Causes of deafness in British Bangladeshi children: a prevalence twice that of the UK population cannot be accounted for by consanguinity alone

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Objective: To study the causes and prevalence of sensorineural deafness in Bangladeshi children resident in East London.

Methods: This was a cross sectional survey of children of Bangladeshi origin living in East London with bilateral sensorineural hearing loss of 40 db HL or more. In this study, 134 patients were included. The study looked primarily at the causes of sensorineural hearing loss in this population.

Results: The prevalence of deafness in Bangladeshi children in East London is approximately 3.86 per 1000 [95% confidence intervals (CI) 3.20, 4.65] which is significantly greater than the average UK prevalence of 1.65 per 1000. The prevalence of deafness in these Bangladeshi children belonging to non-consanguineous families only, the prevalence falls to 2.73 per 1000 (95% CI 2.19, 3.41). In 60% cases the cause of deafness was genetic. The single most common cause of sensorineural hearing loss in this population was mutations in the \(GJB2\) gene (Connexin 26) in 20 of these patients (17%). Parents were consanguineous in 33% of the families.

Conclusion: This study concludes that prevalence of sensorineural deafness in Bangladeshi children is at least 2.3 times the national average. This study also concludes that genetic causes are the common cause of deafness in this ethnic group, with nearly 30% of children with non-syndromic deafness having mutations in \(GJB2\). Although parental consanguinity was very high in this population it did not account for the whole increase in prevalence.

Hearing loss can be broadly divided into sensorineural, conductive or mixed. Sensorineural hearing loss is defined as loss of hearing sensitivity resulting from dysfunction of the inner ear or cochlear nerve, exceeding 20 db HL with an air bone gap of <15 db HL averaged over 0.5,1 and 2 KHz. The prevalence of sensorineural hearing loss >40 dB HL in the UK has been reported as 1–2 per 1000 [95% confidence intervals (CI) 2.02, 2.08] (permanent congenital hearing loss is 0.9/1000 and at age 10 the prevalence is 1.7/1000).\(^1,2\) In nearly half of children with permanent hearing impairment, the cause is genetic.\(^3,4\) Of the genetic causes of hearing loss, syndromic forms of deafness account for 30% and non-syndromic hearing loss accounts for nearly 70% cases.\(^5\)

In 1993, Vanniasegaram et al. reported the prevalence of sensorineural deafness in the Bangladeshi population in East London to be greater than the national average.\(^6\) The ethnic profile of the resident population in the borough of Tower Hamlets in East London shows that 33.4% are of Bangladeshi ethnic origin\(^7\) according to the 2001 Census. Most of these Bangladeshi families originate from Sylhet, a province in Bangladesh, and a large proportion of parents of these children speak little or no English. In view of the expansion of the Bangladeshi population in East London within the last decade, the increase in knowledge of genetic causes of deafness with the possibility of molecular diagnosis and the introduction of Newborn Hearing Screening, it was decided to review the causes of sensorineural deafness in this population in some detail. The objectives of this study were to determine the prevalence of sensorineural deafness and to review the causes among the Bangladeshi population. We also wanted to determine whether consanguinity accounted for the high prevalence of deafness in this population as this has been cited as the reason for the
high prevalence of deafness but was not explicitly addressed.

**Patients and methods**

**Ethical considerations**

Approval for this project was obtained from the Research Ethics committee at Great Ormond Street Hospital and the Institute of Child Health and City and Hackney Primary Care Trusts.

**Methods**

This study was a cross sectional survey of children of Bangladeshi ethnic origin under the Donald Winnicot Centre (a multidisciplinary community clinic in East London) to determine the causes of sensorineural deafness. The study was carried out from October 2003 to October 2006. The Bangladeshi population living in East London is concentrated mainly in Tower Hamlets, Hackney and Newham health districts.

The patients recruited for this study were all the Bangladeshi subjects with bilateral sensorineural hearing loss of all causes more than 40 dB HL, on the records of the Donald Winnicot Centre. Details of children of Bangladeshi ethnic origin with hearing loss were obtained from several sources (Audiology database at the Donald Winnicott Centre, Teachers of Deaf database, and individual Consultants’ records) and the records were cross checked. Bangladeshi ethnic origin of the child was defined as, both the parents of Bangladeshi ethnicity (first generation, i.e. born in Bangladesh or second generation, born elsewhere) and was confirmed by self-reporting on direct questioning. Most of these patients were regularly under the follow-up of Consultant audiological physicians at Donald Winnicot Centre and Great Ormond Street Hospital. Many of the patients had already been investigated for their deafness. The tests included: full blood count, urea and electrolytes, thyroid function tests, ESR, urine analysis, ECG, ultrasound of kidneys, and CT scan of temporal bones. If the history had suggested teratogenic cause, the patients had been tested for common infectious diseases (toxoplasma, rubella, cytomegalovirus (CMV), herpes simplex, syphilis). A pre-printed list of investigations was used to request investigations for these patients at Great Ormond Street hospital. For most of the patients seen until 4–5 years ago, no genetic testing had been requested.

The serial hearing tests of these patients were recorded in the notes or were in the audiology records at Donald Winnicot Centre. The hearing had been assessed by pure tone audiometry in the older children and by sound field audiometry and Brainstem evoked response audiometry in the younger children.

The data collected included detailed history of hearing loss, medical history, family history including history of consanguinity, examination findings, audiological information on patients and parents and results of investigations. After the data collection at this stage patients were discussed at meetings with the senior authors regarding inclusion into or exclusion from the study. At this stage, the patients were classified into two main groups—’Cause of deafness known’ and ‘Cause of deafness unknown’.

One hundred and thirty-four patients (115 families) were eligible to be included in this study (Fig. 1). Of these, 11 patients (11 families) declined to participate and four patients (four families) could not be contacted. Thus, for the purpose of elucidating the cause of deafness 119 patients (100 families) were included. Of these 67 patients (53 families) had children with undetermined cause and 52 patients (47 families) had children with cause of their deafness diagnosed. Those patients in whom the cause of deafness was not known were invited to come to the research clinic.

**Results**

The patients in this study ranged from 9 months to 18 years of age (average age at the time of recruitment in this project was 11 years and 6 months). In this study group, there were 71 (53%) males and 63 (47%) female patients. All the subjects had parents or grandparents...
In 2001, there were 28,497 children <16 years as born in the province of Sylhet in north-eastern Bangladesh. The total population of Bangladeshis living in Tower Hamlets and Hackney districts in East London was 71,525 in 2001. Of these, there were 28,497 children <16 years as per 2001 census. Of the 134 deaf children with a permanent bilateral sensorineural hearing loss >40 db HL in the better hearing ear, living in these two districts at the time of census in 2001, 110 children were aged up to 16 years of age (<16) in 2001. Thus the prevalence of deafness in Bangladeshi children in 2001 was at least 3.86 per 1000 (95% CI 3.20, 4.65 using Wilson’s method). This may be an underestimate as we may have incompletely ascertained some individuals, although all efforts have been made to trace these children using different sources.

Information about consanguinity was available in 105 families, of which parents were consanguineous in 35 (33%). Of these, 26 parents were first cousins, seven were second cousins and two were third cousins.

On calculating the prevalence of deafness in these Bangladeshi children belonging to non-consanguineous families only, the prevalence falls to 2.73 per 1000 (95% CI 2.19, 3.41). This is still higher than the national figures of 1.07 (95% CI 1.03, 1.12) per 1000 for 3-year-old children to 2.05 per 1000 (95% CI 2.02, 2.08) for children aged 9–16 years, so the excess cannot be accounted for by consanguinity alone.

There are no figures for consanguinity rates in Tower Hamlets as this data is neither collected during the census. One can determine whether errors in this estimated consanguinity were likely to affect our calculations of prevalence of deafness. Figure 2 shows that there are no substantial changes in the prevalence of deafness in non-consanguineous marriages with respect to possible values of the proportion of consanguineous marriages (between 5% and 20%) in the background Bangladesh population. For the group as whole (119 patients/100 families) genetic causes appear to be the most common cause of deafness in the Bangladeshi population accounting for 60% of patients. Acquired causes were responsible for hearing loss in 18% patients and in 22% cases the cause of deafness was undetermined. Of the deafness because of genetic causes, 58% were non-syndromic, 25% syndromic and 17% were chromosomal. Amongst the 12 children who had hearing loss because of chromosomal causes, most (93%) of these children had Down syndrome and one child had Trisomy 8. In the 27 families, with non-syndromic deafness nearly all patients (96%) had recessive deafness except one family who had dominant deafness.

For the group as whole (119 patients/100 families), the most common cause of deafness in the background population was genetic causes, which accounted for 58% of patients. Acquired causes were responsible for hearing loss in 18% patients and in 22% cases the cause of deafness was undetermined. Of the deafness because of genetic causes, 58% were non-syndromic, 25% syndromic and 17% were chromosomal. Amongst the 12 children who had hearing loss because of chromosomal causes, most (93%) of these children had Down syndrome and one child had Trisomy 8. In the 27 families, with non-syndromic deafness nearly all patients (96%) had recessive deafness except one family who had dominant deafness.

All non-syndromic children in whom the cause of deafness was unknown were tested for mutations in the GJB2 gene. We have published these results previously but briefly, of the 67 patients, 20 were confirmed to have biallelic pathogenic mutations in GJB2 (30%). The most common mutation in this study was W24X in 55% patients (total-11/20; eight-homozygous, three-compound heterozygous). The mutations M1V, W77X, V95M, IVS1 + 1 and Q124X have all been observed in both homozygous and compound heterozygous form.

In the group with syndromic deafness (18 patients/14 families) the most common cause was an unknown syndrome in nearly one-third of patients. These children had dysmorphic facies and/or other clinical features but no specific diagnosis could be assigned to them. The other syndromes associated with hearing loss found in this...
study are shown in Table 2. Consanguinity in the group of patients with an unknown syndrome was 100% (5/5 families). This reiterates the fact that rare autosomal recessive diseases manifest in highly consanguineous populations.

Amongst the group with deafness because of acquired, environmental or other causes (22 patients/21 families), the hearing loss was associated with factors because of prematurity in nearly one-third of the patients. Overall, amongst the total study group prematurity was associated in about 6% of all patients. In these patients with prematurity other factors may have contributed to the hearing loss. Two of these patients also had associated jaundice and one had intracranial haemorrhage. Other acquired/environmental factors were hypoxic-ischaemia, CMV, otosclerosis, otitis media, meningitis, aminoglycoside toxicity, and infective polyneuropathy (Table 3).

Severity of deafness was calculated as an average of hearing at frequencies 500, 1000, 2000 and 4000 Hz. The severity was classified as mild (25–39 dB HL), moderate (40–69 dB HL), severe (70–89 dB HL) and profound (>90 dB HL) in the better hearing ear, of all causes. The distribution in this group of Bangladeshi children as a whole was: profound deafness in 53 (40%), severe deafness in 35 (26%), moderate in 46 (34%). Another eight children had mild deafness and were not included in this study.

Progression of deafness was confirmed on audiogram in 14 patients (11%) out of 128 on whom this information was available (Table 4). This number of children with progressive deafness may be an underestimate as for some children the deafness was confirmed at a later age and there were no previous records for these children to decide whether the hearing was stable or progressive. It is noteworthy that the majority (10/14 [72%]) patients with progressive deafness had a genetic cause. The cause was acquired in 1/14 (7%) and unknown in 3/14 (21%) patients. None of the children with progressive deafness were positive for mutations in \( \text{GJB2} \). In 13 of these 14 children (93%) the deafness had progressed to severe or profound deafness. In five of these children the parents were consanguineous. The average age of confirmation of

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<tr>
<th>Table 1. Causes of deafness after ( \text{GJB2} ) testing: 119 patients (100 families)</th>
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<tr>
<td><strong>Cause</strong></td>
</tr>
<tr>
<td>Hypoxic-ischaemia</td>
</tr>
<tr>
<td>Prematurity</td>
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<tr>
<td>CMV</td>
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<tr>
<td>?Otosclerosis*</td>
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<tr>
<td>Otitis media†</td>
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<tr>
<td>Meningitis</td>
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<tr>
<td>Aminoglycoside toxicity</td>
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<td>Infective polyneuropathy</td>
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*This patient had a family history of otosclerosis and had cochlear otosclerosis.
†This patient developed sensorineural deafness because of long-standing otitis media.
hearing loss in this group of patients as a whole was at the age of 3 years and 5 months (range- month to 15 years). On dividing these children as per the decade in which they were born, it is quite apparent that with the passage of time (Table 5) the age of detection of deafness has fallen in this study group.

Discussion

Comparison with other studies

In this study, the prevalence of deafness in children of Bangladeshi origin resident in East London up to 16 years of age was calculated to be at least 3.86 per 1000 which is 2.3 times the national average of 1.65\(\/2\) per 1000. Higher prevalence of deafness in a number of different immigrant ethnic groups has been reported in the past.\(^4,6,12\) In these studies, the excess of childhood deafness was also attributed to genetic causes secondary to the practice of consanguineous marriage. In the British Bangladeshi population our analysis suggests that consanguinity contributes to the raised prevalence of deafness. However, removal of those children born of consanguineous marriages from the calculation does not reduce the prevalence to the national figure. Furthermore, we are confident that disclosure of consanguinity by parents of the deaf children is accurate because in those families with GJB2 mutations, self-reported consanguinity by parents was accurately reflected in mutational status (i.e. where parents said that they were not related the deaf children were found to be compound heterozygotes and vice versa). Interestingly, the proportions of deafness because of genetic, acquired and unknown causes do not differ significantly from proportions described in other populations, which supports the conclusion that deafness because of all causes may be increased in this population of Bangladeshi ethnic origin. It is likely therefore that environmental factors may also play a part in the high prevalence of deafness.

The environment of Tower Hamlets is unusual for many reasons; the borough of Tower Hamlets, where 33.4% of residents are of Bangladeshi origin,\(^7\) is ranked as the second most deprived out of 384 in the country, has high unemployment rates and is overcrowded (10 462 people per square kilometre compared with 4679 for the region and 380 for England overall). The total fertility rate in Tower Hamlets is 1.84 compared with 1.64 for UK and Bangladeshis in general tend to have large families. For example in London generally, 57% of Bangladeshi households have two or more dependent children compared with the London average of 17% and only 8% of Bangladeshi households are single person households.\(^13\)

Cytomegalovirus is now recognised as the most frequent cause of congenital infections in humans and is the leading acquired cause of congenital sensorineural hearing loss.\(^14\) It occurs in \(\approx 1\)% of all newborns and hearing loss, which can range from mild to profound, is the most common neurological impairment associated with congenital CMV infection. As only 10% of infants with congenital CMV are

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<th>Table 4. Progressive hearing loss-14 patients</th>
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<tr>
<td><strong>Cause of deafness</strong></td>
</tr>
<tr>
<td>Genetic</td>
</tr>
<tr>
<td>Non-syndromic</td>
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<tr>
<td>Recessive</td>
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<td>Syndromic</td>
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<td>Unknown syndrome</td>
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<td>Pendred syndrome</td>
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<td>Waardenburg syndrome</td>
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<td>Peroxisomal disorder</td>
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<td>Chromosomal</td>
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<td>Trisomy 21</td>
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<tr>
<td>Acquired</td>
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<tr>
<td>Otitis media</td>
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<tr>
<td>Unknown</td>
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Table 5. Age of confirmation of hearing loss in different decades

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<tr>
<th>Children born in decade</th>
<th>Mean age of confirmation of hearing loss</th>
<th>Mode age of confirmation of hearing loss</th>
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<tbody>
<tr>
<td>1980–1989</td>
<td>4 years 5 months</td>
<td>3 years</td>
</tr>
<tr>
<td>1990–1999</td>
<td>3 years 1 month</td>
<td>2 years</td>
</tr>
<tr>
<td>2000 onwards</td>
<td>1 year 3 months</td>
<td>&lt;6 months</td>
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symptomatic at birth it can be extremely difficult to diagnose in the majority of cases.\textsuperscript{15} Cytomegalovirus is more prevalent with overcrowding and is associated with poorer socio-economic conditions.\textsuperscript{16} Thus, although speculative, it is possible that congenital CMV infection may account for some of the increase in prevalence of deafness in the Bangladeshi population of East London.

In this study, the distribution of causes of deafness has been – genetic causes in 60%, acquired/environmental in 18% and unknown in 22% of the 134 subjects. Amongst the genetic causes, most of the children had non-syndromic deafness (58% patients). Even after genetic analysis, the cause of deafness remains undetermined in 22% patients. As this study population originates from a confined geographic region (Sylhet), there might be other unknown recessive genes responsible for these cases of deafness of undetermined aetiology. Characterisation of these genes will be the subject of further research.

The fact that mutations in the \textit{GJB2} gene were found to be the cause of deafness in nearly one-third of Bangladeshi children with non-syndromic deafness has a major implication for the investigation of deaf children of Bangladeshi ethnic origin. If \textit{GJB2} analysis is the first test requested for investigation of deafness, it is likely to be positive in one in three Bangladeshi children, obviating the need for further investigation with potential saving of NHS resources. Knowing the causes of deafness is important as it provides a more logical approach to management of these children informs genetic counselling and may help to organise preventive measures in the future.\textsuperscript{17} The aetiology of deafness should be diagnosed at as early an age as possible as early rehabilitation is important for communication development, educational achievement and better quality of life.\textsuperscript{18–20}

\textbf{Strengths of this study}

This study reviews the causes of deafness in Bangladeshi population in detail, utilising the increase in knowledge of genetic causes of deafness with the possibility of molecular diagnosis. This study also determines whether consanguinity accounted for the high prevalence of deafness in this population as this has not been explicitly addressed previously.

\textbf{Clinical applicability of the study}

This study is of relevance to Bangladeshis living in Bangladesh, other parts of UK (Oldham, Bradford, Luton and Birmingham) and elsewhere in the world.

\textbf{Synopsis of key findings}

- The prevalence of deafness in Bangladeshi children in 2001 was at least 3.86 per 1000 (95% CI 3.20, 4.65) which is at least 2.3 times the national average.
- Parents were consanguineous in 33% families. Of these, 26 parents were first cousins, seven were second cousins and two were third cousins. However, the increase in prevalence is not accounted for by the high rates of consanguinity alone.
- For the group as whole (119 patients/100 families) genetic causes appear to be the most common cause of deafness in the Bangladeshi population accounting for 60% of patients. Acquired causes were responsible for hearing loss in 18% patients and in 22% cases the cause of deafness was undetermined.
- In this study population, nearly 30% of children with non-syndromic deafness having mutations in \textit{GJB2}.

\textbf{Acknowledgements}

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\textbf{Conflict of interest}

None to declare.

\textbf{References}


