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## **Relationship between Hyperuricemia with Auditory Disorder Based on Otoacoustic Emission**

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### **Abstract**

Hyperuricemia will cause changes of microvasculer of cochlea and direct penetration of uric acid in to OHC will cause stiffness of OHC and disturbances in electrical motility responses of OHC that lead to auditory disfunction. The purpose of this study is to know the influence of hyperuricemia to auditory disorder based on otoacoustic emission examination (OAE). This study is a cross sectional study on hyperuricemia patients in Dr Wahidin Sudirohusodo Hospital Makassar that fullfill the inclusion criteria. We performed Pure Tone Audiometry examination, Tympanometry and Otoacoustic Emission Examination. The data analyzed using Mann Whiney U test and Fisher's exact test. The results show that there are distinction of Hearing Limit Value (<0,05) between hyperuricemia group with control, in the same ear of each patient. From 29 hyperuricemia patients, we found 2 patients (6,9%) with refer OAE and mild SNHL. From this study, we can conclude that hyperuricemia could cause disturbances to cochlear function that lead to auditory disorder.

**Keywords:** Auditory Disorder; Hyperuricemia; Otoacoustic Emission (OAE).

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## **1. Introduction**

Hyperuricemia is defined as an increase in serum uric acid levels over 7.0 mg / dl in men and more than 6.0 mg / dl in women [1]. In the study by Hamed et al in US suggested that hyperuricemia as other systemic diseases that play a role in cell metabolism and can disrupt the function of the cochlea. Wilke et al studied 45 patients with hearing loss and found that hyperuricemia (35.9%) as a vascular risk factors as diabetes mellitus (63.8%) The elevation of uric acid in the blood was considered as a sensitive marker for the cause of the inflammation that occurs in various locations of the body. As the local ischemic tissue (hypoxia) that occurs in microvascular disease, ischemic causes the breakdown of RNA-DNA, which results in improved concentration and enzyme purine Xanthine Oxidase (XO). These enzymes will change xanthine to uric acid and superoxide production that stimulate inflammation as a major cause of damage to the target organ. Increasing the amount of oxidant causes oxidative stress which further reduces oxidative production of nitrite (NO) and worsened endothelial dysfunction [2,3]. Their high metabolic activity in the inner ear and the auditory pathway makes the cochlea become targets specific disease damaging cell metabolism, including hyperuricemia. Functional disorders of endocochlear potential (EP) was not solely caused by the malfunction of striae vaskularis (indirect mechanism) the loss due to the change of hyperuricemia [4]. Direct penetration of uric acid into Outer Hair Cells (OHC) will cause stiffness in OHC and motility disorders electrical response of OHC [5,6].

Information on the type and degree of hearing loss can be ascertained from the audiometric examination, where the results of pure tone audiometric examination, obtain information regarding the hearing threshold at the frequency of 125 - 8000 Hz [7]. This examination can provide a picture of a person's ability to hear. Damage to the cochlea as a part of the inner ear can cause sensorineural deafness. This damage can be detected by Otoacoustic Emission testing to obtain information about cochlear function that affects the patient ability to understand the conversation that is needed in communication and interaction between people [8-10]. Multivariate analyzes were performed by [5], showed abnormalities on examination OAE high frequency, related to the length of suffering and the degree of hyperuricemia.

Based on existing data, it was found many visits patients with hyperuricemia problems in the Wahidin Sudirohusodo hospital, Makassar where hyperuricemia can cause sensorineural hearing loss and can reduce the life quality of patients. From the description of the background and some of the above study, we tried to do some research to determine whether there is a hearing loss in patients with hyperuricemia.

## **2. Materials And Method**

### ***2.1 Place and time research***

This research was conducted in hospital of Dr. Wahidin Sudirohusodo, Makassar from September 2015 until April 2016.

### ***2.2 Design and variable of research***

This research is an observational analytic research using cross sectional design, with an examination of PTA

(Pure Tone audiometry), Tympanometry, and OAE (Otoacoustic emission). Variable consisted of independent variables (hyperuricemia), dependent variable (hearing), and variable between (Microangiopathy, striae vaskularis basement membrane thickening and stiffness OHC).

### ***2.3 Population and sample***

The study population was all patients with the results of serum uric acid > 6 mg / dL in women and > 7 mg / dL in men. The samples are all affordable population studies and met the inclusion criteria and had signed a consent form to participate in the study.

### ***2.4 Method of collecting data***

All patients with hyperuricemia in the study met the inclusion criteria listed by name, age, sex, address and occupation, then followed diagnose and questionnaires. For patients with hyperuricemia were willing to participate in the study, they were asked to sign a letter of consent (informed consent). After that, ENT examination was done, examination PTA, Tympanometry and OAE. All data were recorded in the form of research data.

### ***2.5 Data Analysis Techniques***

All the data obtained are recorded in the form of research data, then each analyzed with descriptive method by using SPSS.

## **3. Results**

It has been conducted a cross sectional study to determine whether there is a hearing loss in patients with hyperuricemia. This research was conducted at hospital of Dr.Wahidin Sudirohusodo Makassar in September 2015 until March 2016.

Subjects were patients with hyperuricemia were already diagnosed with the disease in parts that meet the inclusion criteria and willing to participate in this study. It was conducted the examination of PTA, Tympanometry and OAE.

There are 48 samples that participated in this study comprised 29 patients with hyperuricemia and 19 controls. From the whole sample was obtained 2 (6.9%) samples with test result of OAE refer and PTA sensorineural Hearingloss (Sensorineural hearing loss) according to the data analysis using Fisher's exact test where  $p = 0.36$  (Table 1).

Based on the research showed that there was no significant age difference ( $p > 0.05$ ) between hyperuricemia with the control group. Hyperuricemia group uric acid levels ranged from 6.2 to 13.4 g / d and control from 2.7 to 6.0. The duration of hyperuricemia suffer ranged from 6 months to 5 years (Table 2).

**Tables 1:** The comparison of the cochlear function impairment distribution between two groups

Groups	Cochlear function impairment		Total
	No	Yes	
Hyperuricemia	27 (93,1%)	2 (6,9%)	29 (100,0%)
Control	19 (100,0%)	0 (0,0%)	19 (100,0%)
Total	46 (95,8%)	2 (4,2%)	48 (100,0%)

Fisher's exact test → p=0,360

**Table 2:** Characteristics of the study sample

Variables	Min-Max/Mean (SD)		P
	Hyperuricemia (n=19)	Control (n=19)	
age (Year)	25-50/36,7 (6,9)	26-49/34,5	0,557
Urid Acid (gr/dL)	6,2-13,4/8,71 (1,98)	2,7-6,0 / 4,45(0,94)	<0,001
Time of suffering	0,5 – 5 / 2,5 (2,0)		

Based on data analysis using Mann whiney U test, there was a difference NAD significance (p <0.05) between groups with control hyperuricemia, on each same side ear (left or right). Average NAD on the right ear of hyperuricemia group (23.62) was higher than the control (21.71); nor on the left ear hyperuricemia group (23.49) was higher than the control (21.71) (Table 3).

**Table 3:** Comparison of NAD (hearing threshold value) between the two groups on each ear the same parties

Variables	Mean (SD)		P
	Hyperuricemia (n=19)	Control (n=19)	
Right NAD	23,62 (3,51)	21,71 (1,12)	0,029**
Left NAD	23,49 (3,60)	21,71(1,12)	0,029**

\*\*Mann Whiney U test

From this study, it was found that NAD (hearing threshold value) between the right ear and the left ear in hyperuricemia group was not significant (p> 0.05); nor between right and left ears in the control group according to the data analysis using Independent t test.

#### **4. Discussion**

This study shows that there is interference with the function of the cochlea which eventually cause hearing loss in patients with hyperuricemia. It was found 2 (6.9%) samples with results of OAE refer and mild PTA Sensorineural hearing loss.

Hearing loss is a decrease in one's ability to hear well on one or both ears. This will affect the ability of patients to understand the conversation that is needed in communication and interaction between people so as to reduce the life quality of patients [8-10]. Sensorineural hearing loss involves damage to the cochlea or nerve vestibulokoklear [6]. According to [5], one of the causes of hearing loss that is elevated levels of uric acid that can damage the stria vaskularis and stiffness in the OHC.

Cochlear function tests done using OAE, a new cochlear examination techniques, based on the objective, fast, easy, automated principle of electrophysiological and non-invasive with a sensitivity approaching 100%. The disadvantage is affected by noisy environments, the condition of the outer ear and the middle ear, as well as the relatively expensive price [11,12]

From the 48 samples studied, it was consisting of 29 sample groups of hyperuricemia and 19 control samples, obtained a lifespan of between 25-50 years. In this study sample was restricted to age 25-50 years on the grounds that hyperuricemia is rarely at a young age while older age (over 50 years) can already occur presbiakusis so as to obscure the accuracy of the study sample. From the 29 samples of hyperuricemia group in this study, 27 samples are people with asymptomatic hyperuricemia and symptomatic 2 with a complaint history of edema in the legs. In this study, also carried out the questionnaires to obtain data ever suffered hyperuricemia and get rid of other risk factors to the emergence of sensorineural hearing loss such as history of diabetes, hypercholesterolemia, hypertension, head injury, ear infections and the possibility of congenital hearing loss.

In this study, the levels of uric acid from hyperuricemia group ranged from 6.2 to 13.4 g / dl with a long-suffering ranged from 6 months-5 years. While the levels of uric acid in the control group ranged from 2.7 to 6.0 g / dl. From these data when connected with examination results of PTA, it was seen that the increase in patients with hyperuricemia hearing threshold is proportional to the uric acid levels and duration of suffering. The results are consistent with research conducted by [5], which gets the auditory function disorders occur in samples with long-suffering over 2.9 years and uric acid levels above 8.1 g / dl. Impaired function of the cochlea and hearing disorders occur in samples 4 and 5 years old suffer otherwise was not found in samples of hyperuricemia with long suffered less than 4 years and controls (0.0%). In the sample group were the result of hyperuricemia without cochlear function disorders (93.1%) with long-suffering almost the same as the sample impaired cochlear function was found in people who consume drugs regularly anti hyperuricemia.

From this study, there was found NAD significant difference ( $p < 0.05$ ) between groups with control hyperuricemia, on each ear the same side (left or right). The Average NAD on the right ear of hyperuricemia group (23.62) was higher than the control (21.71); nor on the left ear hyperuricemia group (23.49) was higher than the control (21.71). This suggests that hyperuricemia influence on NAD sufferers. It was found 2 sample

groups of hyperuricemia with NAD normal speech frequency hearing threshold but there was a decrease in the frequency of 6000 Hz and 8000 Hz both in air conduction and bone conduction as well as the results of OAE Pass on both ears.

The result of [5] research obtained that there was a decrease in the threshold of hearing, especially at high frequencies (4 and 5 kHz). Another study by [13] was getting a hearing loss especially at high frequencies. There are obtained average NAD right ear was higher than the control group. This is because the results of PTA examination found 5 samples with a mild degree of hearing loss in the right ear while the control samples were obtained NAD all normal; so on the ears left.

The NAD results between right and left ear in hyperuricemia group was not statistically significant ( $p > 0.05$ ) because NAD examination results showed that nearly symmetrical in both ears either on samples with normal NAD as well as those found hearing loss. This research also shows that there is interference with the function of the cochlea on a sample group of hyperuricemia was 2 samples among 29 samples of hyperuricemia (6.9%), although statistically insignificantly different from where the test results of Fisher 's Exact showed  $p > 0.05$ . One of the two samples of the malfunction with the result of unilateral cochlear decline audiogram hearing threshold at frequencies 2000, 3000, 4000, 6000, and 8000 Hz with result of OAE Refer to the right ear. The previous research conducted by Sherifa also show the same thing that hyperuricemia may affect the function of the cochlea and bilateral mild of sensorineural hearing loss. The existence of cochlear function impairment and unilateral hearing loss in one of the samples as a result of hyperuricemia as a risk factor for systemic, where they found about 17% of cases are unilateral.

Limitation of this study was there are no earlier audiometric examination so hearing status was not known before a patient suffering from hyperuricemia.

## **5. Conclusion**

The researchers concluded that the measurement of hearing threshold of hyperuricemia patients in the hospital of Dr.Wahidin Sudirohusodo Makassar obtained average of 23.62 db on the right ear and the left ear with 23.49 db. The mean threshold of hearing people with hyperuricemia higher than controls. There cochlear function impairment in patients with hyperuricemia (6.9%) .There are relationship between hyperuricemia with impaired function of the cochlea. Researchers suggest the cooperation should be made with the internal part especially Rheumatology for hearing evaluation, especially for patients who do not regularly consume anti hyperuricemia. Besides of that, it also needs to be done further research to assess the presence of uric acid in the cochlea of animals.

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