

Volume 10

ISSN 0975-5400

Volume 10, Number 1, 2014

ISSN 0975-5400

Indian Journal of Otology

An Official International Journal
of the Indian Society of Otology



Dr. M. S. Kumar
Editor-in-Chief

Home Ahead of print Instructions Contacts
 About us Current issue Submit article Advertise
 Editorial board Archives Subscribe Login

Editorial Board

Editorial Board: Indian Journal of Otology

Chief Editor: **Dr. M.K Taneja**

Director
 Indian Institute of ear diseases,
 E 982, C.R. Park, New Delhi-110019

Email: ljo_editor@rediffmail.com, tanejaentcenter@gmail.com

Mob: +91 8006000203, 9312933530, Ph: 011-26275101

Associate Editor:

Dr. Kapil Sikka

Associate Professor

Department of ENT & Head Neck Surgery

All India Institute of Medical Science (AIIMS)

Ansari Nagar, New Delhi – 110029

Mob: +91 9810423088, 011-26594922

Email: kapil_sikka@yahoo.com

Executive Editor:

Dr. Vivek Taneja

ENT Consultant & Surgeon

Sr. Resident at Sanjay Gandhi Memorial Hospital, Mangolpuri, New Delhi

Residence: E-982, C. R. Park New Delhi-110019

Email: dr.vivektaneja@gmail.com

Mob: 9205494762

Executive Officer

Dr. Tarini Taneja

Head Department of Indian I.V.F. Center, Muzaffarnagar

Co-Director Indian Institute of Ear Diseases

E- 982, C. R. Park, New Delhi – 110019

Mob: 9412210266, Ph: 011-26275101

E-mail: drtarini@yahoo.com

Dr. Mansi Taneja

M.D. OBGYN

Gynaecologist

E- 982, C. R. Park, New Delhi – 110019

Mob: 9870847506, Ph: 011-26275101

E-mail: mansi.taneja.14@gmail.com

Editorial Advisory Board - Chief

Dr. Saurabh Varshney

Prof. & Head Department of ENT & Head neck Surgery

All India Institute of Medical Sciences, Rishikesh

Type V- 3/2; AIIMS Camus, Rishikesh- 249203 (Uttarakhand)

Mob: 8475000273, 0135-2456062 (Res.)

E-mail ID: drsaurabh63@gmail.com

Editorial Advisory Board


Prof. Dr. Tariq Rafi

Vice Chancellor, JSMU


Professor Emeritus Department of ENT, JSMU


     Users Online: 699

Feedback
 Subscribe
 About the journal


 **Subscribe to this journal**

 **Submit article**

 **Most popular articles**

 **Join as Reviewer**

 **Email alerts**

 **Recommend this journal to your library or friends**

Mob: 9869259450, 8828110545, Ph: 022-23724178

Dr. Khandhar Vinod Mahasukhlal

Professor, ENT C.U.Shah Medical College

H-1 , Meghalay Avenues, Near Sardar Patel colony, Naranpura,
Ahmedabad - 380006

GUJARAT, INDIA

Mob.9824047807, Ph: 079 26575330 / 26585330

E-mail ID:khandhar57@gmail.com

Col (Dr) Poonam Raj

Prof Department of ENT-HNS,

Army Hospital (R&R), Delhi

Residence: P 88/A, Shankar Vihar

Delhi Cantt, New Delhi- 110010

Mob: 9958414385, Phone: 011-26154352

Dr. Prashant E. Natekar

Prof. HOD Department of Anatomy

Goa Medical College, Bambolim

Taleigao Plateau, Taleigao Goa

Goa – 403202, India

Mob: 9158864325, Tel: 08322458787

Email id: drpenatekar@gmail.com/drpenatekar@hotmail.com

Dr. P. Karthikeyan

Prof. & HOD, Department of Oto – Rhino Laryngology (ENT),

Mahatma Gandhi Medical College & Research Institute,

SBV University, Pondy – Cuddalore Main Road, Pillaiyarkuppam,

Pondicherry – 607 403

Phone: (0413) 2615 449 – 458 Extn: 337, 0413 2615302

Cell: 94433 81302.

Email: karthikent73@gmail.com

Dr. Prahlada N.B.

Prof. & Head Department of Otorhinolaryngology,

Basaveshwara Medical College & Hospital,

Chitradurga-577501, Karnataka, India

Residence: "Basava Bhavana". #29, Bheema Samudra Road,

Davalagiri Extension - II Stage,

Chitradurga, Karnataka, 577 501, India.

Mobile: +91-9342310854, Phone: +91-8194-226643.

E-mail: prahladnb@gmail.com

Dr. Saurabh Varshney

Professor & Head

Department Of ENT at All India Institute of Medical Sciences (AIIMS), Rishikesh

Type V- 3/2; AIIMS Camus, Rishikesh- 249203 (Uttarakhand

Mob.: 91-8475000273, 9412944724, Ph: 0135-2456062 (Res.)

Email: drsaurabh68@gmail.com

Dr. Shashi Raheja

Director Professor in Anatomy Department

Lady Hardinge Medical College,

New Delhi- 110001

Mob: 9868906767

Detection of Single-Nucleotide Polymorphism Gap Junction Protein Beta-2 Genes in Deaf Schoolchildren of Javanese Population in Surabaya, Indonesia

Nyilo Purnami, Gwenny Ichsan Prabowo¹, Citrawati Dyah Kencono Wungu¹, Retno Handajani^{1,2}

Department of Otorhinolaryngology Head and Neck Surgery, Faculty of Medicine, Dr. Soetomo General Hospital, Universitas Airlangga, ¹Department of Medical Biochemistry, Faculty of Medicine, Universitas Airlangga, ²Hepatitis Study Group, Institute of Tropical Disease, Universitas Airlangga, Surabaya, Indonesia

Abstract

Background: Genetic factors account for about 50%–75% responsible for hearing loss. The existence of single-nucleotide polymorphism (SNP) as genetic factors that affect hereditary hearing loss. The widely studied SNP was the gap junction protein beta-2 (GJB2) gene encoding the gap junction beta-2 protein (connexin26) that found in cochlea and required to convert sound waves into electrical nerve impulse. This study was aimed to detect the SNP GJB2 gene of hereditary hearing loss patients from Javanese population in Surabaya, Indonesia. **Methods:** The design of this study was a cross-sectional, analytic observational. The participant was taken randomly among the students from a deaf School in Surabaya. The questionnaire was completed by the parents of the deaf children. Blood sampling was taken from venous peripheral blood. DNA was extracted and amplified on GJB2 gene area by polymerase chain reaction (PCR). The positive results of PCR were processed further for sequencing. The sequencing results were analyzed to detect the GJB2 gene SNP with reference sequence/rs-80338939. **Results:** A total of 22 children participated in this study; all were profound sensorineural hearing loss (SNHL). The hereditary hearing loss was obtained with fewer in five children (22.73%), who had a history of hearing loss in their family. It was compared to 17 children (77.27%) who had no family history of hearing loss. It was found that the nucleotide variation in nucleotide number 8473 of GJB2 gene as much as 3 (13.64%) out of 22 children in hereditary hearing loss patients in Deaf School Type B Surabaya. **Conclusions:** This study did not found any SNP GJB2 gene (rs-80338939) of hereditary hearing loss patients from the Javanese population in Surabaya, Indonesia. There was the nucleotide substitution G to A in nucleotide number 8473 of GJB2 gene, which indicated the change of amino acid code genetic code table (valine) to amino acid code genetic code table (isoleucine). It may as the cause of SNHL.

Keywords: Gap junction protein beta-2 gene, hereditary hearing loss, single-nucleotide polymorphism

INTRODUCTION

Sensorineural hearing loss (SNHL) is the most common sensory disorder that affected by environmental, genetic, and interaction among the factors. About 1 in 1000 births, 50%–75% bilateral hearing loss are caused by genetic factors.^[1,2] Since now, there have been 102 genes that cause nonsyndromic hearing loss and one of the genes that have significant associations with SNHL is gap junction protein beta-2 (GJB2, OMIM 1221011).^[2,3] About 50% of GJB2 gene mutations cause autosomal recessive nonsyndromic hearing loss in the world. In Turkey, about 18.9% of hearing loss patients are caused by GJB2 gene mutations.^[4]

The single-nucleotide polymorphism (SNP) GJB2 gene is an important gene located in the DFNB1 locus on chromosome


13q.12^[5] and encodes protein connexin 26 composed of 226 amino acids.^[3,4] Connexin is a gap junction that resides in epithelial cells and connective tissue and is responsible for maintaining electrical potential in cochlea. Gap junctions are used to transport neurotransmitters, metabolites, and potassium ions.^[6] In cochlea, connexin 26 serves to maintain the balance of K⁺ ions used to deliver the stimulation of sound to hair cells during the auditory transduction process.^[7] Mutation of the GJB2 gene results in modification of the codon encoding

Address for correspondence: Dr. Gwenny Ichsan Prabowo, Department of Medical Biochemistry, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia. E-mail: gwenny-i-p@fk.unair.ac.id

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Purnami N, Prabowo GI, Wungu CD, Handajani R. Detection of single-nucleotide polymorphism Gap junction protein Beta-2 genes in deaf schoolchildren of javanese population in Surabaya, Indonesia. *Indian J Otol* 2019;25:6-10.

Access this article online	
Quick Response Code: 	Website: www.indianjotol.org
	DOI: 10.4103/indianjotol.INDIANJOTOL_50_18

the connexin protein 26 and affecting the stability of mRNA. Mutation of the GJB2 gene is the main cause of congenital deafness.^[8] GJB2 c.35delG gene mutations are common in hearing-impaired patients in Europe and America. In Eastern and Central European societies, c.167delT gene mutations are commonly found in hearing-impaired patients, while in the Mongolia race mutations, c.235delC genes that occur in many patients with hearing loss. Thus, gene mutations in hearing-impaired patients can be identified in GJB2 c.35delG, c.167delT, and c.235delC.^[9,10] In Indonesia, there has not been much investigation of the association between genetic mutations and the occurrence of congenital hearing loss, although the number of congenital hearing loss patients in Indonesia is high. A study in Indonesia (1994–1996) obtained the result of a congenital auditory hearing survey in of 0.1% and in 2005 increased by about 0.22%.^[9] Based on the above description GJB2 c.35delG analysis in congenital hearing loss patients in Surabaya, Indonesia needs to be done.

METHODS

The participants of this study were congenital hearing loss patients who met the inclusion criteria in Surabaya, Indonesia. Participant inclusion criteria include children with congenital hearing loss with profound (>80 dB). Exclusion criteria include patients having a history of head trauma, otological disease, meningitis, rubella virus infection, and using ototoxic drugs. Participant's parents who are willing to follow the research in advance fill out informed consent sheets. A self-administered questionnaire was completed by parents of a deaf child participating in a GJB2 testing study. Before the assessment of the research, participant's first conduct ethical test (510/panke. KKE/VIII/2017) at Dr. Soetomo General Hospital Surabaya, Indonesia. The population of congenital hearing loss after being identified in Yayasan Karya Mulia, Surabaya, Indonesia, found 215 participants. After a health history study, 103 participants were selected according to the inclusion criteria, followed by audiometric examination (Grason-Stadler Inc., Eden Prairie, USA) according to the diagnosis of hearing loss according to the WHO and found 36 participants who met the criteria. Participants, who were eligible in this study as many as 22 children, underwent a genetics evaluation.

The design used in this research is observational analytic. Participants were collected 5 ml of venous blood samples which were inserted into the vacutainer tube with ethylenediaminetetraacetic acid. Then, in accordance with the procedure, the peripheral blood mononuclear cells (PBMCs) were separated from the samples and inserted into the Eppendorf tube and stored at -80°C at the Institute of Tropical Disease, Universitas Airlangga, until further analysis.

DNA extraction from PBMC was performed using modification procedure found in DNA Isolation Kit for blood/bone marrow (paint No. 2 032 805), then continued the amplification of GJB2 gene by polymerase chain reaction (PCR) technique. PCR was performed using a pair of primers made using the

primary program of NCBI, and then the primary was selected after multiple alignments using the Computer Program Clone Manager 9 and the optimization test. A pair of primers used for PCR GJB2 genes is: forward 5'-ACG TTC AAG AGG GTT TGG GAA-3' and reverse 5'-CTG CAA GAA CGT GTG CTA CG-3'. The first round PCR was performed for 40 cycles and used the initial hot start temperature at 94°C for 5 min, each cycle consist of denaturation: 94o C for 45 s and final extension for 7 min. In every work, PCR used a negative control (aquadest) and positive control (samples already known to contain GJB2), and research samples are done together. PCR product detection was performed by electrophoresis technique using 2% agarose gel dissolved TBE x0.5 and containing ethidium bromide.

We detected SNP GJB2 gene (rs-80338939) with DNA sequencing technique. The sequencing engine used is a sequence ABI prism 310 genetic analyzer from Applied Biosystems, Inc., using one of the primers (sense) used on PCR. Electropherogram obtained from sequencing results and analyzed using Computer Program Clone manager 9.

RESULTS

Demography data

In the research, participants conducted data collection on gender, mean ± standard deviation (SD), and age range with the unit year. A summary of data on gender, mean ± SD, and age range of study participants as shown in Table 1.

The number of female Deaf School Type B (SLB) students with the inherent deafness in this study was more than male students. The mean age in female SLB students is younger than the mean age in male students. The age range of male study participants has a wider range of ages than females, with the age difference between the youngest and the oldest in the subject of the study were 17 years and in male 10 years in female.

Factors suspected of contributing to the occurrence of hearing loss are as follows: environmental factors, genetic factors, and interactions between the two factors. Factors that are thought to play a very important role in the occurrence of hearing loss is a genetic factor. This study also collected data-interview questionnaire about the history of hearing loss in the family of research participants. A summary of gender distribution data and a history of hearing loss in the study participant's family are shown in Table 2.

Table 1: Distribution of gender, mean ± standard deviation, and age range of the study participants

Gender	n (%)	Age (year)	
		Mean ± SD	Range of age
Male (M)	10 (45.45)	14.50±10.32	8-25
Female (F)	12 (54.55)	11.83±7.44	7-17
n total (%)	22 (100)	13.12±9.13	7-25

SD: Standard deviation

Male participants in this study who had a history of hearing loss in the family were higher (3/10) than female participants (2/12). Overall, the total number of the study participants with a history of hearing loss in the family was lower (22.73%) than the study participants who did not have a history of hearing loss in the family (77.27%).

Polymerase chain reaction examination results and gap junction protein beta-2 gene sequencing

In this study, successfully extracted GJB2 gene DNA from research participants that could be visualized by performing electrophoresis. Documentation of PCR gene purification result in positive GJB2 in the participants, was a DNA fragment with a length of 422 bp that appeared as a band that visualized with ultraviolet light. An example of electrophoresis results from several PCR products of the GJB2 gene in the study participants as shown in Figure 1.

Results of positive GJB2 gene PCR then sequenced to determine the presence of SNP GJB2 gene with rs-80338939. In this study, there was no SNP GJB2 gene with rs-80338939 but found the variation of nucleotide G to A in nucleotide number 8473. Example of fragment resulted from sequencing location around GJB2 gene variation in nucleotide number 8473 in research subject as shown in Figure 2a and b.

SNP GJB2 gene with rs-80338939 is located on chromosome 13q11-q12 in exon 2. In this study did not found SNP GJB2 gene rs-80338939, however, there is nucleotide variation at nucleotide number 8473 GJB2 gene in participants study number 3, 4, and 5, because the SNP is influenced by demographic and ethnic factors.^[11]

Genetic variation in the research participants can be known by doing multiple alignments that are comparing the results of

sequencing all research participants with GJB2 gene standard from Gene Bank NCBI (NM_004004.5) and rs-80338939. In the multiple alignments of the GJB2 gene standard of Gene Bank NCBI (NM_004004.5), rs-80338939, and the sample, it was found that in the research participants 3, 4, and 5 found the variation/substitution of G nucleotides to A. The nucleotide variation resulted in the amino acid change which is coded because the codon genetic code table (GTC) encoding the amino acid valine turns into an amino acid code table (ATC) codon that encodes the amino acid isoleucine. Multiple alignments with the location of variation/substitution of GJB2 gene nucleotide from the sequencing of all study participants with congenital deafness, compare to rs 80338939 and GJB2 gene standard (NM_004004.5) is shown in Figure 3. (Nucleotide number 8473).

Distribution of genotype G/G (homozygote-wild type) is found in male research participants with 70% of inherited deafness (7/10) and in the study participants of female with 100% congenital deafness (12/12). Distribution of genotype A/A (homozygote-mutant type) is only found in the male participants with 30% (3/10) congenital deafness. In the overall study participants with congenital deafness, the genotype A/A distribution was 13.64% (3/22), derived only from male participants. In the study participants with congenital deafness studied, no genotype G/A (heterozygote) was obtained. The distribution of genotypes and alleles of nucleotide variation/substitution in 8473 GJB2 gene in the study participants with congenital deafness is shown in Table 3.

There was a difference in genotype or allele distribution of nucleotide variation/substitution in 8473 GJB2 gene in the study participants with innate deafness between sexes. In the male research participants obtained genotype G/G and A/A, while the female research participants only obtained genotype G/G. The frequency of allele G in male research participants was 94.1% while in female as much as 92.3%.

Table 2: Distribution of gender and history of hearing loss in the family participants of the study

Gender	History of hearing loss in the family, n (%)		n total (%)
	Yes	No	
Male (M)	3 (30)	7 (70)	10 (100)
Female (F)	2 (16.67)	10 (23.1)	12 (100)
n total (%)	5 (22.73)	17 (77.27)	22 (100)

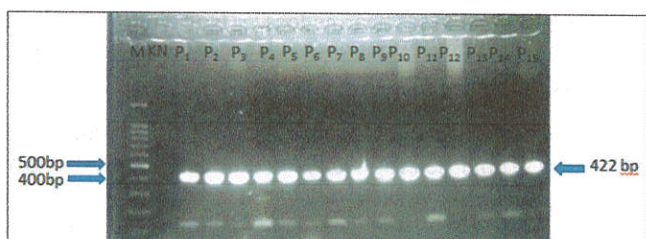


Figure 1: Examples of electrophoresis results of some polymerase chain reaction products of gap junction protein beta-2 genes in the participants' research with positive results. M: Marker 100 bp, KN: Negative control, P1-P15: Sample

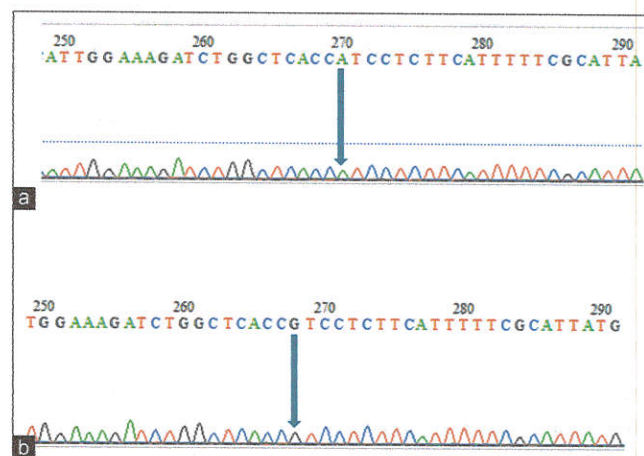


Figure 2: (a) Allele A mutant type, in the research participants number 3, 4, and 5, there was a nucleotide substitution G to A. (b) Allele G wild type, partial example of sequence location fragments around the gap junction protein beta-2 gene variation in nucleotide number 8473 in the study participants

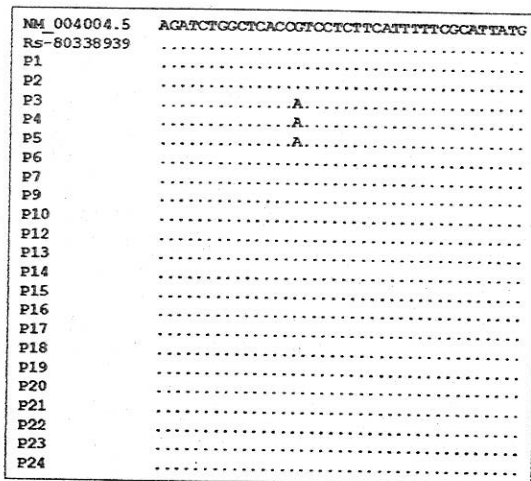


Figure 3: Multiple alignments with location around nucleotide substitution G to A on gap junction protein beta-2 gene single-nucleotide polymorphism (rs-80338939), NM_004004.5, and all samples (P1 - P24). NM_004004.5: Gap junction protein beta-2 gene standard from Gene-Bank NCBI, rs-80338939 and all samples (P1-24)

Nucleotide variation/substitution in 8473 GJB2 gene in the study participants with deafness based on demographic characteristics is shown in Table 4.

DISCUSSION

Molecular diagnosis to detect mutations in congenital deafness has many constraints since the number of genes suspected to be the cause and contribution of each gene in causing deafness is still not fully understood. Types of gene mutations found in congenital deafness influenced by several factors, namely, the differences in demographic and ethnic populations.

Genetic analysis of congenital deafness is an important tool of tracking hereditary disease in research participants with congenital deafness as early as possible so that it can be treated promptly, as well as tracing the hereditary deafness to family members of the study participants and also can be used as premarital screening.^[12] It is important to note that genetic testing should be counted, related with 50% of children with congenital hearing loss are due to genetic factors and about 50% of infants do not have any known risk factors, mandating the implementation of universal newborn hearing screening (UNHS) for both newborns with and without risk factor. However, UNHS may suffer from limitations. First, since the target condition for the majority is permanent hearing loss and given that a genetic cause could not be identified in many hearing-impaired children.^[12]

Delay in diagnosis of hearing loss resulted in a major impact on cognitive development and the ability of children to communicate; hence, it will greatly affect the child's psychosocial development in the future.

Research participants with a history of hearing loss in the family were fewer than those who had no history of hearing loss in the family. The results of this study are not in line

Table 3: Genotype and allele distribution of nucleotide variation/substitution at 8473 gap junction protein beta-2 genes in the study participants with congenital deafness

	Hereditary hearing loss	
	Male (%)	Female (%)
Genotype		
G/G	7 (70)	12 (100)
G/A	0 (0.0)	0 (0.0)
A/A	3 (11.8)	0 (0.0)
Total	10 (100)	12 (100)
Allele		
G	14 (94.1)	24 (92.3)
A	6 (5.9)	0 (0.0)
Total	20 (100)	24 (100)

G/G: Homozygote wild type, A/A: Homozygote mutant type, G/A: Heterozygote

Table 4: Distribution of genotype variation/substitution of gap junction protein beta-2 gene nucleotide based on demographic characteristics on study participants with congenital deafness

Genotype GJB2 gene	A/A (isoleucine/ isoleucine) (mutant type)	G/A (valine/ isoleucine)	G/G (valine/ valine) (wild type)
Mean age (year)	23.3	0	11.92
Gender			
Male	3	0	7
Female	0	0	12
Family history			
Yes	1	0	4
No	2	0	15

A/A: Homozygote mutant type, G/G: Homozygote wild type, G/A: Heterozygote

with previously obtained data, which is about 50% of GJB2 gene mutations causing autosomal recessive nonsyndromic hearing loss in the world.^[2] The GJB2 gene plays a coding protein gap junction beta-2 (connexin 26) which is primarily expressed in the stria vascularis, ligament spiral, spiral limbus, and among the buffer cells in the cochlea. Connexin 26 (gap junction protein) plays a role in the transport of potassium ions in the inner ear. Connexin 26 malfunctions from GJB2 gene mutations will result in impaired potassium ion transport from hair cells through the supporting cell network to the endolymph that induce hearing loss.^[13] Nonsyndromic SNHL can caused by SNP GJB2 gene that it can bother the transport of potassium ion.^[14]

In this study, the GJB2 gene SNP was not found with rs-80338039, the heterogeneity of the results of this study was supported by^[11] who suggested that ethnic diversity and geographic area could influence genotypic variation in the population.^[11] Factors that are suspected to influence the results of this study are the differences in ethnicity because the research participants are all derived from the Javanese population as well as the difference of demographic location

because the research was conducted in Asia, Indonesia. This is supported by the SNP study of the GJB2 gene in Japanese and Korean populations found mainly in SNP 235delC and in African population found R143W.^[13]

In this study, SNP GJB2 gene was found with the prevalence of 13.64% (3/22) in nucleotide number 8473 which resulted GTC codon change to ATC, causing the substitution of amino acid valine to isoleucine. This finding was described consistent with an optimization of the genetic code so as to minimize kinetic energy disturbances during evolution by mutation for processes such as protein folding and dynamics known to be essential for function.^[15] This result provided empirical evidence that genetics evaluation is important to parents regardless of the genetic test result and children have received a genetic explanation for the deafness.^[16] Further research needs to find on the impact of substitution of valine amino acid to leucine in congenital deafness. Efforts to increase awareness of the usefulness of genetics evaluation to ensure appropriate care for deaf children as recommended by the American College of Medical Genetics.^[17]

CONCLUSIONS

There was not find the SNP GJB gene in this study on the congenital deafness of the Java tribe in Surabaya, Indonesia, referring to NCBI with rs-80338939 (SNP is in nucleotide number 8293 [y], 8341 [r], 8361 [y], 8380 [y] 8429 [n], 8444 [y], 8528 [r], and 8543 [k]). Further research on following this finding might demonstrate the clinical utility.

Acknowledgments

The researchers would like to thank all participants who took part in this study. We also thank Mr. M. Amin from the Institute of Tropical Disease who helped us to examine the DNA extraction, PCR, and sequencing.

Financial support and sponsorship

The researchers would like to thank Universitas Airlangga for funding the research through the Annual Work Plan and Budget (Decree: 133/UN3.1.1/KD/2017).

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Petit C, Leveilliers J, Hardelin JP. Molecular genetics of hearing loss. *Annu Rev Genet* 2001;35:589-646.
- Yamamoto N, Mutai H, Namba K, Morita N, Masuda S, Nishi Y, *et al.* Prevalence of TECTA mutation in patients with mid-frequency sensorineural hearing loss. *Orphanet J Rare Dis* 2017;12:157.
- Grillo AP, de Oliveira FM, de Carvalho GQ, Medrano RF, da Silva-Costa SM, Sartorato EL, *et al.* Single nucleotide polymorphisms of the GJB2 and GJB6 genes are associated with autosomal recessive nonsyndromic hearing loss. *Biomed Res Int* 2015;2015:318727.
- Bozdoğan ST, Kuran G, Yüregir ÖÖ, Aslan H, Haytoğlu S, Ayaz A, *et al.* The prevalence of gap junction protein beta 2 (GJB2) mutations in non syndromic sensorineural hearing loss in çukurova region. *J Int Adv Otol* 2015;11:118-21.
- del Castillo I, Villamar M, Moreno-Pelayo MA, del Castillo FJ, Alvarez A, Telleria D, *et al.* A deletion involving the connexin 30 gene in nonsyndromic hearing impairment. *N Engl J Med* 2002;346:243-9.
- Mielczarek M, Zakrzewska A, Olszewski J. GJB2 sequencing in deaf and profound sensorineural hearing loss children. *Otolaryngol Pol* 2016;70:21-5.
- Snoeckx RL, Huygen PL, Feldmann D, Marlin S, Denoyelle F, Waligora J, *et al.* GJB2 mutations and degree of hearing loss: A multicenter study. *Am J Hum Genet* 2005;77:945-57.
- Tlili A, Al Mutery A, Kamal Eddine Ahmad Mohamed W, Mahfood M, Hadj Kacem H. Prevalence of GJB2 mutations in affected individuals from United Arab emirates with autosomal recessive nonsyndromic hearing loss. *Genet Test Mol Biomarkers* 2017;21:686-91.
- Zahara D, Bashiruddin J, Tann G, Munir D, Purnami N, Savitri E, *et al.* Gap junction beta 2 gene mutation in Indonesian patients with non syndromic congenital hearing loss. *Int J Pharm Technol Res* 2015;8:69-76.
- Du W, Zhu YM, Guo YF, Wang QJ, Liu XW. Prevalence of GJB2 mutations in the silk road region of China and a report of three novel variants. *Acta Otolaryngol* 2014;134:373-81.
- Jorde LB, Wooding SP. Genetic variation, classification and 'race'. *Nat Genet* 2004;36:S28-33.
- Wu CC, Hung CC, Lin SY, Hsieh WS, Tsao PN, Lee CN, *et al.* Newborn genetic screening for hearing impairment: A preliminary study at a tertiary center. *PLoS One* 2011;6:e22314.
- Van Laer L, Coucke P, Mueller RF, Caethoven G, Flothmann K, Prasad SD, *et al.* A common founder for the 35delG GJB2 gene mutation in connexin 26 hearing impairment. *J Med Genet* 2001;38:515-8.
- Kenneson A, Van Naarden Braun K, Boyle C. GJB2 (connexin 26) variants and nonsyndromic sensorineural hearing loss: A HuGE review. *Genet Med* 2002;4:258-74.
- Guilloux A, Jestin JL. The genetic code and its optimization for kinetic energy conservation in polypeptide chains. *Biosystems* 2012;109:141-4.
- Alford RL, Arnos KS, Fox M, Lin JW, Palmer CG, Pandya A, *et al.* American college of medical genetics and genomics guideline for the clinical evaluation and etiologic diagnosis of hearing loss. *Genet Med* 2014;16:347-55.
- Rimoin DL. The american college of medical genetics, the first 20 years. *Genet Med* 2011;13:179-87.



Indian Journal of Otology

COUNTRY	SUBJECT AREA AND CATEGORY	PUBLISHER	H-INDEX
India <small>Universities and research institutions in India</small>	Medicine Otorhinolaryngology	Wolters Kluwer Medknow Publications	8
PUBLICATION TYPE	ISSN	COVERAGE	INFORMATION
Journals	22499520, 09717749	1999-2020	Homepage How to publish in this journal Editor@indianjotol.org

SCOPE

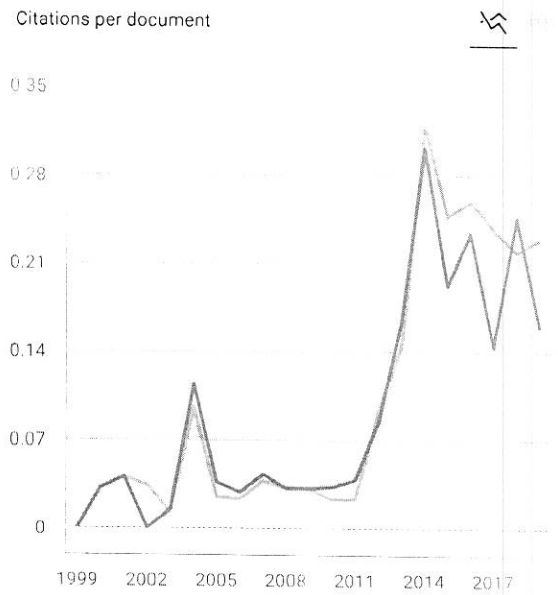
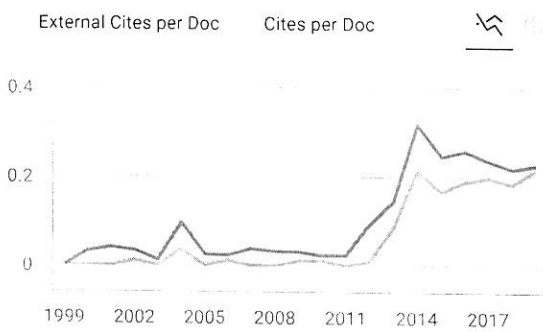
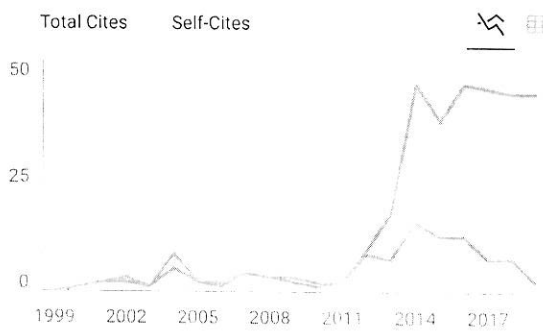
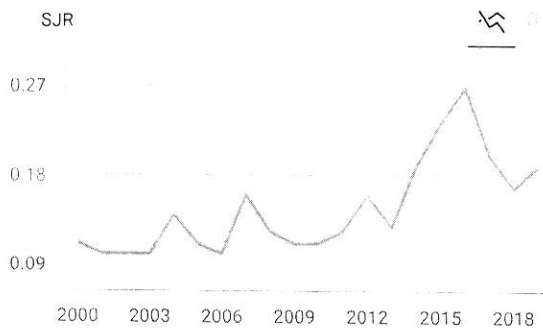
Indian Journal of Otology, a publication of Indian Institute of Ear Diseases, is a peer-reviewed online journal with Quarterly print on demand compilation of issues published. The journal's full text is available online at <http://www.indianjotol.org>. The journal allows free access (Open Access) to its contents and permits authors to self-archive final accepted version of the articles on any OAI-compliant institutional / subject-based repository. The journal does not charge for submission, processing or publication of manuscripts and even for color reproduction of photographs.

Join the conversation about this journal

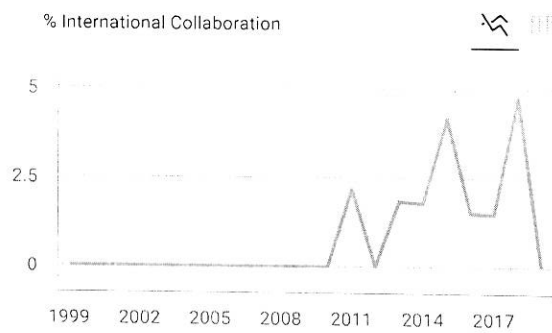
Quartiles

FIND SIMILAR JOURNALS ?

1 Indian Journal of Otolaryngology and Head and Neck Surgery IND 72% similarity	2 International Archives of Otorhinolaryngology USA 69% similarity	3 Egyptian Journal of Ear, Nose, Throat and Allied EGY 65% similarity	4 Journal of Otolaryngology CHN 65% similarity
--	---	--	---

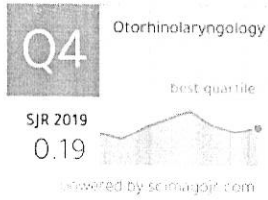


Cites / Doc (4 years)
 Cites / Doc (3 years)
 Cites / Doc (2 years)



Indian Journal of Otology

Show this widget in your own website



Just copy the code below and paste within your html code:

```
<a href="https://www.scima
```

Metrics based on Scopus® data as of April 2020

Leave a comment

Name

Email

(will not be published)

I'm not a robot

reCAPTCHA
Privacy - Terms

Submit

The users of Scimago Journal & Country Rank have the possibility to dialogue through comments linked to a specific journal. The purpose is to have a forum in which general doubts about the processes of publication in the journal, experiences and other issues derived from the publication of papers are resolved. For topics on particular articles, maintain the dialogue through the usual channels with your editor.