Screening for \textit{GJB2}-R143W-Associated Hearing Impairment: Implications for Health Policy and Practice in Ghana

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**Key Messages**

1. \textit{GJB2}-R143W founder mutation is the major cause associated with HI in Ghana, with a relatively high population carrier frequency of 1.45\% amongst healthy Ghanaians.
2. \textit{GJB2}-R143W accounts for nearly 26\% of causes in families segregating congenital non-syndromic HI.
3. There is a rapid test designed for screening for the \textit{GJB2}-R143W variant. We recommend that this test be adopted as part of the universal newborn hearing screening (UNHS) program in Ghana.
4. Early testing for the \textit{GJB2}-R143W variant could lead to early detection of HI and the provision of medical and social services that will help improve the quality of life of affected individuals.
5. Cochlear implant should be developed in Ghana as the method of choice for correcting HI in children diagnosed before the age of language development.

**Keywords**

Health policy · \textit{GJB2}-R143W founder mutation · Hearing impairment · Newborn screening · Ghana

**Abstract**

Genetic factors significantly contribute to the burden of hearing impairment (HI) in Ghana as there is a high carrier frequency (1.5\%) of the connexin 26 gene founder variant \textit{GJB2}-R143W in the healthy Ghanaian population. \textit{GJB2}-R143W mutation accounts for nearly 26\% of causes in families segregating congenital non-syndromic HI. With HI associated with high genetic fitness, this indicates that Ghana will likely sustain an increase in the number of individuals living with inheritable HI. There is a universal newborn hearing screening (UNHS) program in Ghana. However, this program does not include genetic testing. Adding genetic testing of \textit{GJB2}-R143W mutation for the population, prenatal and neonatal stages may lead to guiding genetic counseling for individual and couples, early detection of HI for at-risk infants, and improvement of medical management, including speech therapy and audiologic intervention, as well as provision of the needed social service to enhance parenting and education for children with HI. Based on published research on the genetics of HI in Ghana, we recommend that the UNHS program should include genetic screening for the
**GJB2-R143W** gene variant for newborns who did not pass the initial UNHS tests. This will require an upgrade and resourcing of public health infrastructures to implement the rapid and cost-effective **GJB2-R143W** testing, followed by appropriate genetic and anticipatory guidance for medical care.

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**Background**

Hearing impairment (HI) is the partial or complete loss of hearing in an individual. Globally, about 1–2 of every 1,000 persons present with some form of HI [1]. In Africa, approximately 6 out of every 1,000 live births will have HI [2]. The global prevalence is expected to increase to about 900 million by 2050 [3]. Persons with HI cannot hear sound within the “normal” audible range of hearing [4], and this impacts their ability to effectively communicate with people around them. It could also affect their quality of life, including access to education, health care, and other basic social services [5, 6].

A common form of HI is non-syndromic hearing impairment (NSHI). NSHI is not associated with any known clinical symptoms [7] and presents in different forms and degrees of severity ranging from hearing loss in 1 or both ears to difficulties in understanding soft speech and inability to hear very loud noises. In some cases, the degree of hearing loss may become worse with age. NSHI could be caused by a variety of factors, some of which may be genetic or environmental [8]. The genetic causes are mainly associated with the connexin 26 gene (**GJB2**) mutation which is mostly inherited in an autosomal recessive pattern [9], while environmental causes include, but not limited to, exposure to loud sound, infectious diseases, and certain health conditions. In Ghana, meningitis is the main environmental cause of childhood HI, while the main genetic cause is the inheritance of the **GJB2-R143W** variant [10–13].

Ghana is an English speaking West African country with an estimated population of about 30,280,482 people [14]. About 50 and 15% of rural and urban dwellers in Ghana are living in poverty [15]. To reduce poverty, the government of Ghana has made commitments towards expanding and ensuring free access to formal education [16–18]. In spite of these efforts, an educational performance gap exists between students in urban schools and rural schools, which is possibly as a result of an uneven distribution of educational facilities and resources [19]. Similarly, schools for the deaf are mostly underprivileged and have inadequate resources for effective teaching and learning. Hence, hearing-impaired students are part of the marginalized individuals who receive minimum attention from the government [20]. The structure of the Ghanaian society does not effectively support disabilities [20], especially the negative cultural perception of hearing-impaired people [21], and this affects the participation of hearing-impaired individuals within the society. The low participation of these individuals negatively affects their psychosocial health and makes them feel inferior in many situations [20].

Access to quality health care is a fundamental human right in Ghana, but it is often inaccessible to the hearing impaired [22]. Hearing-impaired patients face major barriers such as finance, the proximity of the facilities, and lack of sign language interpreters when accessing health care in Ghana [22, 23]. A recent study among young hearing-impaired adults underscores the need for healthcare professionals to be trained to communicate using sign language [22]. There is an uneven distribution of health facilities in the country; underdeveloped communities travel many kilometers on foot to access health service in the city centers [24]. In addition to the above challenges, the majority of Ghanaian health facilities cannot effectively diagnose HI at an early age where interventions are most needed [25, 26]. To date, there is no routine clinical investigation of HI genes in Ghana as well as cochlear implants for affected Ghanaians. There is a need therefore to have informed policy on genetic screening for HI in Ghanaian infants who fail universal newborn hearing tests (UNHS) and the provision of early interventions.

**Universal Newborn Hearing Screening**

The UNHS has been implemented in several countries [27–29] with the aim of diagnosing HI in newborn babies to give appropriate interventions, follow-up tests, or treatments to children with permanent HI [29]. The UNHS program is also referred to as early hearing detection and intervention (EHDI) program [28]. The methods used in the UNHS are non-invasive quick tests to assess the physiological status of the infant’s ear and is often conducted soon after birth. The procedure for the UNHS consists of presenting soft sounds (clicks) to the ears of the baby using auto-mated auditory brainstem response or auto-mated otoacoustic emissions. The child’s response to the sound presented is measured by a sensor through the scalp. Special devices with inbuilt algorithms are used to evaluate the auditory brainstem response of...
the child. In most cases, the children who did not pass the first UNHS test are scheduled for a second test and subsequently referred to a specialist when no response is obtained from the initial tests [28, 29].

**HI: A Condition of Public Health Significance in Ghana**

HI adversely affects the cognitive development of children [6], making it challenging for them to learn vocabulary, grammar, and other aspects of verbal communication [5, 6]. This significantly impacts their education, and in some instances persons with HI are considered a social and economic burden to their families and community [30]. For example, over 80% of the deaf children in Ghana are born to hearing parent, and their parents, siblings, and friends struggle to communicate with them [21]. Equally, one-on-one interviews by us with some deaf children in Ghana revealed that they feel neglected and unloved by their parents. Other studies in Ghana have reported difficulties by persons with HI to access social services such as health care and education or to socially adapt to their communities [21, 22, 31]. This could be frustrating for both the deaf children and other people in the community.

Early diagnosis of HI could lead to the early introduction of intervention that could support speech, language, and cognitive development for deaf children [6]. Empirical studies in South Africa and the UK have demonstrated that hearing-impaired children when diagnosed early and given the appropriate intervention, especially within the first 6 months after birth, are likely to have similar cognitive and language development as hearing children of the same age-group [5, 32, 33]. However, in Ghana, the majority of hearing-impaired children are only able to have comprehensive hearing tests after the age of 6 years [12] when they would have passed the age of language development. This impacts negatively on the effectiveness of any interventions that may be introduced to improve on their quality of life.

To facilitate early detection and management of HI in children, several countries have introduced UNHS into their clinical programs. However, UNHS is still not available in many African countries, and many newborn screening programs tend to rely on ontological (ENT) examination to detect hearing loss in infants [5]. Unfortunately, these diagnostic procedures are not able to provide conclusive results in infants [34]. Although UNHS was introduced in Ghana in the early 1970s, this service is still largely unavailable in most health centers across the country [25, 26]. Failure to effectively roll out the UNHS in Ghana could be due to a variety of reasons including high cost of testing, limited infrastructural capacity, and human resources to man the service.

Genetic testing may at this time be costly for populations in sub-Saharan Africa. However, we are of the opinion that we could leverage existing knowledge and genetic programs on HI in Ghana to introduce a cost-effective genetic test for HI as part of the national UNHS package. For example, it is already established that the GJB2 gene accounts for over a quarter (26%) of familial HI cases in Ghana [12], suggesting that 1 out of every 4 hearing-impaired families in Ghana is likely to have the GJB2 gene variants. The reported carrier frequency of nearly 1.5% suggests that among every 145 Ghanaians (without HI), 2 are likely to pass on a defective GJB2 gene to their children. Therefore, genetic screening for hearing loss may identify, at an early stage, children who are likely to develop HI.

In Ghana, there is no clinical investigation for HI genes, especially in the UNHS program. A number of genetic sequencing platforms for HI are now commercially available [35]. However, their use in resource-limited countries may be practically challenging because of limited human and infrastructural capacity to support genetic sequencing as part of routine clinical processes [36–38]. Given this practical challenge, we propose that UNHS Ghana adopts and uses a rapid and effective diagnostic tool for screening for the GJB2-R143W variant [13]. This diagnostic tool was recently developed following genetic studies on HI in Ghana. Unlike most commercially available tools, this diagnostic test is based on the restriction fragment length polymorphism technique and therefore does not require the use of sequencing technology. The tool has the potential to identify the common genetic cause (GJB2-R143W) of HI among Ghanaians and can effectively be used as a first-line genetic testing tool. Adding genetic testing of GJB2-R143W mutation for the population, the prenatal and neonatal level may lead to guiding genetic counseling for individual and couples, early detection of HI for at-risk infants, and improvement of medical management, including speech therapy and audiologic intervention, as well as provision of the needed social service to enhance parenting and education for children with HI. As the UNHS will identify more children with HI, this will further the rationale to develop a cochlear implant service in Ghana as the method of choice for hearing restoration in children diagnosed before the age of language development.
Policy Recommendations

UNHS is an important strategy for reducing the burden of HI. Although it has been introduced in Ghana, it does not incorporate yet the option for genetic HI testing [39, 40]. Therefore, despite the strong evidence for the major contribution of GJB2-R143W mutations to HI, Ghanaian children are unable to receive early HI genetic diagnosis [12]. Therefore, we recommend the following:

1. Early screening of Ghanaian children for HI should be introduced in pediatric programs across the country. For this to be possible, hearing assessment centers in Ghana, as well as the existing Community-Based Health Planning and Services (CHPS) compounds, should be equipped with the necessary logistics and human resources to complement the UNHS program.

2. Children who are found to have HI from the UNHS should be tested for mutations in GJB2 and especially R143W mutation since it accounts for the majority of HI in Ghana. Figure 1 shows an outline of recommended for HI newborn screening program in Ghana.

3. Laboratory diagnosis services should implement the recently developed GJB2-R143W cost-effective for HI in Ghana [13]. This will relatively decrease the cost of HI genetic screening in Ghana compared to existing costs in other African countries. This is because our cost-effective screening tool was developed based on a simple and inexpensive RFLP technic to screen for the common R143W mutation which accounts for over 26% of familial HI cases in Ghana.

4. Health services should develop genetic services including genetics counseling for HI, to accompany the UNHS program.

5. Appropriate intervention programs should be planned accordingly. This will include Cochlear implant services in Ghana; this is a standard treatment for genetic HI in high resources countries such as the UK [33]. This is however not the case in Ghana. This may be due to the inability of Ghanaian health centers to properly diagnose genetic HI. With the implementation of the suggestions above, the HI children under the UNHS scheme can be well characterized and given the appropriate interventions such as provision of hearing aids, cochlear implants, speech therapy, or early language aids. Intervention programs should extend to develop social resources to enhance parenting including sign language courses for families, equipped schools for the deaf in Ghana to improve educational attainment for affected children, and wide speech-language interventions for children and families.

Conclusion

HI is a noncommunicable sensory disorder of major public health concern in Ghana. The majority of congenital HI in Ghana is caused by genetic factors, of which GJB2-R143W is a major contributor. Genetic screening for GJB2-R143W in newborns in Ghana would offer families with options for timely interventions which will improve the living standards and quality of life of deaf children.

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Fig. 1. Flow diagram of recommended screening process for early detection of HI in Ghana. UNHS, universal newborn hearing screening; AABR, automated auditory brainstem response; AOAEs, automated otoacoustic emissions; HI, hearing impairment.
Conflict of Interest Statement

The authors declare no conflicts of interest.

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Author Contributions

Conceptualization: A.W., G.A.A., and S.M.A.; writing – original draft preparation: S.M.A., G.A.A., and A.W.; writing – review and editing: S.M.A., O.Q., G.K.A., G.A.A., and A.W.; supervision: A.W., G.A.A., G.K.A., and O.Q.; funding acquisition: A.W. and G.A.A. All authors contributed important intellectual content presented and have read and agreed to the published version of the manuscript.

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