

Audiometric Findings in Waardenburg's Syndrome Amongst the Institutionalised Deaf / Blind in Kaduna-Nigeria

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Abstract

Introduction: Waardenburg's syndrome is a rare inherited disorder of congenital hearing loss and Pigmentary disturbances of the eyes, hair, skin and neural crest derivatives.

Methodology: 620 students in a deaf/blind school were examined and four had Waardenburg's syndrome with a frequency of 0.65%. 2 males and 2 females with Waardenburg's syndrome and age ranges between 10-19years (mean 15.75years) All 4 subjects had complete blue irides, white forelock and sensorineural hearing loss, and thus met the diagnostic criteria. They were then subjected to Audiometric assessment.

Results: Otoscopy was essentially normal but Audiometry revealed sensorineural hearing loss [SNHL] in all the subjects ranging from severe to profound with one subject being stone deaf.

Conclusion: Waardenburg's syndrome is a rare disorder in our environment although it may be under reported. Two of the subjects benefited from amplification and were given hearing Aids. Provision of early amplification cannot be over emphasized.

Keywords: Waardenburg Syndrome, SNHL, blue irides, white forelock, Amplification.

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Waardenburg's syndrome (WS) is an autosomal dominantly inherited disorder accounting for more than 2%-3% of congenital hearing loss. It is estimated to occur in 1 of 42 000 individuals. It also occurs in both males and females and people of all ethnic backgrounds. Waardenburg's Syndrome was first described by Dutch Ophthalmologist and geneticist Petrus J. Waardenburg. This was later published in 1951 by the American Journal of Human Genetics, as a new entity characterized by congenital SNHL and Pigmentary disturbances of the skin, hair and eyes and various neural crest defects. It is also classified as type I or type II with or without the presence of dystopia canthorum¹.

The presence of congenital hearing loss, the most significant finding in these patients has a penetrance of 35-70% type I and 55-83% type II². Hearing loss in these patients can be complete or partial, bilateral or unilateral³⁻⁵, furthermore, quite a number of patients with WS have both low and high frequency hearing losses and impairments.

Table I Diagnostic criteria for WS types I and II, to be counted as affected a person must have two major or one major plus two minor criteria.

Major Criteria:

- Congenital SNHL -
- Pigmentary Disturbances of the iris:
 - a) Complete heterochromia iridium; two eyes of different color.
 - b) Partial or segmental heterochromia in one or both eyes; or
 - c) Hypoplastic blue eyes; characteristic brilliant blue in both eyes.
- Hair hypopigmentation: White forelock
- Dystopia canthorum: W>1.95
- Affected first degree relative

Minor Criteria

- Congenital Leucoderma: several areas of hypopigmented skin.
- Synophrys or medial eyebrow flae.
- Broad and high nasal root.
- Hypoplasia of alae nasi.
- Premature graying of hair; scalp hair predominantly white before age 30.

Criteria for WS Type II were suggested by Lui et al⁵. These authors recommend that two major features should be present to make the diagnosis of WS Type II. The major features are as in the list above, except for the exclusion of dystopia canthorum and inclusion of premature graying. The hearing loss in WS is SNHL, congenital, and usually non-progressive. It could be

unilateral or bilateral and can vary in degree from slight to profound. It has been reported that 25% of subjects with WS I and 50% of those with WS II have bilateral SNHL⁴.

A profound bilateral loss is the commonest degree of HL in both types, particularly in type I. Hulten, et al⁸ described a profoundly deaf and severely depigmented child born to first cousin parents who both had white forelocks and white skin patches but normal hearing.

Radiological investigation of the auditory system has indicated a normal temporal bone or dysplasia of the lateral semicircular canal (SCC) associated with a normal bony cochlear². The histological appearance of one temporal bone studied by Fisch⁹ was consistent with auditory features of Type I WS being caused by Cochleosaccular degeneration.

Waardenburg's Syndrome type III (Klein-Waardenburg syndrome) is similar to type I but includes muscle contractures. Waardenburg's Syndrome type IV (Waardenburg-Shah) has features of WS in association with Hirschsprung's Disease. WS type IV is a heterogenous disorder with either Autosomal recessive or dominant inheritance.

Both the auditory and Pigmentary abnormalities of WS could be explained by a failure of proper melanocytes differentiation. Melanocytes are required in the stria vascularis for normal cochlear function. With the exception of those in the retina, melanocytes are derived from the embryonic neural crest. Other tissues derived from the neural crest that are involved in WS type I and the rarer WS type III & IV variants include the frontal bone, limb muscles and enteric ganglia. Mutations in multiple genes cause the various forms of WS. In this article we describe Waardenburg's Syndrome and the Audiometric findings in four subjects.

Materials and Method

During a recent survey at the Kaduna state special education school for the deaf/blind, Nigeria. 620 students were evaluated and four⁴ had Waardenburg's Syndrome WS, giving a frequency of 0.65% WS among the institutionalized deaf/blind in Kaduna

Two males & two females with age range of 10-19yrs (mean of 15.75). All four (4) met the diagnostic criteria for WS. We also evaluated Pigmentary disturbances according to the criteria. All 4 subjects had complete blue irides, with 3 of them being bilateral and one unilateral. All 4 subjects had white forelock.

They all had Otosopic, tuning fork, and Ophthalmologic examination and later subjected to Pure Tone Audiometry

(PTA) & Tympanometry.

In all the students Air-conduction thresholds were determined at 500Hz, 1, 2, 4 and 6 kHz by PTA. The degree of hearing loss was determined by taking the mean values across the frequency ranges.

We observed 3 major & 1 minor diagnostic criteria for Waardenburg's Syndrome. At the time of the survey none of WS subjects had any visual defects.

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Discussion

During the survey, the frequency of Waardenburg's Syndrome 0.65% amongst the institutionalized deaf and blind in Kaduna, Nigeria shows how uncommon this syndrome is, compared to studies by Silan et al in Turkey, in which they found 6.8%⁶. Although this may also mean that occurrences are under-reported, as many individuals with WS do not present for evaluation especially those without a hearing loss and considered normal by their families or caregivers and as such lose out on proper counseling and probable amplification⁷. Our subjects met the diagnostic criteria for WS type I.

No skin Pigmentary disturbances were noted, however, complete heterochromia irides and white forelock were noticed in our Waardenburg's Syndrome subjects. Most commonly, the loss affected persons with more than one pigmentation abnormality and is profound, bilateral, and has been stable over time, this also agrees with Newton.¹⁶

Congenital SNHL is clinically the most serious symptom in these individuals, it is also a common denominator in both WS I & II and it is usually severe to profound, as seen in three(3) of the WS subjects (see fig. 2,3 & 4). This was also reported by Hageman et al.³ Liu et al also observed this degree of hearing loss in 58% of WS type I⁵

This hearing impairment is thought to be due to lack of melanocytes in the stria vascularis of the cochlear. Interestingly, we noted that three WS subjects with

bilateral SNHL paralleled their pattern of fundus pigmentation i.e. bilateral complete blue irides. This was also the findings of Andrea Mullner et al⁷ We also did not find any unilateral hearing losses, however, in contrast to other studies where bilateral symmetrical hearing losses are commoner in type II WS, we found this in type I WS. This may be because our subjects were just four!¹⁷

In WS, as in other hearing losses of genetic origin, patients can experience low to high frequency hearing losses. In fact, according to Nadol and Merchant who also showed that audiogram configuration is variable, with low frequency losses being more common¹⁴, however in our study losses were in both low & high frequencies. We however didn't have the luxury of using ABR (Auditory Brain Response Audiometry) or DP-OAE (Distortion product- Otoacoustic emission), as usual in developing countries it is too expensive for large surveys such as this, although it is not usually possible to determine these types of hearing losses by click-ABR, as it is not frequency specific.

Two subjects with hearing thresholds suggestive of severe and profound SNHL respectively passed a hearing

Aid evaluation and where offered amplification which they eagerly accepted (see fig 3 & 4)

We therefore conclude that with availability of genetic studies, families can be traced and counseled to avoid future defects, and that Auditory Brainstem evoked Response Audiometry (ABR) and Distortion product-Otoacoustic Emission (DP-OAE) & Newborn hearing screening be made available and at affordable prices and free if possible to encourage participation. The routine use of DP-OAE in children with WS can detect high frequency hearing losses and thus prevent over-amplification in the lower frequencies during the fitting of hearing Aid, since use of hearing aid is the primary therapy for patients with Waardenburg's Syndrome.

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References

1. Waardenburg PJ. A new syndrome combining developmental anomalies of eyelid, eyebrows and nose root with Pigmentary defects of iris and head hair and congenital deafness. *Am J Hum Genet*: 1951; 3:195-253.
2. Arias S. Genetic heterogeneity in Waardenburg syndrome. *Original Article Ser* 1971; 7:87-101.
3. Hageman MJ. Audiometric findings in 34 patients with Waardenburg syndrome. *J Laryngol Otol* 1977; 91:575-84.
4. Newton V. Hearing loss and Waardenburg syndrome: Implications for genetic counseling. *J Laryngol Otol* 1990; 104:97-103.
5. Liu XZ, Newton VE, Read AP. Waardenburg syndrome type II: Phenotypic findings and diagnostic criteria. *Am J Med Genet* 1995; 55:95-100.
6. Silan F, Zafer C, Onder I. Waardenburg syndrome in the Turkish deaf population. PMID: 16719276
7. Andrea M-E, Elisabeth M. Waardenburg's syndrome type 2 in a Turkish family: implications for the importance of the pattern of fundus pigmentation. *Br J Ophthalmol* 2001; 85:1384
8. Liu XZ, Newton VE. Distortion product emissions in normal-hearing and low-frequency hearing loss carriers of genes for Waardenburg's syndrome. *Ann Otol Rhinol Laryngol* 1997; 106:220-5.
9. Fisch L. Deafness as part of an hereditary syndrome. *J Laryng* 1959; 73:355-82.
10. Harris FP. Distortion-product otoacoustic emissions in humans with high frequency sensorineural hearing loss. *J Speech Hear Res* 1990; 33:594-600.
11. Farrer LA, Grundfast KM, Amos J, et al. Waardenburg's syndrome (WS) type I is caused by defects at multiple loci
12. Reynolds JE, Meyer JM, Landa B, et al. (1995) Analysis of variability of clinical manifestations in WS. *Am J Med Genet* 57:540547.
13. Goldberg MF (1966) Waardenburg syndrome with fundus and other anomalies. *Arch Ophthalmol* 76:797810
14. Nadol Jr JB, Merchant SN: Histopathology and molecular genetics of hearing loss in the human. *Int J Pediatr Otorhinolaryngol* 2001; 61:1.
15. Oysu C: Temporal bone imaging findings in Waardenburg's syndrome. *Int J Pediatr Otorhinolaryngol* 2001; 58:215.
16. Newton VE: Clinical features of the Waardenburg syndromes. *Adv Otorhinolaryngol* 2002; 61:201.