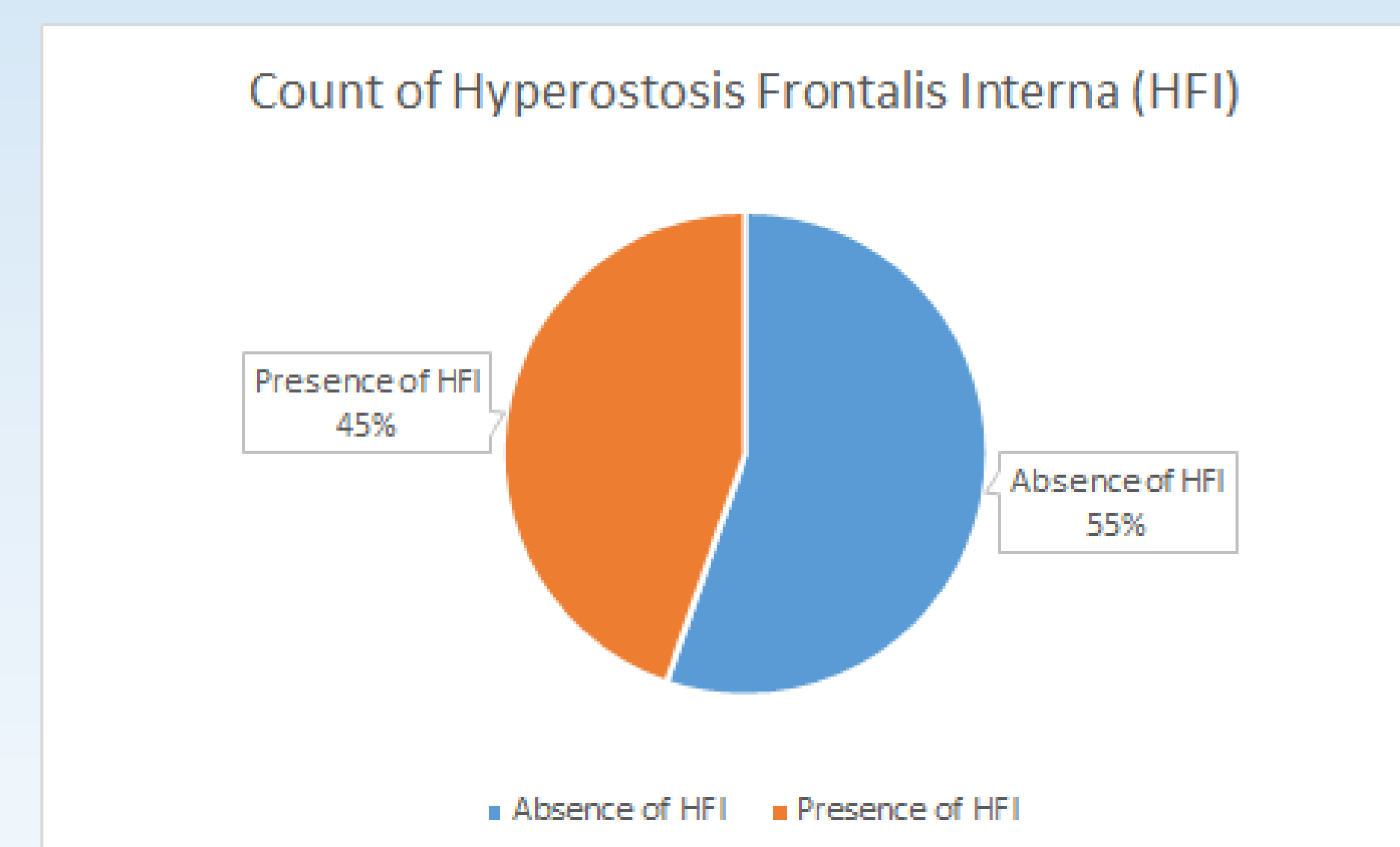
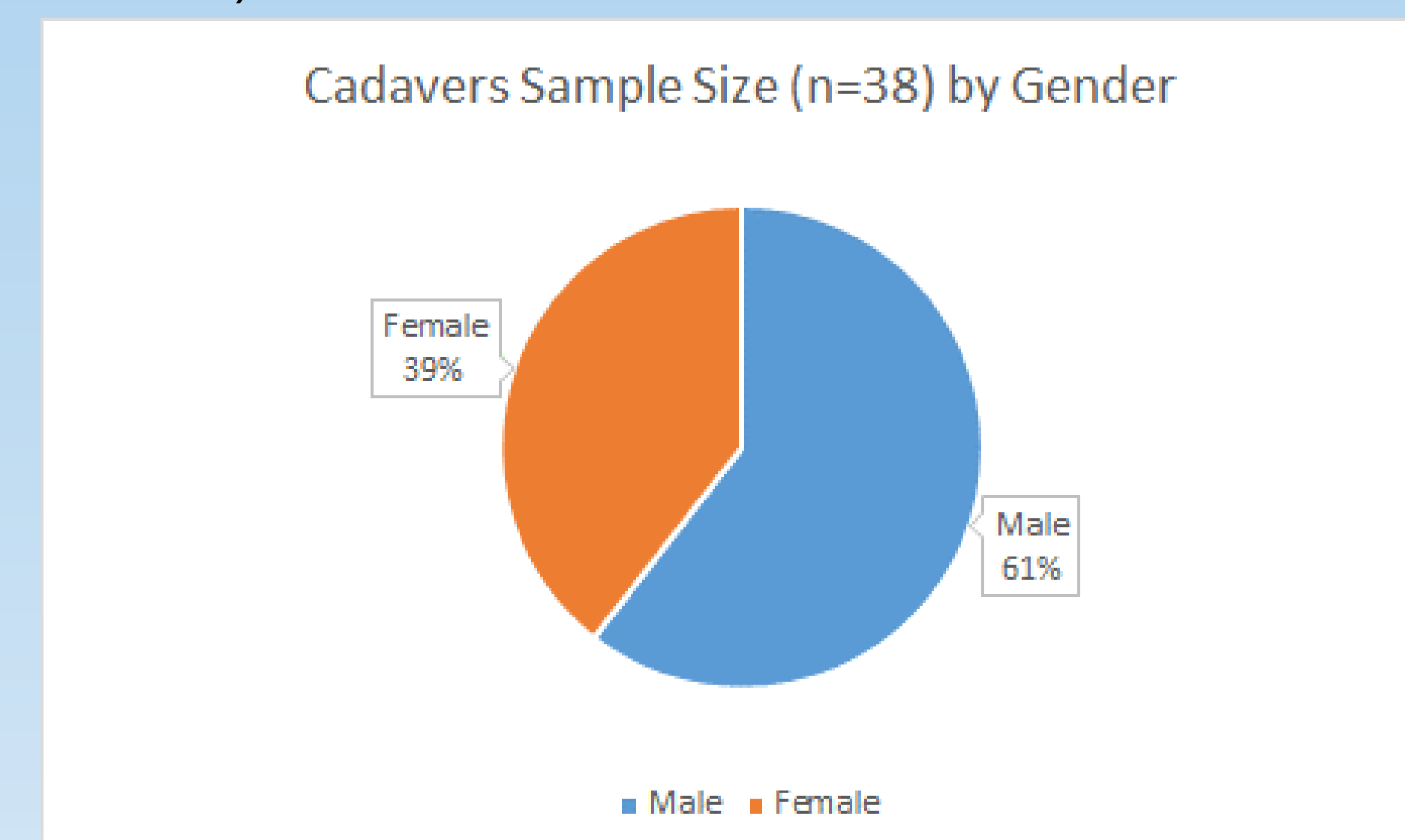
## MATERIAL AND METHODS

- A case study was designed to explore HFI prevalence among sexes in a sample of cadavers (n=38) at two medical education institutions: Philadelphia College of Osteopathic Medicine (Suwanee, GA and Moultrie, GA).
- Dependent variable was whether the cadavers had HFI; diagnosis of HFI was established if frontal bone elevations > 8.02 mm.
- Independent variable was the sex of cadaver.
- Measurements of frontal bone elevations (mm) were obtained utilizing a Vernier digital sliding-caliper.
- Additionally, cadaveric livers were weighed, and the size and weight of testes was measured when available.
- Statistics and graphs were generated using Microsoft Excel.



## RESULTS

- 45% of our cadaveric sample had some evidence of HFI (defined as frontal bone elevations > 8.02 mm).
- Of the 45% diagnosed with HFI, 53% were females and 47% were males.
- Of the 53% females with HFI, 100% (9/9) had liver weight < 1400 g, which is the median liver weight of adult female.<sup>5</sup>
- Of the 47% males with HFI, 87.5% (7/8) had absent testes or testicular atrophy (testes < 15 g in weight and/or 4 cm\*3 cm\*2.5 cm in dimensions, the average weight and dimensions of post-pubertal males' testes.<sup>6,7</sup>)



## DISCUSSION

The overall prevalence of HFI in the general population is 5%-12%.<sup>8</sup> Recent HFI studies suggest an increasing prevalence of the condition, which might explain the high prevalence of HFI (45%) in our study. This increase has been attributed to prolonged estrogen stimulation, characterized by early menarche, late menopause, increased use of contraceptives, low parity, lower prevalence of breastfeeding, as well as incorporation of dietary phytoestrogens.<sup>8</sup> HFI is more common in postmenopausal women due to prolonged estrogen stimulation. Furthermore, as our measurements were plotted on a graph and linear trendlines were generated, it was evident that the HFI extent is directly proportional to increase in females' age, making HFI an age-dependent phenomenon. In males, on the other hand, frontal bone thickness is not directly correlated with the cadaveric age.

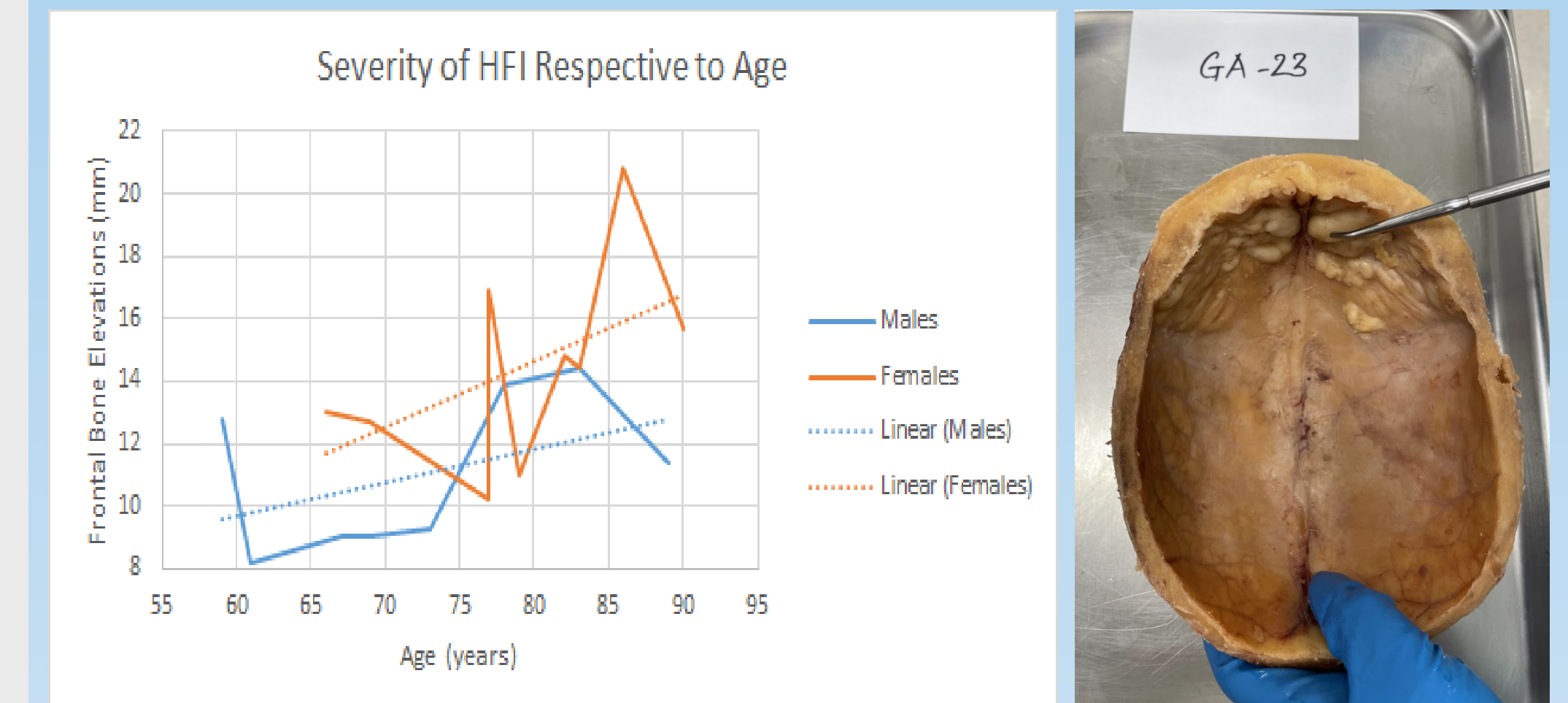
HFI cases in females have been positively correlated with liver pathologies in literature.<sup>9</sup> Similarly, in our cadaveric samples, all females with HFI had lower liver weight than the median liver weight for females in the general population, which could be consistent with liver fibrosis. Also, in previous studies, there was a correlation between decreased Leydig cells in males and presence of HFI.<sup>9,10</sup> Upon examination of our male cadavers' testes with HFI, 87.5% had testicular atrophy or absent testes supportive of possible decrease in Leydig cells.

The differential diagnosis often considered in HFI cases that are also related to some sort of skull thickening are Paget disease, fibrous dysplasia, interosseous meningioma, chronic phenytoin use, renal osteodystrophy, thalassemia, multiple myeloma, hyperparathyroidism, and acromegaly.<sup>11</sup> One of our cadaveric samples displayed frontal bone thickening, but since the patient suffered from multiple myeloma, this was not included as an HFI case, as some of this bone thickening could be due to multiple myeloma itself. Clinically, the most preferred way to diagnose HFI and rule out other differential diagnoses is via CT scan.

HFI may be symptomatic or asymptomatic depending on its severity. Symptomatology is consistent with those of space occupying lesions, such as headaches, seizures, and cognitive impairments, which is further explained by meningeal compression leading to reduction in its blood supply.<sup>12</sup> Thus, supportive management for symptoms, mainly characterized in pain control, is pursued as there is not a treatment protocol for HFI. Nevertheless, early diagnosis of HFI remains crucial as it reduces the burden of unnecessary medical exams for the patient.

## CONCLUSION

- Overall cadaveric prevalence of HFI (45%) is much higher than previously established in literature (5%-12%).
- Frequency of HFI is more common in females (53%) as compared to males (47%).
- Age of females has a direct impact on severity of HFI, characterized by increased frontal bone thickness, while age plays a far less important role in males.
- Role of estrogen on HFI requires further investigations.



## REFERENCES

1. Moreno-Ballesteros A, León-Asuero-Moreno I, Marín-Melero I, García-Gómez aFJ. Hyperostosis frontalis interna by bone scintigraphy. *Japanese Journal of clinical oncology*. 2021;51(4):664-665. doi:10.1093/jco/hyaa150
2. Djonc D, Bracanovic D, Rakocevic Z, et al. Hyperostosis frontalis interna in postmenopausal women—Possible relation to osteoporosis. *Women & Health*. 2016;56(8):994. doi:10.1080/03630242.2016.1178685
3. Hershkovitz I, Greenwald C, Rothschild BM, et al. Hyperostosis frontalis interna: an anthropological perspective. *Am J Phys Anthropol*. 1999;109(3):303-325. doi:10.1002/(SICI)1096-8644(199907)109:3<303::AID-AJPA3>3.0.CO;2-I
4. May H, Peled N, Dar G, et al. Hyperostosis Frontalis Interna and Androgen Suppression. *Anatomical record (Hoboken, N.J. : 2007)*. 2010;293(8):1333-1336. doi:10.1002/ar.21175
5. Tajiri K, Shimizu Y. Chapter 26 - liver diseases in the elderly. *Liver Pathophysiology*. 2017:331-339. doi: 10.1016/B978-0-12-804274-8.00026-6.
6. Silber S. Adult testis anatomy. *Fundamentals of Male Infertility*. 2018:19-21. doi: 10.1007/978-3-319-76523-5\_3.
7. Yang DM, Hyeon-II Choi, Hyun CK, Sang WK, Sung KM, Joo WL. Small testes: Clinical characteristics and ultrasonographic findings. *Ultrasonography*. 2021;40(3):455-463. doi: 10.14366/usg.20133.
8. Morita K, Nagai A, Naitoh M, Tagami A, Ikeda Y. A rare case of hyperostosis frontalis interna in an 86-year-old Japanese female cadaver. *Anatomical Science International*. 2021;96(2):315-318. doi:10.1007/s12565-020-00577-5
9. Beatty K(1,2), Putcha K(1), Shah A(1), Li K(3). Organ histopathological associations with hyperostosis frontalis interna in humans. *International Journal of Morphology*. 2021;39(1):77; 77-83; 83. doi: 10.4067/S0717-95022021000100077.
10. Raikos A, Paraskevas GK, Yusuf F, et al. Etiopathogenesis of hyperostosis frontalis interna: A mystery still. *Annals of Anatomy*. 2011;193(5):453-458. doi:10.1016/j.aanat.2011.05.004
11. Murphy E, Kortyna R, Flaherty D. Hyperostosis frontalis. *JBJS Journal of Orthopaedics for Physician Assistants*. 2018;6(2):e17. doi: 10.2106/JBJS.JOPA.17.00032.
12. Priyambada P, Joshi K, Ozdemir B. Hyperostosis frontalis interna (HFI): A case report and review of literature. *Case reports in internal medicine*. 2017;4(1):57. doi: 10.5430/crim.v4n1p57.

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