JERVELL AND LANGE-NIELSEN SYNDROME IN DEAF SCHOOL CHILDREN POPULATION

Huma Farrukh[1], Arshad Khushdil[2], Farrukh Saleem[3], Azra Ehsan[4]

ABSTRACT

Objective: *To identify the patients of Jervell and Lange-Nielsen syndrome (JLNS) amongst congenitally deaf children.*

Methodology: *This was a cross-sectional study, conducted at Hamza Foundation Academy for the Deaf, and Combined Military Hospital Lahore over a period of 4 months from February to May 2012. A total of 379 children with congenital sensorineural hearing loss were included in this study. Echocardiographs of all children (ages 4-18 years) were obtained. The corrected QT (QTc) intervals of all 379 ECGs were calculated using the Bazett's formula. Using the Schwartz's criteria, patients with long QTc intervals were further evaluated for Jervell and Lange-Nielsen Syndrome.*

Results: *Out of 379 children, 84 (22.1%) were found to have QTc intervals equal to or longer than 0.44 seconds. As per Schwartz's criteria, 31 (36.9%) out of 84 children with Long QTc (8.17% in sample population), scored high points (4.0 to 6.0), proving presence of JLNS.*

Conclusion: *A sizable proportion of congenitally deaf children had Jervell and Lange-Nielsen Syndrome in our study.*

Key Words: *Long QT interval, Jervell and Lange-Nielsen Syndrome (JLNS), Congenital deafness, Electrocardiographs.*

This article may be cited as: Farrukh H, Khushdil A, Saleem F, Ehsan A. Jervell and Lange-Nielsen syndrome in deaf school children population. J Postgrad Med Inst 2013; 27(3):274-9.

INTRODUCTION

Jervell and Lange-Nielsen Syndrome (JLNS) is a rare condition that causes bilateral hearing loss from birth and a disruption of the normal heart's rhythm (arrhythmia). It is a sub-variant of long QT syndrome, which is a heart condition that causes cardiac muscle to take longer than usual to recharge between beats characterized by prolonged QT interval on an electrocardiograph (ECG) and associated with a high risk for syncope, fits and sudden death[1].

[1,2,4] Department of Paediatrics, Combine Militry Hospital, Lahore - Pakistan.

[3] Department of Psychiatry, Combine Militry Hospital, Lahore - Pakistan.

Address for Correspondence:
Dr. Arshad Khushdil
Department of Paediatrics, Combine Militry Hospital, Lahore - Pakistan.
E-mail: drarshad104589@yahoo.com

Date Received: November 27, 2012
Date Revised: May 01, 2013
Date Accepted: May 21, 2013

Jervell and Lange-Nielsen, for the first time in 1957, described four siblings who had a combination of congenital deafness and long QT intervals on ECG, who otherwise seemed to be quite healthy but suffered recurrent attacks of fainting, often provoked by exercise or fear. Three of the 4 children suddenly died at the ages of 4, 5 and 9 years[1].

The prevalence of Jervell and Lange-Nielsen syndrome in deaf population has been investigated in different studies. It is shown that Norway has an unusually high prevalence of at least one in 200,000 total population[2]. In 10 different studies, 6557 children had been screened who were congenitally and bilaterally deaf, and studies showed that the prevalence was 0.21% with a range of 0 - 0.43%[3]. The underlying genetic causes of such prolonged QT interval syndromes are heterogeneous, with at least seven genes responsible for the clinical syndromes[4]. In another study, it was said that genetic pathology involved in causing JLNS is the mutation in the genes for potassium channel, KCNQ1 or KCNE1. Both the mutations can be congenital or one congenital and the other one de novo[5]. It is an inherited disorder of heart and hearing and the pattern

of inheritance is autosomal recessive, which means both copies of the gene in each cell have mutations.

JLNS is predominantly detected during early childhood with onset usually by the age of three years; however, onset by the age of 30 years[6] (without deafness) and the age of 61 years[7] (with deafness) have been reported. The aim of this present study was to know the frequency of this syndrome among a selected sample of deaf school children with prolong QT interval.

METHODOLOGY

This cross sectional study was conducted among 379 children who were all having bilateral congenital deafness at the Hamza Foundation Academy for the Deaf and Combined Military Hospital, Lahore, Pakistan from February 2012 to May 2012. None of the child in the school has acquired deafness and all of the children were already evaluated by an Otolaryngologist. Only those children are given admission in foundation who have severe to profound hearing loss. Records of pure tone audiogram of all children were examined. A preformed questionnaire was employed and information about age, class, symptoms, associated findings and family history were sought.

Rhythm strip ECGs were recorded with an electrocardiographic recorder (New tech ECG 1102) at a paper speed of 25 mm/s. QT intervals were manually calculated from the first deflection of the QRS complex to the point of T wave offset, defined by return of the end of T wave to the isoelectric T-P interval baseline. If the end of the T wave could not be determined correctly, the lead was excluded. Corrected QT interval was calculated (QTc) according to Bazett's formula[8]. The longest QTc interval found on a 12 lead ECG was recorded. The average heart rate was taken to determine the RR intervals because of sinus arrhythmia. Bundle branch blocks or arrhythmias were not found in any of the patients.

Children who had QTc intervals longer than 440 ms were further evaluated. Echocardiography, exercise testing and 24 hour Holter monitoring were performed in these children. Echocardiography was used to assess left ventricular function and any structural lesions. The exercise test was performed as a symptom-limited treadmill effort test. Heart rate, blood pressure, and QTc interval were determined at rest, at the maximal effort, and at the first and third minute of recovery period. Twenty-four hour ambulatory Holter monitoring was evaluated for arrhythmias, heart rate, and T wave configuration. ECG examination of family members was also performed for determination of QTc interval. All available data were evaluated according to original criteria (Table 1) and Schwartz criteria[9] (Table 2). Statistical analysis was done using SPSS 16.0.

RESULTS

Our study included total 379 children, that were congenitally deaf ranging from severe to profound sensorineural hearing loss bilaterally. Out of total, 201 (53.0%) were male and 178 (46.9%) were female. All children were divided in different age groups as shown in figure 1 with mean age of 11 ± 3.76 years (range 4 to 18 years).

In our study, out of 379, 84 (22.1%) were diagnosed to have long QTc interval, and of them 53 (63.0%) were male and 31 (36.9%) were female. QTc intervals were found to be between 290 ms and 590 ms, and heart rates between 62 and 120 bpm (78.04±5.9 bpm). Thirty one (8.17%) out of 379 had definite diagnostic criteria for LQTS according to Schwartz criteria and 17 (54.8%) of them were male and 14 (45.2%) were female.

Table 3 shows cross tabulation of gender and age.

Table 1: Original criteria*

Major Criteria	Prolonged QT interval (QTc>440ms)
	Stress induced syncope
	Family members with LQTS
Minor Criteria	Congenital deafness
	Episodes of T wave alternans
	Slow heart rate
	Abnormal ventricular repolarization

*The diagnosis of LQTS is made in the presence of two major criteria or one major and two minor criteria.

Table 2: Schwartz criteria[9]

ECG FINDINGS	
Qtc > 470 ms	3
460-470 ms	2
450 ms	1
Torsade de points	2
T wave alternans	1
Notched T wave in 3 leads	1
Low heart rate for age	0.5
CLINICAL HISTORY	
Syncope with stress	2
Without stress	1
Congenital deafness	0.5
FAMILY HISTORY	
Family members with definite LQTS	1
Un explained sudden cardiac death	0.5
SCORING	
<1 = low probability of LQTS	
2-3 = intermediate probability of LQTS	
> 4= definite probability of LQTS	

Figure 1: Frequency of children in different age groups

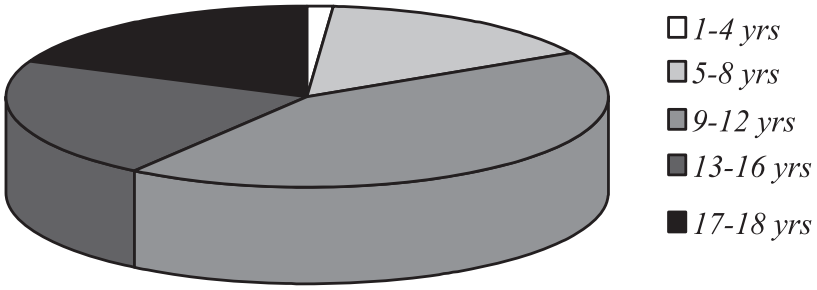

Table 3: Cross tabulation of age and gender

Age (years)	**Gender**		**Total**
	Male	**Female**	
1-4	03	0	03
5-8	44	30	74
9-12	74	63	137
13-16	51	38	89
17-18	29	47	76
Total	201	178	379

Table 4: Qtc interval frequencies among deaf children

QTc interval	Frequency	Percent
less than 0.44	295	77.8
between 0.44 - 0.47	59	15.6
more than 0.47	25	6.6
Total	379	100.0

Table 5: Evaluation of children with LQTS

Particular finding	Frequency of children with particular finding	% of children with particular finding
Children Fulfilling Schwartz criteria	31	36.9
Syncope attack	5	5.95
Sudden death of father b/t age 35-45	2	2.38
Ventricular septal defect	1	1.19

Our study shows random prevalence of JLNS among different age groups. Electrocardiogram of all 264 children (age range 4-18 years) were recorded and found out that there was no abnormal ECG finding, characteristic of the syndrome, such as T wave configuration changes, Bundle branch blocks or arrhythmias were not found in any of the patients.

QTc interval longer than 440 ms were found in 84 of the 379 patients (22.1%) detail of which is shown in table 4.

History of cousin marriage was present in all the 31 patients in the sample population fulfilling the definitive diagnostic criteria for JLNS. ECGs of the immediate relatives revealed that brothers of 5 children and sisters of 6 children had long QT intervals on ECG. Only two among them fulfilled the diagnostic criteria. Sixty nine children out of 379 had family history of congenital deafness.

Further analysis of these 84 children with QTc interval > 440 showed following details in the table 5.

DISCUSSION

In our study we found 31 cases (8.17%) out of total 379, definitely have LQTS according to Schwartz criteria[10]. All children with a prolonged QT interval do not have the LQTS and therefore are not at risk for sudden death, however it is very difficult to predict which of them have this syndrome and will experience sudden cardiac death. In a study of 3,015 LQTS children, the cumulative probability of a first life threatening cardiac event from age 1 to 12 years was 5% in boys compared with only 1% among girls[11] whereas in the age range of 12 to 20 years, Hobbs et al[12] showed that there is no significant gender difference. Hearing loss in JLNS may be treated successfully with cochlear implantation (CI), an intervention that does not interfere with bipolar pacemakers. To date, the cumulative published experience includes approximately 20 individuals with JLNS who have received cochlear implantation[10].

A study conducted in 1976 showed that the patients suffering from this disorder are apparently healthy and asymptomatic except for episodes which may include either : (a) transient episodes of palpitations, numbness, or angina type of chest pain without loss of consciousness; (b) sudden loss of consciousness usually associated with exertion or emotional stress; or (c) sudden death[13]. In our study, Five of the patients with JLNS had non-stress induced syncope attacks. The clinical diagnosis of JLNS is definitively established in individuals with all of the following as shown in a study: (a) Congenital sensorineural deafness; (b) Long QT interval, often manifest as syncope, most often elicited by emotion or exercise; (c) Presence of two disease-causing mutations in either KCNQ1 or KCNE1[14].

However, some carriers of a KCNQ1 or KCNE1 mutation have signs and symptoms affecting the heart, but their hearing is usually normal[15]. While according to another study, some patients with Jervell and Lange-Nielsen Syndrome can have only hearing defect and no cardiac abnormality[16]. In our study, all cases were congenitally deaf with only 22.1% showing cardiac problems.

Prevalence of JLNS varies, depending on the population group studied. In a study of 350 children with congenital deafness in Turkey, one in 175 had JLNS[17] and the first study done in Pakistan previously showed the incidence to be 24.6% in a sample of 114 congenitally deaf children[18]. This syndrome is more common in cultures in which consanguineous marriages are common. Most of the children attending the school of our study were of consanguineous marriage. As JLNS is an autosomal recessive disease, the accumulation of genetic mutations in inter-family marriages is understandable. In another study family history for deafness was positive in 59 (50.8 %) patients out of a sample of 116, and consanguineous marriage was present in parents of 50 children (43.1 %) in the same sample. Qtc interval was prolonged in 7.7% of the sample population[19]. One study reviewed 46 patients presenting between the years 1957 and 1991and found that 17 of these 46 patients (37%) had consanguineous parents[20] comparable to our study where all the children were of the parents with cousin marriage.

CONCLUSION

JLNS is a rare disorder with highly variable spectrum of the disease. On the basis of our study, we recommend to perform an ECG at least once in every deaf child especially in our social setup where there is a high prevalence of consanguineous marriages. We hope to create awareness among the health care professionals that handle special education centers to this potentially fatal disease, so that timely management can be started.

REFERENCES

1. Jervell A, Lange-Nielsen F. Congenital deal-mutism, functional heart disease with prolongation of the Q-T interval and sudden death. Am Heart J 1957;54:59-68.

2. Tranebjaerg L, Bathen J, Tyson J, Bitner-Glindzicz M. Jervell and Lange-Nielsen syndrome: a norwegian perspective. Am J Med Genet 1999;89:137-46.

3. Schwartz PJ, Periti M, Malliani A. The long QT syndrome. Am Heart J 1975;89:378-90.

4. Towben JA, Vatta M. Molecular biology and the prolonged QT syndromes. Am J Med 2001;110:385-98.

5. Schwartz PJ, Spazzolini C, Crotti L, Bathen J, Amlie JP, Timothy K, et al. The Jervell and Lange-Nielsen syndrome: natural history, molecular basis, and clinical outcome. Circulation 2006;113:783-90.

6. Yankowitz F, Preston JB, Abildskov JA. Functional distribution of right and left stellate innervations to the ventricles: production of neurogenic electrocardiographic changes by unilateral alteration of sympathetic tone. Circ Res1966;18:416-28.

7. Gale GE, Bosman CK, Tucker RBK, Barlow JB. Hereditary prolongation of Q-T interval. Br Heart J 1970;32:505.

8. Jackman WM, Friday KJ, Anderson JL, Aliot EM, Clark M, Lazzara R. The long QT syndromes: a critical review, new clinical observations and a unifying hypothesis. Prog Cardiovasc Dis 1988;31:115-72.

9. Schwartz PJ. Idiopathic long QT syndrome: progress and questions. Am Heart J 1985;2:399-411.

10. Tranebjaerg L, Samson RA, Green GE. Jervell and Lange-Nielsen syndrome. In: Pagon RA, Bird TD, Dolan CR, Stephens K, Adam MP, editors. GeneReviews™. Seattle (WA): University of Washington, Seattle; 1993.

11. Goldenberg I, Moss AJ, Peterson DR, McNitt S, Zareba W, Andrews ML, et al. Risk factors for aborted cardiac arrest and sudden cardiac death in children with the congenital long-QT syndrome. Circulation 2008;117:2184-91.

12. Hobbs JB, Peterson DR, Moss AJ, McNitt S, Zareba W, Goldenberg I, et al. Risk of aborted cardiac arrest or sudden cardiac death during adolescence in the long-QT syndrome. JAMA 2006;296:1249-54.

13. Moothart RW, Pryor R, Hawley RL, Clifford NJ, Blount SG Jr. The heritable syndrome of prolonged Q-T interval, syncope, and sudden death. Chest 1976;70:263-6.

14. Priori SG, Barhanin J, Hauer RN, Haverkamp W, Jongsma HJ, Kleber AG, et al. Genetic and molecular basis of cardiac arrhythmias: impact on clinical management parts I and II. Circulation 1999;99:518-28.

15. Towbin JA, Wang Z, Li H. Genotype and severity of long QT syndrome. Drug Metab Dispos 2001;29:574-9.

16. Cusimano F, Martines E, Rizzo C. The Jervell

and Lange-Nielsen syndrome. Int J Pediatr Otorhinolaryngol 1991;22:49-58.

17. 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.

18. Anwer A, Shakeel A, Ikram MH, Zaman SM. Jervell and Lange-Nielsen syndrome: prevalence in deaf children and its significance in relation to cousin marriage. Professional Med J 2011;18:638-43.

19. Kocak G, Kara CO, Karaduman D, Kaftan A. Jervell and Lange-Nielsen syndrome in a deaf children population. Internet J Cordiol 2001;2:10.

20. Priori SG, Napolitano C, Schwartz PJ. Low penetrance in the long QT syndrome. Circulation 1999;99:529-33.

CONTRIBUTORS

HF conceived the idea, planned and wrote the manuscript of the study. AK, FS & AE assisted in the interpretation of data and gave input in the write-up of the manuscript. All the authors contributed significantly to the research that resulted in the submitted manuscript.