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Original Article

Cochlear Implantation in Congenital Long–QT Syndrome: A Comprehensive Study

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OBJECTIVES: Jervell and Lange–Nielsen syndrome is a rare autosomal recessive disease characterized by congenital sensorineural deafness and significant QT interval prolongation. Aims were to study the prevalence of long QT in congenital hearing loss, complications encountered, outcomes by Categories of auditory Performance (CAP) scores and Speech Intelligibility Rating (SIR) scores and to create an algorithm with precautions to be followed in Long QT children.

MATERIALS and METHODS: Study was done at Auditory implant center at a tertiary referral care ENT hospital which includes 41 paediatric patients who were diagnosed to have Long QT during preoperative assessment and underwent cochlear implantation. A standard Protocol was followed in all candidates which includes comprehensive targeted history and investigations, preoperative and intraoperative precautions, and the findings were recorded.

RESULTS: Preoperative prophylactic Beta blockers, avoiding sympathetic stimulation and drugs prolonging QT interval with rational use of Magnesium Sulphate and standby of defibrillator were the standard precautions practised. Fatal Arrhythmias were encountered intra-operatively in five patients which was treated with cardiac pacing. Cardiac monitoring was done intraoperatively and during switch-on. Significant improvement in CAP and SIR scores were observed at 3 and 6 months when compared to their base line values.

CONCLUSION: With special attention to preoperative evaluation, appropriate intraoperative precautions and monitoring, judicious surgical planning and post surgical follow-up cochlear implantation may be performed safely in patients with JLNS with good postoperative results allowing for improved audition.

KEYWORDS: Cochlear implantation, sensorineural hearing loss, jervell and lange-nielsen syndrome, long QT syndrome

INTRODUCTION

The prevalence of congenital hearing loss worldwide is 3 out of every 1000 live births[1]. Hearing loss is often referred to as a double tragedy because a congenitally hearing-challenged child cannot experience normal speech and language development, and hence is deprived of normal communication skills. The consequences of hearing loss in children include significant educational and occupational disadvantage, social isolation, and stigmatization. Cochlear implantation (CI) is a well-recognized treatment for pediatric patients who had severe to profound sensorineural hearing loss for several years [2]. Children who undergo early implantation and regular postoperative habilitation after CI have speech and language acquisition comparable to the one of their normal peers.

Hereditary hearing loss can be classified as syndromic and nonsyndromic [3]. Hearing impairment may be a part of a syndrome associated with other systemic disturbances, in which case, it is termed syndromic hearing impairment. Inherited hearing impairment in the absence of other systemic involvement is termed as nonsyndromic. More than 400 forms of syndromic hearing loss have been characterized [4], of which some of these syndromes offer significant anesthetic challenges in children requiring CI.

The two classical types of long QT syndrome (LQTS) include the Romano–Ward syndrome with a prevalence of 1:2,000 and 1:5,000 individuals who present only with cardiac conduction abnormalities [5], and Jervell and Lange-Nielsen syndrome (JLNS), with an estimated prevalence between 1:1,000,000 and 1:4,000,000, who present with congenital bilateral hearing loss in addition to a prolonged QT interval revealed on electrocardiogram (ECG) [6]. The other rare forms of extra-cardiac LQTS include Andersen–Taw-

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il syndrome, associated with bone abnormalities and intermittent weakness, and Timothy syndrome, associated with autism spectrum disorder [7].

Freidrich Ludwig Meissner is the first person to describe JLNS in 1856, but the first complete elaboration of this syndrome was given by Anton Jervell and Fred Lange-Nielsen in 1957 [6]. The syndrome is characterized by the dysfunction of the sodium and potassium ion channels with QT prolongation, morphological change in the T waves, and torsades de pointes type of ventricular arrhythmia [8].

Patients with LQTS pose significant anesthetic challenge, and undiagnosed patients are at a very high risk of cardiac complications during surgery. Stringent criteria have to be formulated in the preoperative evaluation of a congenitally hearing-challenged child, and a multidisplinary team approach involving the pediatrician and cardiologist is mandatory to diagnose this syndrome. Routine preoperative ECG is essential to identify this syndrome. Once the diagnosis is established through appropriate preoperative investigations, special precautions have to be initiated, and the patient has to be under constant surveillance during CI and during subsequent switch-on to prevent complications [8].

Aims and Objectives

1. To study the prevalence of LQTS among children with congenital profound hearing loss.
2. To study the intraoperative and postoperative complications in LQTS.
3. To establish an appropriate management algorithm in children with LQTS.
4. To study the outcomes in children with JLN after CI.

Inclusion Criteria: All children aged <6 years with bilateral profound hearing loss and corrected QT >440ms in preoperative ECG.

Exclusion criteria: Nonsyndromic children and children with syndromes other than JLN.

Study Method

This is a retrospective, prospective observational study of 41 pediatric patients diagnosed with long QT during preoperative assessment, who underwent CI at the Department of Auditory Implantation in our hospital from May 2014 to May 2018.

All children <6 years of age presenting with hearing loss since birth and delayed speech and language development to our cochlear implant clinic were to be evaluated using a standard protocol, which included essential ENT (Ear, nose and throat) evaluation, audiological test battery, computed tomography, and magnetic resonance imaging of the temporal bone and cochlea, blood investigations, ECG, cardiac, and ophthalmology opinions. A comprehensive targeted history, especially family history of sudden death, was to be taken in all patients and also assessed from previous records. Established preoperative and intra operative precautions undertaken in all cases were recorded.

Postoperatively, the device was switched on after 3 weeks following intensive auditory verbal habilitation therapy. Outcomes are evaluated by categories of auditory performance (CAP) and speech intelligibility rating (SIR) scores at 3 and 6 months postoperatively. Auditory performance is measured using the CAP scores, which range from 0 to 7, and spontaneous speech was quantified using SIR scores, which range from 1 to 5 [9].

Statistical Analysis

The numerical data of the cohort of 41 patients were analyzed using appropriate statistical tests using Statistical Package for the Social Sciences (SPSS) version 23.0 (IBM Corp.; Armonk, NY, USA). Comparative analysis of CAP and SIR scores of an individual patient at 3rd and 6th monthly follow-up was done using the analysis of variance (ANOVA) F test.

The Operative Procedure and Management Protocol

The surgery is carried out under general anesthesia. Appropriate preoperative counselling to parents regarding potential cardiac risk during or after surgery should be explained. The transmastoid route is the most preferred of CI [10].

The postaural incision is made, and cortical mastoidectomy and posterior tympanotomy are done. A bed for the receiver stimulator is made, and electrode insertion is completed through the round window or cochleostomy. Intraoperative neural response telemetry is done to confirm the correct electrode position, and postaural wound is closed. Patient is discharged after 1 to 2 days.

RESULTS

In our retro-prospective study among 831 cochlear implantees, 41 children were diagnosed with long QT preoperatively through a standard protocol (Table 1), which includes a comprehensive targeted history, and investigations which include audiological evaluation, ECG, and cardiac opinion. Thus the prevalence of patients with long QT who presented with bilateral profound hearing loss for CI in the present study is 4.98% (n=41) (Figure 1). Also, consanguineous marriage was found in 51.2% (n=21), favoring increased prevalence of long QT in consanguineous marriage.

Among 41 study participants, 17% (n=7) members had borderline QT prolongation (corrected QT 440–460 ms), 68.2% (n=28) had moderate QT prolongation (corrected QT 460–490 ms), and 14.6% had severe QT prolongation (corrected QT >490 ms) (Figure 2). Cardiac monitoring was done intraoperatively in all patients with LQTS (Figure 3). Children with QTc >480 ms were started on prophylactic beta-blockers preoperatively [metoprolol (Prolomet XL, Sun pharmaceutical, Mumbai, India)] and magnesium sulphate infusion (Magnesium Sulphate, Vulcan Laboratories, West Bengal, India) (if required) during the surgery. Derangement of electrolyte levels predisposed to arrhythmias in LQTS and thus correction of magnesium and calcium levels are done preoperatively. Since stress is a documented factor that can trigger LQTS, anxiolytic premedication with triclofos sodium syrup (Pedicloryl, Dr Reddys Laboratories, Hyderabad, India) is given to all patients with LQTS preoperatively as a standard protocol.

A standardized protocol by avoiding sympathetic stimulation and drugs prolonging the QT interval including inhalation anesthetics (Figure 4) and standby of defibrillator (HeartStart MRx, Philips, Amsterdam, Netherlands) (Figure 5) were the standard precautions practiced in the present study. Defibrillator patches were applied before

Table 1. Algorithm of Management in Children with Long QT during Cochlear Implantation

Preoperative	Avoiding drugs that further prolong the QT interval
	Anxiolytic premedication (triclofos sodium syrup) given
	Correction of QT with therapeutic beta-blockers (metaprolol/amiodarone)
	If symptomatic, pacing done by cardiologist
	If pacemaker/ICD in situ, settings checked
	Correction of serum electrolyte levels (preoperative serum magnesium and calcium levels are assessed)
Perioperative	Preinduction monitoring of 12 lead ECG
	Propofol for induction (inhalational drugs avoided)
	Maintenance with propofol, intermittent fentanyl, atracurium, and oxygen
	Avoidance of QT prolonging drugs (inhalational anesthetics, adrenaline, ephedrine, dopamine, dobutamine, domperidone, ondansetron)
	Avoidance of electrocautery
	Avoiding reversal (neostigmine) and allowing for spontaneous recovery
	Maintain normoxia, normocarbia, normothermia, and normoglycaemia
	Maintain normal serum Postassium, Calcium, and Magnesium levels
	Minimizing sympathetic stimulation by limiting usage of adrenaline with topical Local Anaesthesia
	Availability of magnesium sulphate, antiarrhythmic agents (esmolol), and defibrillator–pacer in the operation theatre
	Temporary pacing done if needed (internal or external) by cardiologist standby
Postoperative	Continuous ECG monitoring done for 12 hours
	Demand pacing done if needed and restarted with beta-blocker therapy
	Intensive care unit monitoring done
	Good analgesia
	Avoiding drugs that further prolong the QT interval (macrolides and quinolones antibiotics, anti histamines such as ebastine, diphenhydramine)

ECG: Electrocardiogram; ICD: Implantable cardioverter defibrillators

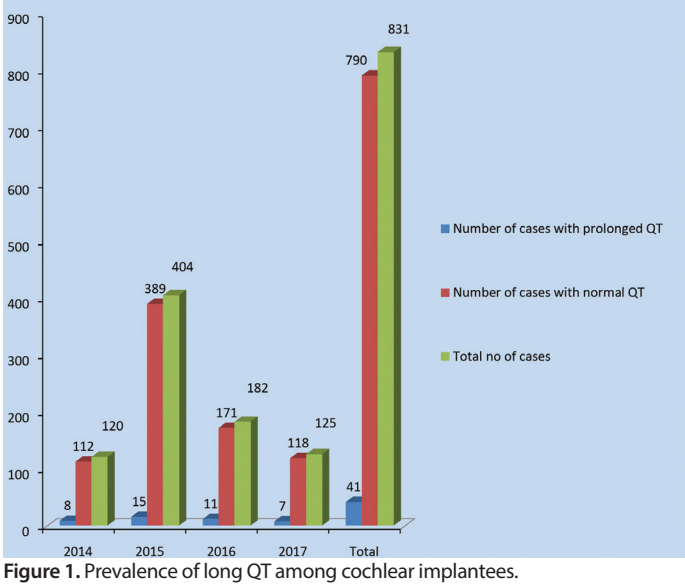

Figure 1. Prevalence of long QT among cochlear implantees.

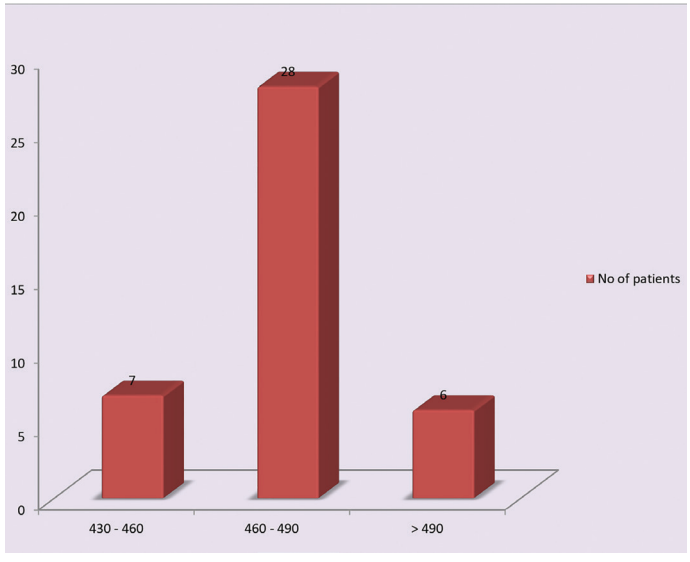

Figure 2. Distribution of QT interval.

the procedure to avoid compromising the patient safety. A detailed discussion was conducted with the cardiologist both preoperatively and intraoperatively about pacemaker and implantable cardioverter defibrillators (ICD) settings if present, and the recommendations were managed accordingly. Since the use of electrocautery predispose to potential arrhythmias and will also interfere with the functioning of pacemaker, use of cautery is avoided as much as possible. Propofol (Neorof, Neon Laboratories, Mumbai, India) with the intermittent use of fentanyl (Fent, Neon Laboratories, Mumbai, India) is applied for the maintenance of anesthesia. Spontaneous recovery from anes-

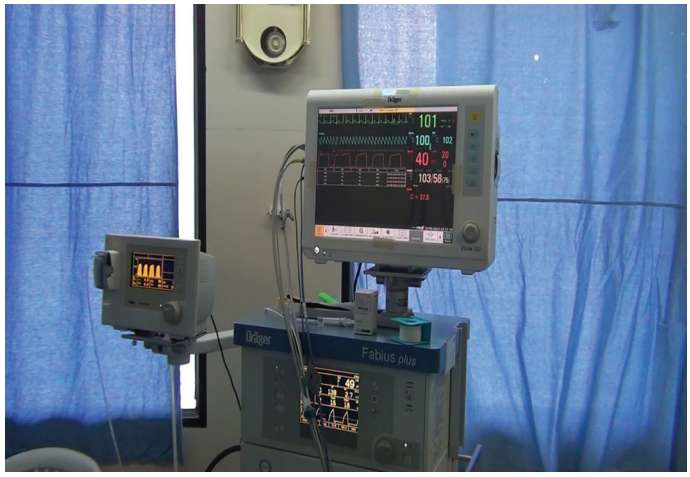

Figure 3. Intraoperative cardiac monitoring in cochlear implantation in long-QT syndrome.

Figure 4. Cardiac defibrillator kept standby for all cases intraoperatively in cochlear implantation for long-QT syndrome.

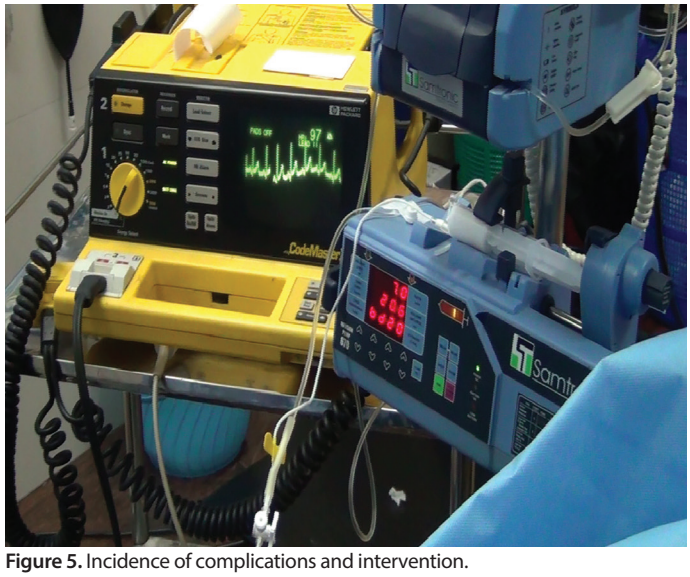

Figure 5. Incidence of complications and intervention.

thesia is practiced in the present study, and all reversal agents, such as neostigmine, are avoided. Fatal arrhythmias and bradycardia were

Table 2. Potential Complications During Switch-On (ECG monitoring was done in all cases during switch-on)

Fainting episodes	Yes/no
Seizure episode	Yes/no
Lightheaded or dizzy	Yes/no
Breathlessness	Yes/no
Fatal arrhythmias	Yes/no

ECG: Electrocardiogram

Table 3. Comparison of CAP and SIR scores at 3 and 6 months after cochlear implantation among children with long QT. Statistical significance in the improvement of CAP and SIR scores at 3 and 6 months after cochlear implantation among children with long QT

	ANOVA F value	p
CAP Baseline	73.928	0.000**
CAP 3 Months		
CAP 6 Months		
SIR Baseline	7.883	0.001**
SIR 3 Months		
SIR 6 Months		

** Significant at 1% level
CAP: Categories of auditory performance; SIR: Speech intelligibility rating

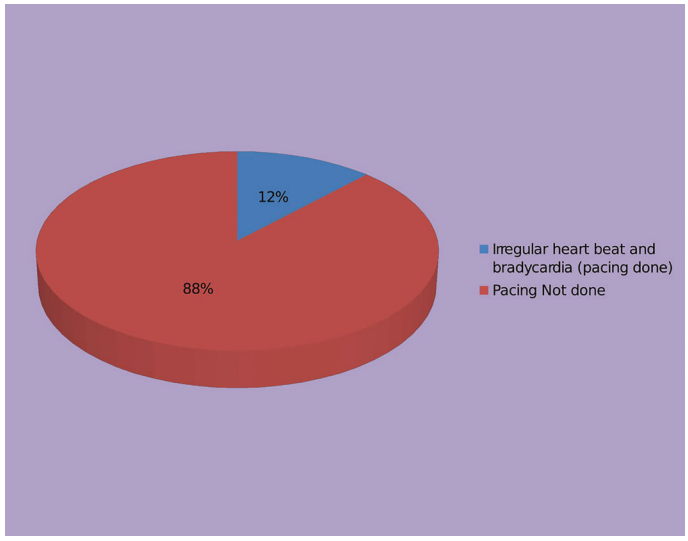

Figure 6. Incidence of complications and intervention.

encountered intraoperatively during the CI in five patients (12.2%) treated with cardiac pacing (Figure 6).

Cardiac monitoring was done in all cases of long QT during the switch-on of the cochlear implant device (Table 2). As adequate safety measures were carried out during the switch-on, no adverse events were reported in the present study.

Our study also showed a significant improvement in CAP (p=0.000 and ANOVA F=73.928) and SIR (p=0.001 and ANOVA F=7.883) scores at 3 and 6 months postoperatively when compared to the base line CAP and SIR scores (Table 3). This proved that an improvement of

CAP and SIR scores at 3 and 6 months after CI among children with long QT was statistically significant.

DISCUSSION

Congenital deafness in children undergoing CI surgery may be associated with various syndromes, and LQTS may be one of them [11].

Jervell and Lange-Nielsen syndrome is a cardiac repolarization disorder and is associated with clinical symptoms such as dizziness, fainting, life-threatening ventricular arrhythmias, and sudden cardiac death [12].

The treatment of patients with LQTS presents a challenge. Thus, for effective and safe management of these patients, it is crucial to provide a treatment environment that is as stress free as possible. Among the considerations in planning surgical procedures, attention must be given to preoperative evaluation, intraoperative precautions and monitoring, and postsurgical follow-up. Perhaps an even greater treatment challenge is for those individuals having undiagnosed LQTS [13].

The prevalence of patients with LQTS with bilateral profound loss in the present study is 4.98%. A similar study done in Iran by Eftekharian and Mahani showed that the prevalence of LQTS was 0.79%, which is in the range with literature reports, ranging between 0% and 2.6% [14]. The cause of increased prevalence of children with long QT in the present study was attributed to increased prevalence of consanguineous marriage in the study group.

Genetic association study done by G. Michael Vincent revealed that since LQTS is an autosomal recessive disease, it is equally present in males and females. In LQTS, both parents must be heterozygous for a mutation of either the KCNQ1 or KCNE1 genes, which usually occurs in consanguineous marriage. For normal potassium production and balance in the endolymph of the inner ear, at least one normal KCNQ1 allele is required. Thus, in children with long QT, no endolymph is formed due to non-functioning KCNQ1 gene, resulting in congenital profound deafness [15]. It was found that 51.2% children in the present study came from a consanguineous marriage, which is in compliance with the study done by Michael favoring increased prevalence of long QT in consanguineous marriage.

Yanmei et al. [16] reported that beta-blockers were the drug of choice to reduce the episodes of syncopal attack and even sudden death. Goyal et al. [17] also mentions that management of long-QT candidates consists of beta-blockers and implantable cardioverters preoperatively and defibrillators for the cardiac condition with CI for the management of deafness.

The protocol followed by Kumar et al. [18] in children with long QT with deafness includes perioperative continuation of beta blockade and avoidance of sympathetic stimulation, which may trigger ventricular arrhythmia, providing adequate premedication, perioperative analgesia, and careful use of anesthetics and other drugs to avoid QT prolongation, and ready availability of magnesium sulphate and defibrillator–pacer in case any arrhythmia occurs. Similarly, the use of prophylactic beta-blockers, avoiding sympathetic stimulation and drugs prolonging QT interval and standby of defibrillator were the standard precautions practiced in the present study.

Eftekharian and Mahani emphasized that since the auditory stimuli are reported as a specific trigger, it is essential that continuous monitoring of the cardiac status must be done during the device switch-on. They also reported no cardiac adverse event during the switch-on, and proved that CI is a safe procedure that can be done in candidates with LQTS, provided that adequate precautions are taken accordingly [14]. Since cardiac monitoring and adequate safety measures were carried out during the switch-on, no adverse events were reported in the present study.

A study conducted by Daneshi and Ghassemi, which showed CI done in three children with LQTS, was noted to have the CAP and SIR scores of 6 and 4, respectively, at the 2-year follow-up. The authors concluded that CI is a safe procedure that can be undertaken in children with LQTS with good postoperative results [19]. The results of the present study correlate with a similar study done by Green, which showed that candidates with long QT have shown good postoperative improvement after 11 following CI and have achieved improved speech with good word comprehension, as expected for their age comparable to non-long QT cochlear implantee children [20].

As inferred from the present study, by following a comprehensive protocol (Table 1), CI is a safe procedure that can be performed in children with LQTS, and it offers significant improvement in the quality of life of these children.

CONCLUSION

The selection criteria for CI have expanded to include children with special auditory, otologic, and medical problems over the recent years.[2] The present study reflects the management of a cohort of 41 LQTS patients who underwent CI in our premier tertiary referral care ENT institute. With a prudent preoperative evaluation, careful cardiac monitoring, and precautions during anesthesia, CI can be performed in children with LQTS with excellent results in auditory performance postoperatively without any complications. Prophylactic beta-blockers, and intraoperative judicious use of magnesium sulphate and selective beta-blockers with cardiac pacing for fatal arrhythmias, significantly reduced the occurrence of adverse cardiac events in our case series. As inferred from the present study, CI is a safe procedure that can be performed in children with LQTS, and it offers significant improvement in the quality of life of these children.

Future Direction

A standardized and established protocol must be followed for children with long QT undergoing implantation. A study of this nature will add strength to the existing evidence in literature that CI is a relatively safe procedure in children with a long QT interval, and when appropriate preventive measures are undertaken, complications can be avoided. All centers that are performing CI must have an established and prudent protocol for children with long QT to avoid cardiac complication during surgery and switch-on. Genetic study in these groups of patients with long QT and consanguinity with profound hearing loss may help to take further steps in prevention.

Ethics Committee Approval: Ethics committee approval was received for this study from the Institutional Review Board of Madras ENT Research Foundation (P) Ltd and MERF-Institute of Speech and Hearing (Ref No: MERF/EC-AUG.17/03).

Informed Consent: Informed consent form was received from all the patients participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - R.A., S.M., M.K.; Design - R.A., S.M.; Supervision - M.K.; Resource - R.A., S.V.; Materials - R.A., S.M., S.V.; Data Collection and/or Processing - R.A., S.M., S.V.; Analysis and/or Interpretation - R.A., S.V.; Literature Search - R.A., S.M., S.V.; Writing - R.A., S.M., M.K.; Critical Reviews - S.M., M.K.

Conflict of Interest: The authors have no conflict of interest to declare.

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