Chart Based Insights into Neurofibromatosis Type 1: A Single Center Database

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Introduction

- Neurofibromatosis Type 1 (NF1) is a common autosomal dominant disorder (1:2500) caused by heterozygous pathogenic variants in *NF1* (a tumor suppressor gene).
- NF1 presents with pigmentary café-aul-lait macules, skinfold freckling, and dermal neurofibromas.
- Other systems can be affected including skeletal, central, and peripheral nervous systems.
- The primary objectives of this database are to characterize and identify trends within the patient population at the Children's Hospital New Orleans (CHNOLA) NF1 and related disorders clinic.
- By consolidating patient data, this database aims to enhance clinical care and inform patient decision-making.
- Additionally, the centralized data will facilitate and support future research projects related to the NF1 and related disorders population.

Methods

- A retrospective chart review was conducted on all patients seen in the CHNOLA NF1 and related disorders clinic from July 2018 to May 2024.
- Data was collected and stored using LSU (Louisiana State University) REDCap software encompassing:
  - Demographics
  - Clinical manifestations
  - Laboratory test results
  - Treatments (including the use of selumetinib)
  - Genotype data

References

1. Friedman JM. Neurofibromatosis 1. 1998 Oct 2 [Updated 2022 Apr 21]. In: Adam MP, Feldman J, Mirzaa GM, et al., editors. *GeneReviews* [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1109/
- Legius E, et al; International Consensus Group on Neurofibromatosis Diagnostic Criteria (I-NF-DC); Huson SM, Evans DG, Plotkin SR. Revised diagnostic criteria for neurofibromatosis type 1 and Legius syndrome: an international consensus recommendation. Genet Med. 2021 Aug;23(8):1506-1513. doi: 10.1038/s41436-021-01170-5. Epub 2021 May 19. PMID: 34012067; PMCID: PMC8354850.

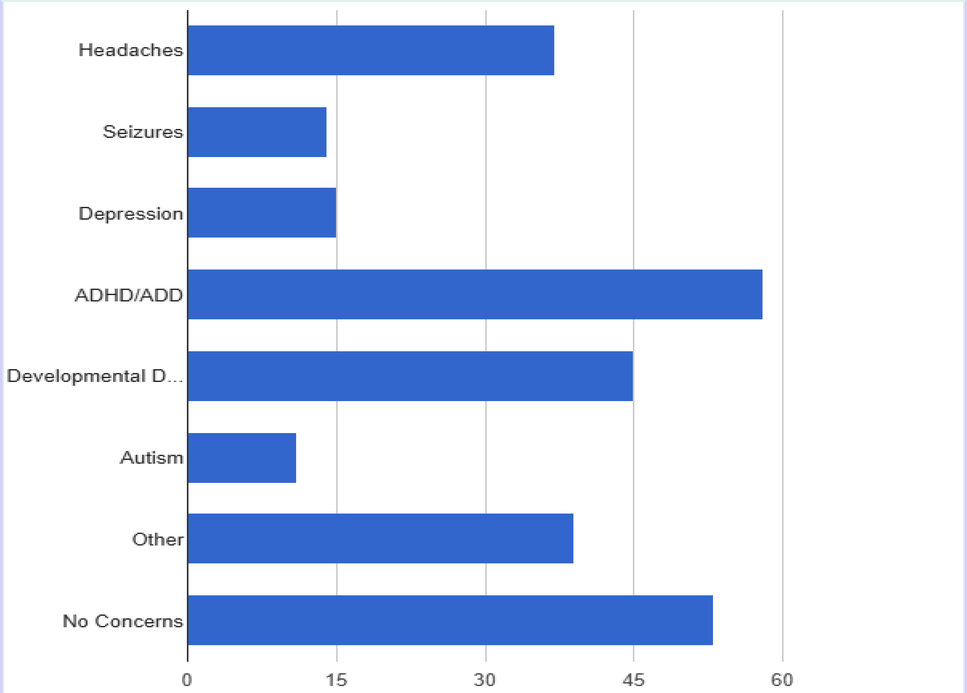
Results

Presence of Clinical Characteristics (Total = 207 patients)	Yes	No	NF1 general population[1]
Café-au-lait macules	207 (100%)	0 (0%)	>99%
Freckling in Axillary or Inguinal Regions or Skin Folds	165 (79.7%)	42 (20.3%)	85%
Plexiform Neurofibromas	81 (39.1%)	126 (60.9%)	30%
Cutaneous Neurofibromas	79 (38.2%)	128 (61.8%)	99% (infrequent in childhood)
Optic Nerve Pathway Glioma	27 (13.0%)	180 (87.0%)	15-20%
Lisch Nodules	56 (27.1%)	151 (72.9%)	95% (frequency increases with age)

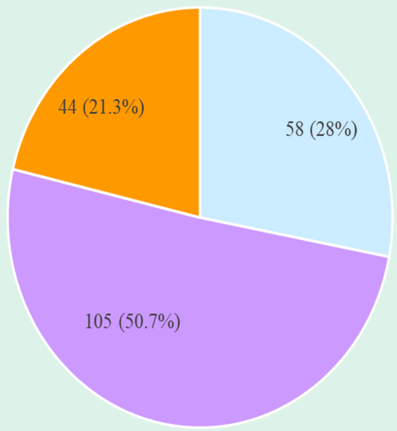
	Yes	No
Selumetinib (N=81)	24/81 (29.6%)	57/81 (70.4%)

Bone Abnormalities	Prevalence	NF1 general population[1]
Pectus Deformity	13 (6.2%)	N/A
Sphenoid Wing Dysplasia	4(1.9%)	N/A
Scoliosis	39 (18.8%)	10%
Bowing of the Legs/Pseudoarthrosis of the Tibia	8 (3.8%)	2%

Neurobehavioral Concerns:



Inheritance Patterns:



- N = 207 patients between July 2018-May 2024
- Demographics
  - 159 (76.8%) are pediatric (21 years or younger)
  - 48 (23.2%) are adults (older than 21)
  - 98 (47.3%) are male
  - 109 (52.7%) are female
- Inheritance patterns:
  - 105 (50.7%) were inherited
  - 58 (28%) de novo
  - 44 (21.3%) unknown
  - Of the patients who met clinical diagnosis of NF1, 7 were found to not have a genetic variant upon molecular testing
  - Optic Nerve Pathway Glioma Type
    - 16/27 (59.3%) Unilateral
    - 11/27 (40.7%) Bilateral

Conclusion

- NF1 patient clinical characteristics at CHNOLA followed trends seen in the general NF1 population.
- The CHNOLA NF1 clinic is a pediatric clinic, however, 23.2% of patients were adults, highlighting the importance for continued care into adulthood for this chronic disorder.
- The addition of a psychologist as a member of the NF1 clinic team will hopefully help address the neurobehavioral concerns in our population.
- Selumetinib is only approved between the ages of 2-18 to treat plexiform neurofibromas. The approval of a *MEK* inhibitor for the adult population would potentially improve treatment for plexiform neurofibromas in that population.
- The Children's Tumor Foundation revised the diagnostic criteria for NF1 in May 2021 to include genetic testing as criteria. We are working to provide genetic testing to all patients at the NF1 clinic.[2]