ORIGINAL RESEARCH PAPER

General Medicine

A CASE SERIES OF WAARDENBURG SYNDROME BASED ON COMMUNITY TRACING.

KEY WORDS: Waardenburg syndrome, white forelock, blue iris, sensorineural hearing loss.

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ABSTRACT

Background: Waardenburg syndrome is rare autosomal dominant genetic disorder.During embryogenesis, there is an abnormal distribution of melanocytes, which results in patchy areas of depigmentation. It is a rare disease, caused by loss of pigmentary cells in eyes, skin, stria vascularis of the cochlea, and hair. It is characterized by a broad nasal root, lateral displacement of medial canthi with the dystopia of lacrimal puncta, pigmentary abnormalities of the iris, hypertrichosis of the medial part of the eyebrows, white forelock, and deaf-mutism.A 19 year old female who was admitted for evaluation and treatment of fever had distinct white forelock of hair in midline along with striking bilateral blue iris. She was deaf-mute and her developmental milestones are otherwise normal. Family history revealed that her elder brother, mother and about 14 of her relatives had similar features with a few differences. The features fit into Waardenburg syndrome. Because of rarity, this series is reported. **Conclusion:** As patients may present with non specific symptoms awareness and genetic counselling are essential ingredients of care in this condition.

BACKGROUND:

Waardenburg syndrome (WS) is a neurocristopathy with an autosomal dominant mode of inheritance, and exhibits considerable clinical and genetic heterogeneity

- During embryogenesis, there is an abnormal distribution of melanocytes, which results in patchy areas of depigmentation.
- A uncommon disease caused by loss of pigmentary cells in eyes, skin, stria vascularis of the cochlea and hair.

Waardenburg syndrome is named after a Dutch ophthalmologist, P J Waardenburg, who described a syndrome comprising of six distinctive features[(1)]:

1. A broad nasal root
2. Lateral displacement of medial canthi with the dystopia of lacrimal puncta
3. Pigmentary abnormalities of the iris
4. Hypertrichosis of the medial part of the eyebrows
5. White forelock and
6. Deaf-mutism

INTRODUCTION:

- Waardenburg syndrome (WS) is an uncommon autosomally inherited and genetically heterogeneous disorder of neural crest cell development.
- Depending on additional symptoms, WS is classified into four types, WS1, WS2, WS3 and WS4.
- Waardenburg syndrome (WS) type I results from genetic defects at several loci, including a region near the ALPP gene located on chromosome 2. This condition is characterized by distinctive clinical features such as hearing loss and changes in pigmentation[(2)].
- WS1 and WS3 are attributed to mutations in PAX3[(3)]
- WS2 is heterogeneous, being caused by mutations in the microphthalmia-associated transcription factor(MITF), SOX10, and SNAI2 gene in some but not all affected families[(4)]
- Apart from the associated upper limb anomalies (e.g. hypoplasia, syndactyly) WS type 3 (WS3)Klein-Waardenburg syndrome is similar to WS1.[2],[4]
- Type 3 is the rarest form of WS.
- WS4 is attributed to mutations in the endothelin-3 or the endothelin-B receptor genes and SOX10 gene usually autosomal recessive.
- In addition to the features of WS1, type 4 WS (WS4; Shah-Waardenburg syndrome is associated with features of Hirschsprung disease.[5]
- As it is a genetic disease, there is no definitive treatment for Waardenburg syndrome, but supportive treatment with cochlear implants and surgery in case of association with Hirschsprung syndrome can be done.
- Genetic counseling is necessary.
- According to the diagnostic criteria proposed by the Waardenburg consortium [6] ,a person must have two major or one major plus two minor criteria to be diagnosed as WS type1.

The Major Criteria

- Sensorineural hearing loss
- Iris pigmentary abnormality (two eyes different color or iris bicolor or characteristic brilliant blue iris)
- Hair hypopigmentation (white forelock or white hairs at other sites on the body),
- Dystopia canthorum (lateral displacement of inner canthi)
- The presence of a first-degree relative previously diagnosed with WS.

The Minor Criteria

- Skin hypopigmentation (congenital leukoderma/white skin patches),
- Medial eyebrow flare (synophrys)
- Broad nasal root, hypoplasia of alae nasi
- Premature graying of hairs (before age 30).
- However, the patients rarely display all the clinical signs.
- WS type 2 lacks dystopia canthorum of WS1

A 19 year old female who was admitted for evaluation and

treatment of fever had distinct white forelock of hair in midline along with striking bilateral blue iris.

She was deaf-mute and her developmental milestones are otherwise normal.

Family history revealed that her elder brother, mother and about 14 of her relatives had similar features with a few differences. The features fit into Waardenburg syndrome. Because of rarity, this series is reported.

MATERIALS AND METHODS:

- **Type Of Method Of Study:** Descriptive ,observational type

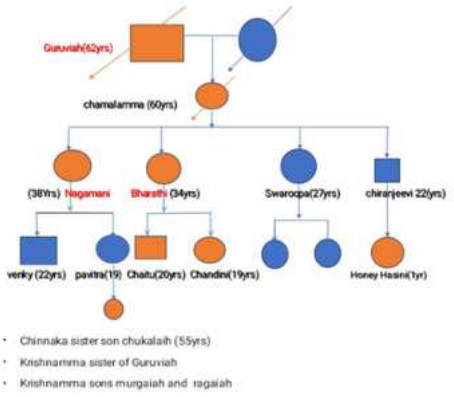
Participants:

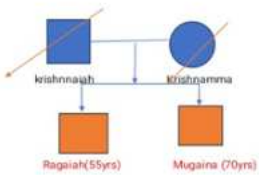
- This is based on findings in 14 individuals -6 Males and 8Females.
- Thorough clinical history was obtained and detailed audio logical and ophthalmological examinations were carried out. All patients were diagnosed according to the Waardenburg Consortium criteria [6]

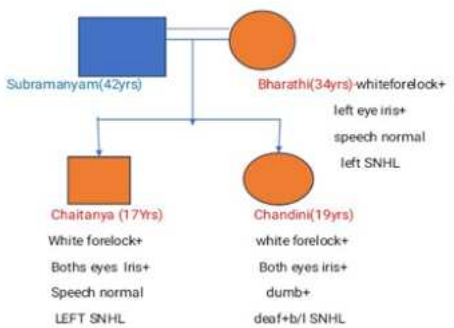
RESULTS:

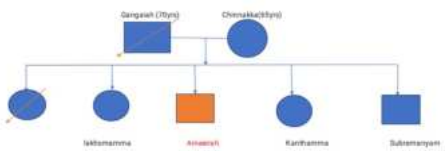
Clinical description:

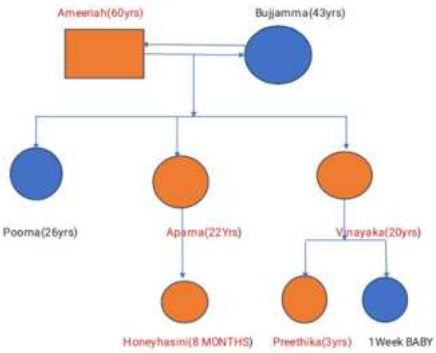
- Totally, 14 WS patients, 5 WS1, 9 WS2 patients, including 6 men and 8 women from 6 families, and their healthy family members were enrolled.
- The study population comprised 6 familial groups ranging from 12 months to 70 years old.











Type 1 WS –

- Ameeriah(60 yrs)
- Mugaina (70yrs)
- Chandini(19yrs)
- Vinayaka(20yrs)
- Preethika(3yrs)

Type 2 WS –

Chukalaih(55yrs)
Ragaiah(57yrs)
Bharathi(34yrs)
Nagamani(37Yrs)
Aparna (22yrs)
Bhanupriya (1yr)
Honey Hasini (8 MONTHS)
Preethika (3yrs)
Chaitanya (17YRS)

Female -8 Male-6 From 6 Families

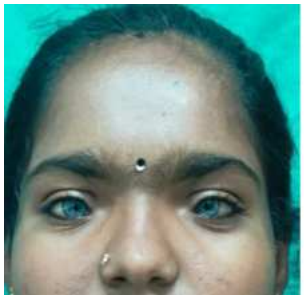


Fig (a)

Fig(b)

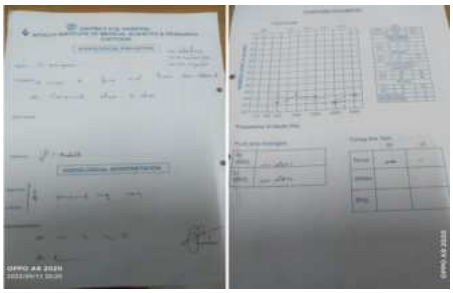
Fig (a): Chandini ws type1 heterochromia iridis,b/l SNHL,mute,white forelock covered by hair dye .
Fig(b): Bharathi ,ws type2,heterochromia iridis in left eye left ear SNHL,premature greying of hair.

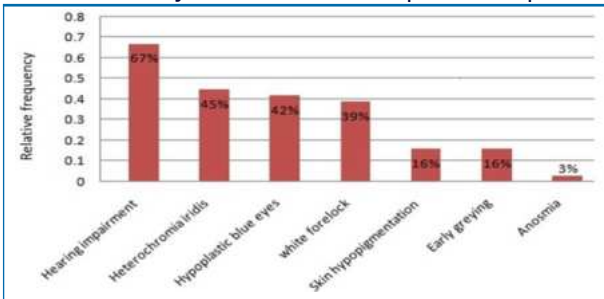
Fig(c)

Fig(d)

Fig(c):Preethika 3yrs wstype1, Chaitanya 17yrs wstype2
Fig(d): vinayaka ws type1 heterochromia iridis,b/l SNHL,mute,white forelock covered by hairdye

Audiological evaluation in Vinayaka –B/L SNHL





CONCLUSION

- In conclusion, this study presents a clinical description of WS in group of Rural Indians in Chittoor district
- The etiology was elucidated in 6 studied families.
- Further investigations of these cases using novel technologies (e.g. next-generation sequencing) could help greatly in unraveling the molecular mechanisms underlying WS.
- Consultations with geneticists are crucial for understanding type I Waardenburg syndrome, which is inherited in an autosomal dominant manner. Individuals with this condition often have family members who are also affected. Although prenatal testing can identify the presence of the associated genetic mutations, it cannot predict how severely the disease will manifest in an individual. Therefore, a collaborative approach involving various healthcare professionals is essential for effectively addressing the complications associated with the condition([8,9]).

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