

ORIGINAL ARTICLE

PREVALENCE OF LONG QT SYNDROME AND OTHER CARDIAC DEFECTS IN DEAF-MUTE CHILDREN

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Background: Long QT syndrome is considered a fatal disease because of its association with ventricular arrhythmias and sudden cardiac death. Objectives of study were to determine the prevalence of long QT syndrome and other heart diseases, in deaf-mute children. **Methods:** A Cross-sectional descriptive study was conducted at Cholistan special education centre and Cardiology department, Sheikh Zayed hospital Rahim Yar Khan, Pakistan in September 2006. A total of 104 congenitally deaf-mute children were assessed. Height, weight and blood pressure measured, 12-lead electrocardiogram done and QTc calculated using Bazette's formula. Children with prolonged QTc underwent 24-hour ambulatory ECG recording. All were auscultated following complete protocol. A child with murmur was further evaluated with colour Doppler echocardiography. Audiometry was performed on all the children and the result interpreted according to WHO recommendations. Diagnosis of LQTS was based on Revised Schwartz criteria. **Results:** Out of 104 children, 62 were male with mean age 11.89 yrs. The average systolic and diastolic BP was 97/67 mmHg. Average height was 126 Cm. All children had moderate to severe bilateral sensorineural hearing loss (40–80 dB). One child had associated Patent Ductus Arteriosus. Fifteen had an innocent murmur. Prevalence of congenital heart disease was found to be 0.1/1000. Four children had QT interval more than 440 mSec, (range 0.46–0.47 mSec.). Both genders were equally affected. Three children had high probability of LQTS and one had intermediate probability. Screening of family of these 4 patients showed prolonged QT interval in the sibling of one patient. **Conclusion:** Our study highlights the significant prevalence of Jervell Lange-Nielsen Syndrome in Pakistani deaf-mute children, which may be associated to the high level of consanguinity in this region. Awareness of this syndrome among health care providers is needed as timely diagnosis and subsequent treatment may prevent fatal complications.

Keywords: Long QT Syndrome, Deafness, Congenital Heart Defects

INTRODUCTION

The association of bilateral sensorineural hearing loss with cardiac pathology was first documented by Jervell and Lange-Nielsen in 1957.¹ They described a Norwegian family where four out of six siblings with congenital deafness had fainting spells since infancy. They noticed prolongation of QT interval on electrocardiogram of three of the four children. This association of prolonged QT interval, syncopal attacks and congenital deafness was called the cardio-auditory syndrome by James.² Now this condition is more commonly known as Jervell Lange-Nielsen Syndrome (JLNS), a variant of the Long QT Syndromes (LQTS).

Long QT syndrome is considered a fatal disease because of its association with ventricular arrhythmias and sudden cardiac death.³ Literature reveals that although a few studies have been conducted worldwide to determine the prevalence of JLNS, no such study has been reported from Pakistan. Being a developing country, medical facilities may not always be available to the people, and in such circumstances, the deaf-mute are often overlooked, being a more neglected segment of community. With a 49.9% literacy rate⁴, most of the people resort to manual labour as a mean of earning livelihood. In such circumstances, a deaf-mute child may be considered by some, more of a

liability than an asset, and hence neglected. The health care professionals are themselves, not particularly trained in the handling of deaf-mute children and are unaware of other defects that may be associated with the deafness. Access to professionals may not always be possible. Furthermore, the practice of interfamily marriages is highly prevalent in Pakistan as shown by Sajjad and colleagues.⁵ This may lead to the accumulation of genetic mutations and a higher prevalence of recessive diseases.

We have attempted to identify cases of JLNS and determine its prevalence, and simultaneously look for other cardiac defects that may have previously gone unnoticed.

MATERIAL AND METHODS

It was a cross-sectional survey of Cholistan Special Education Centre, Rahim Yar Khan. A field team consisting of trained senior medical officer, ECG technician and a female nurse from Department of Cardiology, SZMC, Rahim Yar Khan visited the school after arranging an appropriate time and date with the school authorities.

Height, weight, and blood pressure were recorded by paramedical staff. Sphygmomanometer with different sizes of paediatric cuffs was used. Blood

pressure was recorded in sitting position on a chair with back support. 12-lead ECG was done by a trained ECG technician with standard lead placement and automatic computerised report. All ECGs were mounted on ECG report proforma and read by two different experts before a final decision was taken. QT interval was calculated by using Bazett's formula.⁶

$$QT^c = QT / \sqrt{(R-R)}$$

Measurements were compared with computerised readings. Prolonged QT was defined to be >440 mSec. Long QT syndrome was diagnosed following Revised Schwartz criterion.⁷ Children with prolonged QT interval underwent 24-hr ambulatory ECG recording to document any arrhythmia.

All children were auscultated in supine, left lateral and sitting with leaning forward position by a trained Medical officer in cardiology. Any child having murmur of any intensity was further evaluated by colour Doppler Echo using Toshiba Nemio 35 Echocardiographic system.

Audiometry was performed using Grason Stadler GSI 61 clinical audiometer on all children and records taken. The grading of deafness was done according to WHO recommendations (1980): mild (26–40 dB), moderate (41–55 dB), moderately severe (56–70dB), severe (71–91dB) and profound (>91 dB) deafness.⁸

Table-1: Revised criteria (1993)

Parameters	Points
ECG findings:*	
A. QTc**	
≥480 mSec	3
460–470 mSec	2
450 mSec (in males)	1
B. Torsade de Pointes†	2
C. T-wave alternans	1
D. Notched T-wave in three leads	1
E. Low heart rate for age††	0.5
Clinical history:	
A. Syncope†	
With stress	2
Without stress	1
B. Congenital deafness	0.5
Family history:‡	
A. Family member with definite LQTS[§]	1
B. Unexplained sudden cardiac death below age 30 among immediate family members	0.5

*In the absence of medications or disorders known to affect these electrocardiographic features

**QTc calculated by Bazette's formula, † Mutually exclusive

†† Resting heart rate below the second percentile for age

‡ The same family member cannot be counted in A and B

§ Definite LQTS is defined by an LQTS score ≥4

Scoring: ≤1 point, low probability of LQTS

2–3 points, intermediate probability of LQTS

≥4 points, high probability of LQTS

RESULTS

This study group consisted of 104 children, 62 male (M/F 3:2) with mean age of 11.89 (range 4–22 years).

The systolic BP ranged from 70–130 mmHg (average 97.62 mmHg) and diastolic BP ranged 40–90 mmHg (average 66.87 mmHg). The height ranged from 69–183 Cm with the average of 126 Cm. All children

had moderate to severe bilateral sensorineural hearing loss (40–80 dBs). One child had associated Patent Ductus Arteriosus. Fifteen had innocent murmur. Prevalence of congenital heart disease was found to be 0.1/1000.

Four children had QTc interval more than 440 mSec according to Bazette's formula. It ranged from 0.46 to 0.47 mSec affecting both genders equally. All available data was evaluated according to the Schwartz Revised LQTS Diagnostic Criteria. The children were divided into 4 different cases. Their clinical and ECG findings are shown in the Table-2.

Table-2: Clinical and ECG findings of the cases

Case No	Age (Yr) /Sex	QTc Interval (mSec)	Syncope and Deafness	Sudden Death in Family Members	Family members with Deafness	Score
1.	11 /F	0.47	Stress induced	+	-	5
2.	14 /M	0.46	Stress induced	+	-	5
3.	9 /M	0.46	Without Stress	+	+	4
4.	12 /F	0.46	-	-	Family Members with long QT 0.45 mSec	3.5

Cases 1, 2 and 3 had a high probability of LQTS and case 4 has intermediate probability of LQTS. Echocardiography of these 4 children showed no cardiac anomaly with normal ventricular function. Holter monitoring failed to disclose any important cardiac arrhythmia or T-wave abnormality. ECG screening of the family members of these 4 children documented lengthening of QT interval in a sister of case No. 4.

DISCUSSION

Jervell Lange Nielson Syndrome is a rare syndrome.⁹ However, our study, conducted on 104 deaf-mute kids, showed 4 children completely fulfilled the criteria of LQTS (JLNS) laid down by Schwartz. This is a very high prevalence, as no other study has so far yielded such a number. In 1969, Sanchez-Cascos, Sanchez-Harguindey and DeRabago found one case in 511 deaf-mute kids¹⁰ and in 1971, 5 cases of LQTS were seen in 1126 deaf kids in Ontario.¹¹ Even recent studies conducted in Turkey¹² and Songhla¹³ yield a prevalence of 0.57% and 0.7% respectively. This high prevalence of JLNS is most probably linked to the high incidence of consanguinity in our population. Most of the children attending this school, and all of our diagnosed cases, were from a consanguineous marriage. As JLNS is an autosomal recessive disease, the accumulation of genetic mutations in inter-family marriages is understandable. The parents of the Pakistani child diagnosed with JLNS in 2005 in Hong Kong¹⁴ were also first cousins. Furthermore, review of our four children showed that 3 had a history of sudden death in their family. Medical records of the deceased

individuals were not available, but it may be possible that they too suffered from LQTS. One deaf child had a sister with LQTS, although she was not deaf. No such history of sudden death was retrieved from the deaf children with normal QT interval.

We conducted audiometric studies on all the children. Deafness was bilateral and severe in the children with JLNS. In the rest it varied from moderate to severe. Both the sexes were equally affected, which may be a coincidental finding, as the disease is autosomal recessive.

In this study, we also looked for other congenital cardiac defects that may be present with deafness. Congenital deafness has been linked to other cardiac diseases previously. Csanády *et al*¹⁵ suspected an association between congenital deaf-mutism and hypertrophic cardiomyopathy. This association was also described in a study conducted in Maryland where MYO6 was suspected to cause Familial hypertrophic cardiomyopathy and sensorineural deafness.¹⁶ Schonberger *et al* conducted a study¹⁷ to determine a link between dilated cardiomyopathy and sensorineural hearing loss. Ucar T and colleagues hypothesised that decreased sympathetic/ parasympathetic balance as a result of the absence of auditory stimuli on the autonomic nervous system might be an explanation for finding of lower mean heart rate in congenitally deaf children.¹⁸ However, their study did not support this hypothesis.

In our study, one child had patent ductus arteriosus (1%) out of 104. The patient's mother did not give a history of Rubella infection in pregnancy. Nor did the child show any other signs of congenital Rubella. So, whether this PDA is an isolated finding, or whether it has a genetic link with deafness, is hard to say. Further genetic testing is required to ascertain this link. However, such advanced testing was beyond the scope of this study. Innocent murmur was present in 15 patients (14%). No cardiomyopathy was detected in any child on echocardiography. This may be due to a relatively small sample size, or it may be due to the absence of addition of new genes, and hence new mutations, in the gene pool owing to the high rate of consanguinity.

Jervell Lange Nielsen Syndrome is not curable, but it can be treated. The main aim is to control arrhythmias with beta blockers or prevent them with ICD (Implantable cardioverter defibrillator) implantation.¹⁹ Care must be taken to avoid situations that precipitate a syncopal attack. Drugs that prolong QT interval should not be prescribed so as to prevent arrhythmias like Torsade de Pointe. However, these precautions are only possible if the person and his treating physician are aware of his/her condition.

In light of all these findings, we agree with Siem *et al*²⁰ that any deaf child with fainting spells or a

family history of sudden cardiac death, must be evaluated, at least once, with 12-lead ECG. Deafness by itself has a marked impact on the development of a child and a cardiac defect may adversely affect it further by limiting the physical activity of the child.

LIMITATIONS OF STUDY

- Our study involved a relatively small number of children, and the bigger picture may, although not necessarily, differ.
- Stress test was not performed. Hence, some children with stress induced syncope may have been overlooked.
- Molecular study was not carried out and further differentiation between the types of LQTS is not possible. Molecular screening may have implications in management.

CONCLUSION

Jervell Lange Nielsen Syndrome is highly prevalent in our deaf-mute children, possibly due to the high rate of consanguinity, but unfortunately these children remain undiagnosed and untreated. We hope to create awareness among the health care professionals *and* the authorities that handle special education centres to this potentially fatal disease, so that timely treatment can be initiated. A nationwide survey be conducted to determine the exact magnitude of this fatal disease among this special group of children. By doing so, we may be able to improve the quality of care provided not only to the deaf-mute children in our country, but also to other countries like us.

REFERENCES

1. Jervell A, Lange-Nielsen F. Congenital deaf-mutism, functional heart disease with prolongation of the QT interval and sudden death. *Am Heart J* 1957;54:59-68
2. James TN. Congenital deafness and cardiac arrhythmias. *Am J Cardiol* 1967;19:627-30
3. Morita H, Wu J, Zipes DP. The QT syndromes: long and short. *Lancet* 2008;372:750-63
4. Pakistan Demographics Profile. Available at: http://www.indexmundi.com/pakistan/demographics_profile.html
5. Sajjad M, Khattak AA, Bunn JE, Mackenzie I. Causes of childhood deafness in Pukhtoonkwa Province of Pakistan and the role of consanguinity. *J Laryngol Otol* 2008;122:1057-63.
6. Bazett HC. An analysis of the time-relations of the electrocardiogram. *Heart* 1920;7:353-370
7. Schwartz PJ, Moss AJ, Vincent GM, Crampton RS: Diagnostic criteria for the long QT syndrome. An update. *Circulation* 1993;88:782-784
8. Dhingra PL. Hearing loss. In: *Diseases of Ear, Nose and Throat*. New Delhi: Elsevier; 2005:38-51.
9. Fraser GR, Froggatt P, James TN. Congenital deafness associated with electrocardiographic abnormalities, fainting attacks and sudden death: a recessive syndrome. *QJ Med* 1964;33:361-85.
10. Sanchez-Cascos A, Sanchez- Harguindey L, DeRabago P. Cardio-auditory syndrome; cardiac and genetic study of 511 deaf-mute children. *Br Heart J* 1969;31:26-30.
11. Jay FE, Olley PM, Partington MW, Kavety VB, Ahmad G. Surdo-cardiac syndrome: Incidence among children in schools for the deaf. *Can Med Assoc J* 1971;105:718-20.

12. Ocal B, Imamoglu A, Atalay S, Ercan Tutar H. Prevalence of idiopathic long QT syndrome in children with congenital deafness. *Pediatr Cardiol* 1997;18:401–5.
13. Sopontammarak S, Khongphatthanayothin A, Sa-Nguanchua P. Prevalence of idiopathic long QT syndrome in congenital sensori-neural hearing loss students of Songkhla School for the Deaf. *J Med Assoc Thai* 2003;86:1149–55.
14. Yuen LK, Lam CW, Fong NC, Tang PM, Shek CC, Chan YW, *et al.* Jervell-Lange Nielsen syndrome in a Pakistani family. *Hong Kong Med J* 2004;10:351–4.
15. Csanády M, Hogue M, Forster T. Hypertrophic cardiomyopathy associated with congenital deaf-mutism. *Eur Heart J* 1987;8(5):528–34.
16. Mohiddin SA, Ahmed ZM, Griffith AJ, Tripodi D, Friedman TB, Fananapazir L, *et al.* Novel association of hypertrophic cardiomyopathy, sensorineural deafness, and a mutation in unconventional myosin VI (MYO6). *J Med Genet* 2004;41:309–14.
17. Schönberger J, Levy H, Grünig E, Sangwatanaroj S, Fatkin D, MacRae C, *et al.* Dilated Cardiomyopathy and Sensorineural Hearing Loss: A Heritable Syndrome That Maps to 6q23–24. *Circulation* 2000;101:1812–8.
18. Uçar T, Tutar E, Tekin M, Atalay S. Heart rate variability in children with congenital sensorineural deafness. *Turk J Pediatr* 2010;52(2):173–8.
19. Priori SG, Napolitano C, Schwartz PJ. Association of long QT syndrome loci and cardiac events among patients treated with beta-blockers. *JAMA* 2004;292:1341–4.
20. Siem G, Früh A, Leren TP, Heimdal K, Teig E, Harris S. Jervell and Lange-Nielsen syndrome in Norwegian children: aspects around cochlear implantation, hearing, and balance. *Ear Hear* 2008;29(2):261–9.

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