

Factors associated with time of diagnosis and habilitation of congenital hearing loss in Indonesia: A multicenter study

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ABSTRACT

Objectives: To investigate factors associated with time of diagnosis and habilitation of congenital hearing loss in Indonesia.

Method: A retrospective cohort study was conducted from January to December 2020 by collecting data on patients with congenital hearing loss using validated questionnaires.

Result: Among 535 children with congenital hearing loss, 2.7% had a family history of congenital hearing loss, 11.2% and 37.4% had a maternal history of ototoxic drugs and herbal medicine use during pregnancy, respectively, and 17.8% had prenatal exposure to TORCH infection. Lower maternal education level was shown to be associated with older age at diagnosis ($p = 0.045$), while older maternal age ($p < 0.001$), non-housewife mothers ($p = 0.029$), and out-of-pocket payment scheme ($p = 0.027$) were associated with a higher rate of habilitation.

Conclusion: The present study showed that the presence of family history, the use of certain medications during pregnancy, and prenatal TORCH infection are prevalent in children with congenital hearing loss in Indonesia. Several factors such as maternal education level, age, occupation, and habilitation payment scheme may be associated with time of diagnosis and habilitation of congenital hearing loss.

1. Introduction

Congenital hearing loss is one of the most prevalent chronic conditions in children with a global prevalence of about 1–3 cases out of every 1000 births [1]. In Indonesia, the prevalence of congenital hearing loss is about 0.11% in 2018 up from 0.08% in 2013 [2,3]. If left undetected or untreated, congenital hearing loss may affect the children's quality of life due to speech, social, and cognitive developmental delay, as well as poor academic performance. The condition is caused by an impairment of the ability of the ear to convert sound vibration into electrical nerve impulses, which can result from one or more factors during pregnancy (prenatal) or at birth (perinatal and postnatal). The fetus is most vulnerable to congenital hearing loss during the first trimester of pregnancy where the presence of any disturbance such as TORCH infection (infection caused by *Toxoplasma gondii*, rubella virus, cytomegalovirus, or herpes simplex virus) or certain ototoxic drugs (e.g., salicylates, quinine, neomycin, barbiturates, and gentamicin) may cause detrimental errors in the development of hearing functions. On the other hand, several perinatal conditions that may pose risks for hearing loss include premature birth, low birthweight (<2500 g), hyperbilirubinemia, and asphyxia. Hearing loss occurring during this period usually presents bilaterally with a severe to profound sensorineural hearing loss. Lastly, hearing loss occurring during the postnatal period usually presents as sensorineural, conductive, or mixed type hearing loss, and may be caused by either bacterial or viral infections such as mumps, measles, rubella, brain infections, or middle ear and/or temporal bleeding and trauma.

In developed countries, early detection of congenital hearing loss is usually performed by neonatal hearing screening programs followed by early interventions to prevent further speech and developmental delays. However, in developing countries, such programs are usually hindered by the lack of appropriate technology and human resources. In Indonesia, hearing screening programs are implemented voluntarily as some healthcare facilities do not have access to hearing test devices. In addition, it is not uncommon for the parents to be reluctant to undergo follow-up visits due to the lack of knowledge and understanding of the objectives of the screening programs [4]. This is especially concerning considering that the time of diagnosis and immediate habilitation of congenital hearing loss are paramount in determining the patients' morbidity and quality of life. In this study, we analyze factors associated with the time of diagnosis and habilitation of patients with congenital hearing loss from 23 hospitals across 17 provinces in Indonesia.

2. Material and methods

The present retrospective cohort study was conducted from January to December 2020, collecting data on patients with congenital hearing loss using questionnaires that had been validated through validity and reliability tests. The diagnosis of congenital hearing loss was confirmed by brain evoked response auditory (BERA) examinations. Parents of children with congenital hearing impairment who visited outpatient clinic were given written and verbal informed consent about the study. Parents or the child's guardian signed the consent prior to the enrollment to the study. This study has been approved by the Health Research Ethics Committee, Faculty of Medicine Universitas Indonesia and Cipto Mangunkusumo National General Hospital (KET-749/UN2.F1/ETIK/PPM.February 00, 2020).

2.1. Data collection

Data collection was performed in 23 hospitals across 17 provinces in Indonesia, including: Zainoel Abidin Hospital (Banda Aceh, Aceh), H. Adam Malik Hospital (Medan, North Sumatra), M. Jamil Hospital (Padang, West Sumatra), Awal Bros Hospital (Pekanbaru, Riau), M. Husin Hospital (Palembang, South Sumatra), Mitra Husada Pringsewu Hospital (Lampung), Dr. Cipto Mangunkusumo National General Hospital (Jakarta), Fatmawati Hospital (Jakarta), Persahabatan Hospital (Jakarta), Tangerang City Hospital (Tangerang, Banten), dr. Hasan Sadikin Hospital (Bandung, West Java), Dustira Hospital (Cimahi, West Java), Dr. Sardjito Hospital (Yogyakarta), Academic UGM Hospital (Yogyakarta), dr. Kariadi Hospital (Semarang, Central Java), Wonogiri Hospital (Solo, Central Java), dr. Soeradji Tirtonegoro Hospital (Klaten, Central Java), dr. Soetomo Hospital (Surabaya, East Java), dr. Saiful Anwar Hospital (Malang, East Java), Sanglah Hospital (Denpasar, Bali), Panglima Sebaya Hospital (Tanah Grogot, North Kalimantan), Mitra Medika Pontianak Hospital (Pontianak, West Kalimantan), dr. Wahidin Sudirohusodo Hospital (Makassar, South Sulawesi) and Kandou Hospital (Manado, North Sulawesi).

The questionnaire consists of information on the patients' family history of congenital hearing loss, history of medication and herbal use, and prior exposure to TORCH infections during pregnancy. The patients' age was dichotomized into under/over one year, while the maternal age was dichotomized into under/over 30 years. The maternal education level was classified to high school graduates and diploma/university graduates, the maternal occupation to housewife and non-housewife, and the habilitation payment method to insurance and out-of-pocket/

donors.

2.2. Outcome measures

The primary outcomes in this study are time of diagnosis and habilitation. The time of diagnosis is defined as the age when the subject was first diagnosed with congenital hearing loss, while habilitation is the presence of interventions to improve hearing functions.

2.3. Data analysis

The retrieved data were tabulated and visualized for descriptive purposes. All of the collected variables were considered as potential risk factors for congenital hearing loss. The association between independent variables including maternal age, maternal education status, maternal occupation, habilitation payment method, and family history of congenital hearing loss were analyzed, with time of diagnosis and habilitation were analyzed using Pearson's chi square tests. All analyses were performed using SPSS 25.0 (SPSS Inc., Chicago, IL).

3. Results

A total of 535 patients participated in this study, with a mean maternal age of 34.10 years and a mean patient age of 5.52 years. Most of the mothers were housewives (71.8%) and were high school graduates (74.3%), while about 55.9% of the patients were boys (Table 1). Fig. 1 shows that about 3.6% of the subjects had a maternal family history of congenital hearing loss (19 patients), 3.2% had a paternal family history of congenital hearing loss (17 patients), and 1.3% had siblings with congenital hearing loss (7 patients).

Fig. 2 illustrates the history of medications that might be related to the patients' congenital hearing loss. The most common ototoxic drugs consumed by the mothers during pregnancy were analgesics (6.9%), followed by antihypertensive drugs (3.2%), cardiovascular medicines (0.7%), as well as anticancer and antimalarial drugs (0.2% each; Fig. 2A), while about 37.4% of the mothers consumed herbal medicines during pregnancy (Fig. 2B).

Out of 535 mothers who had a child with congenital hearing loss, 95 (17.8%) were infected by TORCH during pregnancy (Fig. 3A). Among them, rubella was the most prevalent infection (35.0%), followed by toxoplasmosis (23.6%) and herpes zoster (12.2%; Fig. 3B).

The results of the univariate analysis is shown on Table 1. Lower maternal educational level was shown to be associated with older age at diagnosis ($p = 0.045$), while no other variables were significantly correlated with age at diagnosis. Meanwhile, older maternal age, non-housewives, and out-of-pocket payment scheme were associated with a higher rate of habilitation (vs < 30 years old: 63.4% vs 38.8%, $p <$

0.001; vs housewives: 64.9% vs 54.4%, $p = 0.029$; and vs insurance payment scheme: 98.9% vs 94.6%, $p = 0.027$; respectively).

4. Discussion

In the present study, we provided evidence suggesting that several risk factors such as family history of congenital hearing loss, ototoxic drugs and herbal medicine use, and prenatal TORCH infection were identified among congenital hearing loss cases in Indonesia. Our findings showed a remarkably lower prevalence of patients with a history of affected siblings (1.3%) as compared to the study by Driscoll et al. in Australia which found that about 1.09% of affected children had a family history with a similar condition [4]. In addition, we found a prevalence of family history of congenital hearing loss of 2.7%, which is slightly lower than a similar study in Australia with a prevalence of 7.3% [4]. The relatively low prevalence observed in this study might be due to undetected hearing impairment in the screened population, or due to recall bias considering that the collected data was based on one-time interview. Nonetheless, the present study adds the body of evidence supporting the association between family history and congenital hearing loss, where a previous study have shown that the risk of congenital hearing loss was 1.92-fold higher in children with a family history of hearing loss [5].

It is estimated that about half of congenital hearing loss is caused by environmental factors such as the use of ototoxic drugs during pregnancy and prenatal TORCH infection [6,7]. Our research showed that, among the included patients, analgesics and antihypertensive drugs were the most common ototoxic drugs used by the mothers during pregnancy. However, as our study did not further explore the type of analgesics used and the duration of usage, and considering that previous studies failed to show a firm association between the use of acetaminophen or ibuprofen during pregnancy (as the most commonly used non-prescription analgesics) and congenital hearing loss, further studies are required to confirm our findings. In addition, antihypertensive drugs especially renin-angiotensin-aldosterone inhibitors are known to be linked to congenital hearing loss [8]. As the present study revealed a relatively high consumption of antihypertensive drugs during pregnancy, further drug stewardship strategies are required to minimize the use of these ototoxic drugs during pregnancy.

Other drugs shown to be associated with congenital hearing loss in this study were anticancer and antimalarial drugs, each of which accounts for about 0.2% out of the total cases. These observations are reinforced by previous reports showing that cisplatin and chloroquine use during pregnancy were linked to congenital hearing loss [9,10]. Lastly, this study also found that congenital hearing loss was prevalent in mothers who consumed herbal medicine which are extensively consumed in Indonesia, during pregnancy, accounting for about 34% of

Table 1
Association between risk factors and time of diagnosis and habilitation.

Variable	Total	Age Diagnosis			Total	Habilitation		
		<1 y.o	3 ¹ y.o	P value		No	Yes	P value
Maternal Age								
<30 y.o	129(100%)	32(24.8%)	97 (75.2%)	0.504	129(100%)	79 (61.2%)	50 (38.8%)	0.000*
3 ³ 30 y.o	396(100%)	87(22.0%)	309(78.0%)		396(100%)	145(36.6%)	251(63.4%)	
Mother's education								
Primary/Junior high/high school	390(100%)	80(20.5%)	310(79.5%)	0.045*	390(100%)	171(43.8%)	219(56.2%)	0.353
Diploma/Bachelor/Master	135(100%)	39(28.9%)	96(71.1%)		135(100%)	56(39.3%)	82(60.7%)	
Mother Occupation								
Housewives	377(100%)	83(22.0%)	294(78.0%)	0.570	377(100%)	172(45.6%)	205(54.4%)	0.029*
Non-housewives	148(100%)	36(24.3%)	112(75.7%)		148(100%)	52 (35.1%)	96(64.9%)	
Habilitation payment								
Government	130(100%)	28(21.5%)	102(78.5%)	0.550	130(100%)	7(5.4%)	123(94.6%)	0.027*
Independent/donation	180(100%)	44(24.4%)	136(75.6%)		180(100%)	2(1.1%)	178(98.9%)	
Hearing loss in other children								
No	518(100%)	116(22.4%)	402(77.6%)	0.199	518(100%)	221(42.7%)	297(57.3%)	0.992
Yes	7(100%)	3(42.9%)	4(57.1%)		7(100%)	3(42.9%)	4(57.1%)	

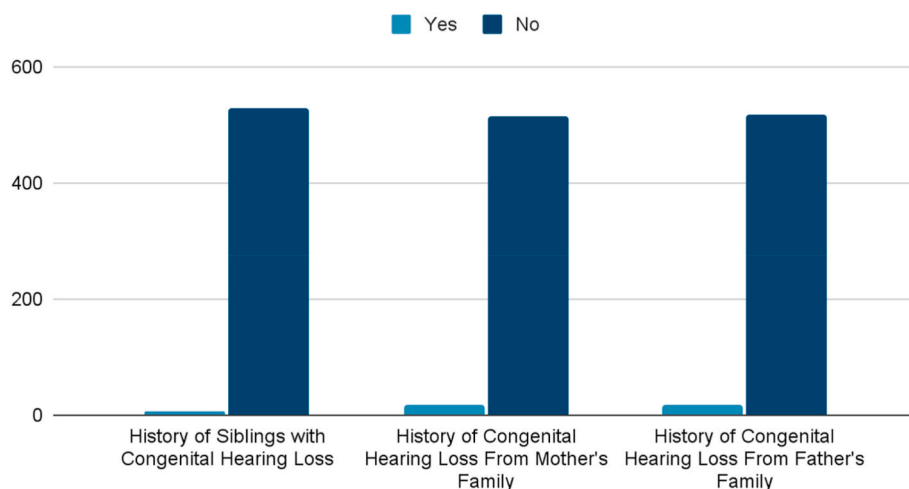


Fig. 1. Family history of patients with congenital hearing loss.

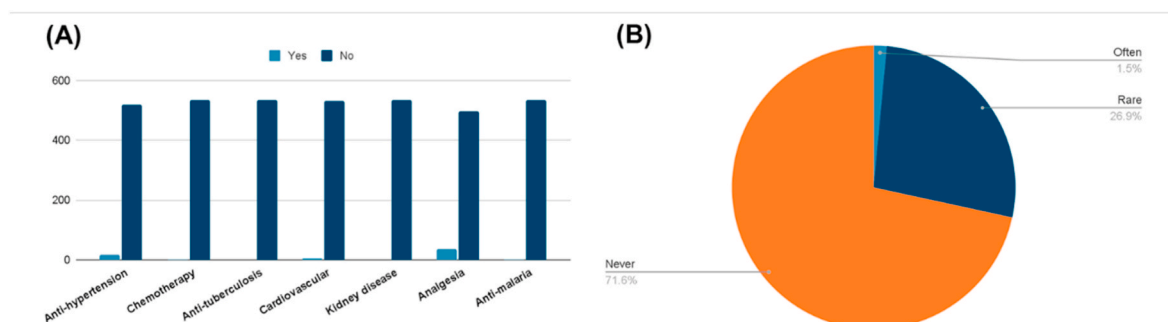


Fig. 2. Maternal use of (A) ototoxic drugs and (B) herbal medicines during pregnancy.

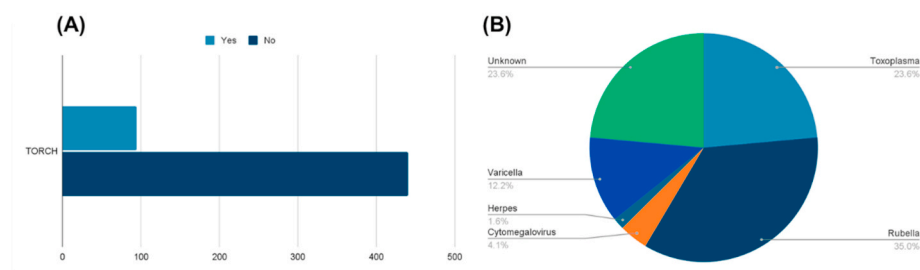


Fig. 3. (A) Prevalence and (B) types of TORCH infections during pregnancy.

all cases.

A history of TORCH infection was identified in 17.8% mothers in this study, among which rubella and toxoplasmosis were the most common infection associated with congenital hearing loss. This finding is in contrast with previous studies conducted in developed countries which found that cytomegalovirus was the most common TORCH microorganism causing congenital hearing loss [11,12]. Our findings are supported by previous studies showing that cytomegalovirus, rubella virus, and *T. gondii*, among other microorganisms such as herpes simplex virus, Zika virus, and lymphocytic choriomeningitis virus, may cause congenital hearing loss through prenatal intrauterine infection [13].

In this study, we underwent Chi Square test of several variables, namely maternal age, mother's education, mother's occupation, habilitation payment and hearing loss in other children to the age of diagnosis and the presence of habilitation. Our finding shows that there is a significant relationship between mother's education and the age of

diagnosis of the congenital hearing impairment children ($p < 0.05$). We also find a statistically significant association between mother's age, occupation and type of habilitation payment and the presence of habilitation ($p < 0.05$). Study by Sahli AS (2019) of 473 children who attended training center with the complaints of hearing and speech disorders in Turkey found a statistically significant association between the age at onset of training and several factors, such as the cause of admission, parental education level, employment status of the mother, occupation of the father, and socioeconomic status of the family [14]. Jeddi Z et al. (2012) research in Iran showed a significant decrease in the age at cochlear implantation with the increase of the level of education of the children's father and mother [15].

5. Conclusion

The present study suggests that children with a family history of

congenital hearing loss, a prenatal exposure to TORCH infection, and a maternal history of ototoxic drugs and herbal medicine use during pregnancy should be screened for hearing impairment at birth and be monitored throughout their childhood. Furthermore, as both maternal and paternal family history of congenital hearing loss is shown to be significant risk factors, we recommend young adults with family history of congenital hearing loss to undergo premarital screening and genetic counseling programs. Further research are required to confirm our findings on the association between the observed risk factors and the occurrence of congenital hearing loss.

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