APPENDIX I

ETHICS APPROVAL LETTER

SRI RAMACHANDRA UNIVERSITY
INSTITUTIONAL ETHICS COMMITTEE
(Declared under Section 3 of the UGC Act, 1956)
(Other than Clinical Evaluation of Drugs / Procedures / Devices / Diagnostics / Vaccines / Herbal Remedies)

Chairperson:
Dr. A. Nalini

Member Secretary:
Dr. Pankaj B. Shah

Members:
Dr. Padma Vathi R.
Dr. Nirupa
Dr. Ramesh Harigha Iyer
Dr. C. D. Narayanan
Dr. T. S. Lokeswari
Dr. Leena Dennis Joseph
Dr. Porkodi
Dr. L. V. K. S. Bhaskar
Dr. Vamsi Lavu
Mr. S. Rethiha Kumar
Mrs. Sheeba Vinod

To
Dr. S. Heramba Ganapathy
Reader
Department of SLHS
SRU.

19.06.2012

REF: IEC-NI/08/Mar/03/11
SUB: Study of association between high risk factors and hearing impairment in infants & newborns and to develop a structured modular parents counseling program.
Changed as: Association of high risk factors and hearing impairment in infants - A Hospital Based Study.
- Research Proposal - Approval - Reg.

With reference to your letter dated 7.6.12 the Ethics Committee approved the amendment.

You are advised to be familiar with ICMR guidelines on Biomedical Research in human beings and also to adhere to the Principles of good clinical practice. You are required to submit the final report on the completion of study to the Institutional Ethics Committee.

Yours Sincerely,

(DR. PANKAJ B. SHAH)

Note: Please quote IEC Reference number in all future communications.
INSTITUTIONAL ETHICS COMMITTEE (NI) Other than Clinical Evaluation of Drugs/Devices/Diagnostics/Vaccines/Herbal Remedies

Chairman:
Dr. Venkatesan

Member Secretary:
Dr. Padmavathi R

Members:
Dr. Ramesh Hari Hara Iyer
Dr. Darling Cheellathai David
Dr. Radhakumar
Dr. C. D. Narayanan
Ms. A. G. Shanthi
Mr. S. Rethinakumar - Legal Consultant
Mrs. Sheeba Vinod
Dr. T. S. Lokeshwari

To
Dr. S. Heramba Ganapathy
Associate Professor
Department of SLHS
SRU.

Dear Dr. Heramba Ganapathy,

REF: IEC-NI/08/Mar/03/11

SUB: Study of association between high risk factors and hearing impairment in infants & newborns and to develop a structured modular parents counseling program – Research Proposal - Resubmission - Reg.

Thank you for submitting the above proposal to the Institutional Ethics Committee, which was discussed in the meeting, held on 26.03.08. The Institutional Ethics Committee request you to resubmit the proposal with the following changes:

- To include a neonatologist/ Pediatrician in the study.
To include in the consent about the possibility of giving a sedative (with the dose) to the child for conducting the tests and mention the side effects of the sedative.

- Study design can be modified to a case control study design as the objective of the study to look at association of risk factors and hearing impairment and study population can be children selected from special schools. The current study design is not appropriate for the objective of the study.

- Sample size to be recalculated based on the study design

Yours Sincerely,

(DR.R.PADMAVATHI)
Member Secretary

Note: Please quote IEC Reference number in all future communication.
APPENDIX II

CONSENT FORM

Mother’s / Father’s Name: ___________________ Date: ____________

Child’s Name: ___________________ HP/OP/IP No.: ____________

Age/Sex

Address:

I have been told about the procedure of hearing testing of my child and all of my questions have been answered to my satisfaction. I have been informed that the data of the test result and the information of the medical records of my child is going to be used for the study purpose.

I have been told that in rare condition my child can sleep 2 or 3hrs longer than the required time as side effect, when sedative is administered for the purpose of testing. With the clear knowledge of above, I give consent for the hearing testing and use of this data for study purpose.

Signature:

Name:

Relationship to the Child:
## APPENDIX III

## DATA COLLECTION SHEET 1

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<th>S.No.</th>
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<th>Name:</th>
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<th>OP/PP/IP No.:</th>
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<th>Parent’s Name:</th>
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<th>ABR Results:</th>
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<th>High Risk factor noted:</th>
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<table>
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<th>History of regression of hearing loss:</th>
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<td>Sl no</td>
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FH - Family History  
IUI - In-Utero Infections  
CN - Consanguinity  
HB - Hyperbilirubinemia  
PT - Preterm  
OT - Ototoxicity  
NICU - Neonatal Intensive Care Unit  
S - Seizures  
MV - Mechanical ventilation
APPENDIX IV
PRESENTATIONS

International

“Association of acquired risk factors with hearing impairment in infants in India.”
Asia pacific symposium on cochlear implants, Hyderabad, November, 2013.

Association of hereditary risk factors with hearing loss. Heramba Ganapathy. S,
conference on updates in research ethics and research methodology, SRU, Chennai,
March, 2013.

Two papers titled
i) “Mothers views on hearing loss and NHS in India” and
ii) “Hearing loss and Newborn screening in India – Opinions of grandmothers of
newborn children”

conference on speech, language and hearing, Christchurch, NewZealand, January,
2011.
National


Invited Lecture

APPENDIX V

PUBLICATION

Original Article

Association of family history and consanguinity with permanent hearing impairment

Heramba Ganapathy Selvarajan, Ravi Kumar Arunachalam, Rajashekhar Bellur, Kalyani Mandke, Roopa Nagarajan

Department of Speech, Language and Hearing Sciences, Sri Ramachandra University, Chennai, *Department of ENT and Head and Neck Surgery, Sri Ramachandra University, Chennai, Tamil Nadu, *Manipal College of Allied Health Science, Manipal University, Manipal, *Mandke Hearing Services, Pune, India

ABSTRACT

Background: Risk factors for hearing impairment can offer important information for both the family and health-care providers regarding etiology, other associated health problems, and risk of recurrence in subsequent pregnancy. Family history and consanguinity indicates the possible involvement of genetic factors.

Objective: The aim of the study is to find the strength of association of family history and consanguinity with permanent hearing impairment in infants. Materials and Methods: A case-control study was designed on 420 infants with permanent hearing impairment and normal hearing from the year 2008 to 2012. The case control ratio was 1:1. Alternate sampling method was used in a hospital for selecting the control group. Parent interview was carried out to collect the information of family history of hearing impairment and consanguineous marriage. Results: Family history and consanguinity was seen in 18.6% and 39.5% of the hearing-impaired group. These factors were associated with hearing impairment with a high significance (odds ratio (OR) 6.6; 95% Confidence interval (CI) 2.8, 15.1; \( P = 0.0000 \) and OR: 2.7; 95% CI 1.9, 3.9; \( P = 0.0000 \)). The combination of risk factors is seen in 10% of the hearing-impaired group, whereas only 0.5% had it in the control group. Conclusion: Family history and consanguinity seems to be an important risk factor of hearing impairment both in isolation and in combination.

KEYWORDS: Consanguinity, Family history, Hearing impairment

INTRODUCTION

Data on the existence of risk factors for hearing impairment will have significant clinical relevance because they can offer important information for both the family and health-care providers about etiology, other associated health problems, and risk of recurrence in a subsequent pregnancy.\(^{11}\) Family history and consanguinity indicates the possible involvement of genetic etiology. Consanguinity is a term derived from two Latin words “con” meaning common or of the same and “sanguineus” meaning blood. It is a marriage relationship between two close relatives. At present, about 20% of world populations live in communities with a preference for consanguineous marriage,\(^{11}\) which includes South India.

More than 50% of congenital hearing impairment is genetic, most often due to autosomal recessive inheritance.\(^{13}\) And consanguinity is highly associated with autosomal recessive inheritance.\(^{14}\) It increases chances of the defective gene sharing in the off-spring, which in turn increases the chances of occurrence of hearing impairment running in the family. There are 25% and 12.5% of gene sharing in second and third degree consanguinity.\(^{15}\)

Apart from consanguinity, family history of childhood hearing impairment can directly influence the occurrence

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of hearing impairment. This particular history can guide
diagnosis and evaluate the need for additional diagnostic
tests. The first information collected for the genetic testing
is always the family history. It also helps in knowing the
pattern of inheritance of hearing impairment. The
existence of consanguinity increases the importance of family history
showing clear pattern of inheritance of hearing loss.

There are several studies in the western literature to associate
the family history with hearing impairment. In general, it
is considered as low prevalent risk factor. In India, it is
important to know the strength of association of family history
and consanguinity with hearing impairment in India. This data
will be helpful in planning national programs like “Prevention
of deafness.” Moreover, in a place like south India where
consanguinity is very high, there is scarcity of the literature.

AIM

The aim of this study was to find the strength of association
of family history and consanguinity with permanent hearing
impairment in infants.

MATERIALS AND METHODS

A case-control study was designed on 420 infants (6 month
to 2 years) with permanent hearing impairment and normal
hearing from 2008 to 2012. The cases were infants with
permanent hearing impairment and controls were normal
hearing infants. Infants with sensorineural hearing loss
were considered as permanent hearing impairment. The
case-control ratio was 1:1. Sample size was determined based
on the prevalence of risk factors as per Vohra et al. for
the power of 80%. Alternate sampling method was used in a
hospital for selecting the control group. Infants with hearing
impairment were selected from four hospitals in Chennai city
of Tamil Nadu state, India. Exclusion criteria were history of
middle ear discharge, gross developmental delay, and infants
with less than 1500 g of birth weight. Institutional Ethics
Committee of Sri Ramachandra University has given approval
for the study.

Along with the parental opinion about the hearing status,
Auditory Brainstem Response screening using Beraphone
MB11 (It is the model name and doesn’t need expansion)
was carried out for all the controls to rule out the hearing
impairment. Diagnostic ABR instruments such as Grason
Stadler Incorporation-Audera and Intelligent Hearing
System-Junior instruments were used to confirm the sensori
neural loss in hearing impairment group. Parent interview
was carried out to collect the information of family history of
childhood hearing impairment and consanguineous marriage
for both the control and hearing impairment group. Statistical
analysis of odds ratio, Chi square test, 95% confidence
interval (CI) and spearman correlation was applied to the data.

RESULTS

As shown in Figure 1, family history of childhood hearing
impairment and consanguinity were higher in the Hearing
Impairment group compared to the control group with high
statistical significance (P = 0.000). The combination of
risk factors were also significantly higher in the HI
group (P = 0.000).

As the Table 1 indicates, the risk estimate for family history
and Consanguinity was 6.5 and 3.7 with narrow CI showing
the good precision of the findings. When both the risk-factors
are combined together, the risk estimate is very high. The CI
is very large due to less number of this factor in the control
group. There was only one family in the control group for the
combined risk factor.

When the risk factors were correlated with different types
of sensori neural hearing impairment [Table 2], none were statistically significant. Family history was having
moderate correlation with bilateral severe to profound hearing
impairment. Almost 100% of infants with the combination of
family history and consanguinity had severe – profound
impairment.

Figure 2 shows the percentage of second and third degree
consanguinity in HI and control group. Both the factors
are significantly higher in the hearing impairment group
(P = 0.000).

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Family history (Odds ratio)</th>
<th>Consanguinity (Second degree)</th>
<th>Consanguinity (Third degree)</th>
<th>Combination (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall 6</td>
<td>3</td>
<td>3</td>
<td>6</td>
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<td></td>
<td>3.14</td>
<td>2.4</td>
<td>1.4</td>
<td>3.155</td>
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Confidence interval

<table>
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<tr>
<th>Table 1: Risk estimate</th>
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<tr>
<td>Risk factors</td>
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95% CI: Confidence interval

<table>
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<th>Table 2: Correlation of risk factors with permanent hearing</th>
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<tr>
<td>Spearman correlation</td>
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<tr>
<td>FH (N=39)</td>
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<tr>
<td>Correlation coefficient</td>
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<td>Sig. (2 tailed)</td>
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<tr>
<td>CN** (N=83)</td>
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<tr>
<td>Correlation coefficient</td>
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<td>Sig. (2 tailed)</td>
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<td>FH+CN (N=21)</td>
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<tr>
<td>Correlation coefficient</td>
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<tr>
<td>Sig. (2 tailed)</td>
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</table>

SNHL: Sensorineural hearing loss, FH: Family history, CN: Consanguinity
Table 1 shows that risk estimate is slightly different for second and third degree consanguinity with former having a higher risk. Both of it is having narrow CI showing the high precision of the finding.

**DISCUSSION**

The incidence of consanguinity is very high in developing countries than in developed countries. This increases the probabilities of incidence of hearing impairment. In a Saudi Arabian population survey,[43] between 45% and 47% had consanguineous marriage in first and second degree. In that same population between 60% and 37% had hereditary sensorineural hearing impairment. In a large-scale national study of Oman,[44] 70% of deaf children had consanguineous parents. 61.4% of consanguinity was found in hearing impaired population in a recent study in Iran.[12] They also found 77.1% of persons who had more than one handicapped child in the family had consanguineous marriage. Prevalence of consanguinity seems to be slightly less in Indian population. In a South Indian school based study,[13] 41% of hearing impaired students had the history of consanguineous parents. Studies are also showing that there is a link between consanguinity and susceptibility to infections both in humans and in animals.[14,15]

Second degree and third degree consanguinity can cause 25% and 12.5% chances of gene sharing in the off-spring.[45] Therefore, there are proportionate chances of incidence of hearing impairment in the family. This is the reason why risk estimate of 2nd and 3rd degree consanguinity slightly vary in the present study [Table 1]. A difference in the gene sharing had a direct influence in the association of consanguinity with hearing impairment. It was noticed that the prevalence of consanguinity in the total population of the present study is slightly less than what is reported earlier. Earlier literature shows there is 30-50% of consanguinity in south India.[16] In the present study, 28% had consanguineous marriage. This is in the lower limit of earlier prevalence literature.

Family history of childhood hearing impairment is another crucial risk factor, which is closely linked with consanguinity among the genetic cause of hearing impairment. There are many studies in India showing the prevalence of family history in children with hearing impairment. A school based study in Mumbai[46] found family history as a statistically significant risk factor for hearing impairment. Nearly 30% of children with hearing impairment were having this risk factor, causing the highest association among the risk factors such as prematurity, low birth weight, infections etc. The risk estimate, when extracted appears to be 67. A study in Karnataka,[47] found 25% of babies with hearing impairment were having a family history. In Kerala,[48] 38% of children with hearing impairment were having a family history. These data are highlighting the need of creating awareness on a preventable cause of hearing impairment in India.

The risk factors are not having correlation with different types of permanent hearing impairment statistically. In terms of percentage, more than 90% of Family History and Family History with Consanguinity category [Table 2] were having bilateral severe-profound hearing loss. In Netherlands,[11] 39% of permanent hearing loss is attributed to hereditary reasons in which 49% were having severe and profound hearing impairment. The effect of hereditary reasons on permanent hearing impairment seems to differ with the population.

**CONCLUSION**

Family history and consanguinity are strongly associated with congenital permanent hearing impairment. A child with family history has six times more chances of having permanent hearing impairment. Family history is still continuing to be an important risk factor as in the past in the southern part of India. A child with consanguineous parents has three times more chances for developing permanent hearing impairment. The second degree consanguinity is having three times chances, and third degree is having two times chances of occurrence of hearing impairment.

**REFERENCES**


Source of Support: Nil. Conflict of Interest: None declared.