ORIGINAL ARTICLE

INDEX COPERNICUS INTERNATIONAL

# Is the Monocyte/HDL Ratio a Prognostic Marker of Idiopathic Sudden Hearing Loss?

**Authors' Contribution:**
**A** – Study Design
**B** – Data Collection
**C** – Statistical Analysis
**D** – Data Interpretation
**E** – Manuscript Preparation
**F** – Literature Search
**G** – Funds Collection

Hasan Emre Koçak[ABCE], Harun Acipayam[ABCE], Mustafa Suphi Elbistanlı[DF], Ayşe Pelin Yiğider[DF], Wesam Alakhras[DG], Mehmet Nurettin Kıral[EF], Fatma Tülin Kayhan[ACDF]

Bakırköy Dr.Sadi Konuk Training and Research Hospital, Department of Otorhinolaryngology - Head and Neck Surgery, Istanbul, Turkey

Article history: Received: 09.05.2016 Accepted: 02.06.2016 Published: 23.08.2016

**ABSTRACT:**

**Objective:** In this study, our aim was to investigate whether Monocyte/HDL ratio is a marker of the prognosis of the idiopathic sudden hearing loss (ISHL).

**Study design:** Retrospective, case-control clinical trial.

**Materials and Methods:** 45 patients, who were diagnosed with idiopathic sudden hearing loss and were treated with the same therapy regime and 47 healthy volunteers, who applied to the hospital for routine controls and had audiological and laboratory examination between March 2014 and December 2015, were included in the study. Monocyte/HDL ratios of the patients in the study and control groups were calculated from the results of the blood counts and biochemical analysis. Additionally, the study group was divided into two sub-groups regarding their responses (responders and non-responders) to the treatment determined by the audiological examination, which was carried out after 3 months according to the Siegel criteria. The Monocyte/HDL ratios between the groups were statistically evaluated.

**Results:** There was no statistically significant difference between the MHRs of the study and control groups (p=0.574). However, the MHR was significantly higher in the non-responders' group compared with the responders' group, although they were treated with the same therapy regimen (p=0.005).

**Conclusion:** There was no difference in MHRs between study and control groups. However, as MHR was higher in the patients with good prognosis compared with the patients with bad prognosis, we believe that regarding the ISHL, MHR is not a predictive value but might have prognostic marker.

**KEYWORDS:** hearing loss, HDL, Monocyte, Ratio

## INTRODUCTION

Idiopathic sudden hearing loss (ISHL) is defined as a sensorineural hearing loss greater than 30 dB measured over at least three contiguous frequencies and lasting at least 72 hours. It is believed that it has a multi-factorial etiology and viral infections, vascular failure and obstructions, inflammatory events, autoimmune and immunological disorders were considered as possible causes of ISHL (1). Nevertheless, none them has been demonstrated to be a definitive etiological factor in the development of ISHL. In recent studies, chronic inflammation and oxidative stress were reported as contributing factors (1,2). Monocytes and macrophages are the most abundant cells that secrete proinflammatory and prooxidant cytokines as part of inflammatory reactions[3]. Moreover, it was demonstrated that high-density lipoproteins (HDL) protected endothelial cells against the noxious effects of the low-density proteins (LDL) and prevented the oxidation of the LDL molecules. Therefore, it was believed that HDL had both anti-inflammatory and anti-oxidant effects[4]. In recent studies, the ratio of the monocyte count to the HDL cholesterol level (MHR) was defined as an easy calculable cardiovascular prognostic marker indicating the extent of inflammattion and oxidative stress (4,5,6).

The objective of our study was to investigate whether the MHR was a prognostic marker in ISHL.


DOI: 10.5604/00306657.1209435

## MATERIALS AND METHODS

### Participants

This study had a retrospective design. The approval of the local ethics committee was obtained (Ethics Committee No: 2016-03-04). The data were accessed in patient files and were subseqiently analyzed. We included 45 patients diagnosed with idiopathic sudden hearing loss and receving the same treatment and 47 healthy volunteers who undergoing routine audiological and laboratory examinations between March 2014 and December 2015. Patients with a sensineurl hearing loss greater than 30 dB, measured over at least three contiguous frequencies and lasting at least for 72 hours, were diagnosed with ISHL. In all patients, systemic physical examination, detailed otological examination, hematological and biochemical studies, audiological evaluation and Magnetic Resonance Imaging (MRI) were carried out. Patients who had hearing loss due to retro-cochlear disorders, autoimmune inner ear disorders, infections, bilateral ISHL or smoked were excluded from the study.

### Hematological Evaluation

Blood samples were taken from patients at admission. The MHR was calculated as a simple proportion of the monocyte count to the HDL value. The monocyte count was determined with the Pentra 120 Retic Hematology Analyzer (ABX, Montpellier, France) as part of the routine complete blood count. The reference value for monocyte in our laboratory is 4,4–12,7%.

### Hearing Evaluation

All patients were evaluated with pure tone audiogram and tympanometry. Air and bone conduction at frequencies of 250Hz, 500Hz, 1kHz, 2kHz, 4kHz, and 8kHz were evaluated. With the analytic mean of these 6 frequencies, the pure-tone average was calculated. Patients with non-type A tympanogram were excluded from the study. All patients had audiological evaluations at admission and in the third month after the completion of treatment. Siegel (7) criteria were used for the assessment of treatment response (Tab. I.).

The patients were divided into two subgroups according to their recovery status – as responders and non-responders. According to the Siegel criteria, full, partial and poor recovery (Type 1, 2, 3) was defined as "responding to treatment" and no recovery (Type 4) was defined as "non-responding to treatment." All patients received 1mg/kg parenteral methylprednisolone (Prednol-L®, Mustafa Nevzat, Istanbul Turkey) for 14 days (full dose in the first 3 days, then the dose was decreased by 5mg every day) and intratympanic dexamethasone (Dekort® 8 mg/2mL, 1 vial, Deva, Istanbul, Turkey) every second day (a total of 8 doses).

**Tab. I.** Siegel criteria * Final hearing level: 500,1000,2000 and 4000 Hz arithmetic mean (Committee on Hearing and Equilibrium of the American Academy of Otolaryngology-Head and Neck Surgery)

| TYPE | EVALUATION | EXPLANATION |
|---|---|---|
| 1 | Complete recovery | Final hearing level* is 25 dB or better, regardless of the amount of gain |
| 2 | Partial recovery | More than 15 dB hearing gain and final hearing is between 25-45dB |
| 3 | Poor recovery | More than 15 dB hearing gain and final hearing is 45 dB or worse |
| 4 | No recovery | Gain less than 15 dB |

### Statistical Analysis

Mean, standard deviation, range, frequency and ratio values were used for the descriptive analysis of the data. The normality of distribution of variables was tested with the Kolmogorov-Smirnov Test. The Mann-Whitney U Test and the independent samples t-Test were used for the analysis of the qualitative data. For quantitative data the Chi-square test was used. Calculations were carried out with the use of SPSS v22.0 software (PASW for Windows, Rel. 18.0.0. 2009; SPSS Inc., Chicago, IL, USA).

## RESULTS

Forty-five SHL patients and 47 healthy controls were included in the study. Twenty-seven patients were classified as "responders" and 18 patients as "non-responders" according to the Siegel criteria. The mean age of patients was 31.1 ± 7.4 years and 32.4 ± 8.1 years in controls, respectively. Twenty-eight patients were female and 25 male. Twenty-eight controls were female and 19 male. There was no significant differences between the groups regarding the age and gender (Tab. II.).

The demographic characteristics and laboratory findings of patients and healthy controls are presented in Table 2. The average monocyte counts were 563±238x$10^9$/L in patients and 524±173x$10^9$/L in controls, respectively. The mean HDL value was 46.0±8.9 mg/dL in patients and 46.7±10.3 mg/dL controls, respectively. The differences between these values were not statistically significant (p=0.793; p=0.659 respec-

**Tab. II.** Demographic characteristics and laboratory findings of patients and healthy controls

| | | STUDY GROUP | | CONTROL GROUP | | |
|---|---|---|---|---|---|---|
| | | MEAN±.S.D./N-% | MED (MIN-MAX) | MEAN±.S.D./N-% | MED(MIN-MAX) | P |
| Age | | 31,1 (+7,4) | 32 (16,0–47,0) | 32,4 (+8,1) | 34,0 (16,0–49,0) | 0,360 |
| Gender | Female | 20 (44,4%) | | 28 (62,2%) | | 0,146 |
| | Male | 25 (55,6%) | | 19 (42,2%) | | |
| Monocytes | | 563 (+238) | 510 (100-1320) | 524 (+173) | 510 (100-1000) | 0,793 |
| HDL | | 46,0 (+8,9) | 44,0 (33,0-69,0) | 46,7 (+10,3) | 44,0 (28,–79,0) | 0,659 |
| Monocytes/HDL | | 12,8 (+6,1) | 12,1 (1,6–32,2) | 11,8 (+4,9) | 11,1 (2,3–26,8) | 0,524 |

Mann-whitney u test / t test / Chi-square test

**Tab. III.** Demographic characteristics and laboratory findings of responders and non-responders

| | RESPONDERS | | NON-RESPONDERS | | |
|---|---|---|---|---|---|
| | MEAN±.S.D./N-% | MED (MIN-MAX) | MEAN±.S.D./N-% | MED(MIN-MAX) | P |
| Age | 30,4 (+8,3) | 32,0 (16,0–47,0) | 32,1 (+5,8) | 31,5 (22,0–44,0) | 0,360 |
| Monocytes | 476 (+156) | 400 (280–894) | 693 (+281) | 700 (100–1320) | 0,002 |
| HDL | 46,3 (+9,0) | 44,0 (35,0–69,0) | 45,7 (+8,9) | 43,5 (33,0–63,0) | 0,754 |
| Monocytes/HDL | 10,7 (+4,3) | 10,8 (4,3–23,5) | 15,9 (+7,2) | 14,4 (1,6–32,2) | 0,005 |

Mann-whitney u test / Chi-square test

tively). The MHR was 12.8±6.1 in patients and 11.8±4.9 in controls, respectively. The difference of the MHR values between the groups was also not statistically significant (p=0.524), (Tab. II).

The group of patients was divided into two subgroups according to the results of the audiological examination performed in the 3rd month. According to the Siegel criteria, Type e1, 2 and 3 were classified as responders and type 4 as non-responders. The mean monocyte count was 476±156 in responders and 693±281 in non-responders, respectively. This difference was statistically significant (p=0.002). HDL values were 46.3±9 and 45.7±8.9 respectively, but the difference was not significant (p=0.754). The MHR was 10.7±4.3 in the responders and 15.9±7.2 in non-responders, and this difference was significant (p=0.005) (Tab. III).

## DISCUSSION

SHL is a disorder with an unknown etiology and is usually defined as idiopathic. It is believed that it develops as a result of multifactorial processes. Several hypotheses were proposed to explain its etiology. The most emphasized factors were inflammation, viral infections, and hypoxia (8). The main rationale behind the systemic and intratympanic steroid administration for the treatment of the sudden hearing loss is to reduce inflammation[2]. Hyperbaric oxygen treatment, used in combination with steroids in the treatment of SHL or as an alternative intervention in the salvage therapy, supported the SHL treatment by increasing the oxygenation in the inner ear. Therefore, it was believed that the cochlear hypo-oxygenation, which was assumed to play a role in the etiology of SHL, might be related to cochlear vasospasm or cochlear artery obstruction or occlusion (9).

We believe that an unstable atherosclerotic plaque, which might cause an occlusion of the cochlear artery, might be a basis for the development of SHL. Moreover, factors accelerating the progress of atherosclerosis might be correlated with the histopathology of the disease. Monocytes and macrophages might lead to the emergence of the foam cells within the atherosclerotic plaques as a result of phagocytosis of oxidized LDLs, and thus, they might decrease the stability of plaques (10). It was already demonstrated that monocyte count was an important and independent factor for the development and progression of the atherosclerotic plaques (6,11). In contrast to the pro-atherosclerotic properties of monocytes, HDL has a vasoprotective role by way of prevention of LDL oxidation and due to anti-inflammatory, antithrombotic, and antioxidant effects (12). Recently, it was believed that the MHR was a new cardiovascular prognostic marker indicating inflammation and oxidative stress (4-6). It was already shown that the MHR was correlated with

high serum levels of high-sensitive C-reactive protein (hs-CRP) (4,13). Canpolat et al. (4) demonstrated that the MHR was correlated with diffuse atherosclerosis, inflammation, and microvascular dysfunction and decreased the coronary flow in cardiovascular disorders. As similar factors might play a role in the etiopathogenesis of SHL, we believe that the MHR might be correlated with the prognosis of the disease. The most important feature of our research is that it is the first to study this topic.

Comparison of the MHR values between all SHL patients and the control group did not reveal any significant difference (p=0.524). There was also no statistically significant difference between the groups regarding monocyte counts and HDL values (p=0.793 and p=0.659 respectively). However, in the audiological examination performed in the 3rd month, MHR values in responders was lower than in non-responders (according to the Siegel criteria) (p=0.005). Moreover, monocyte counts were also low in the responders' group (p=0.002), but there was no significant difference with respect to HDL values (p=0.754).

In light of these findings - no difference between patients and controls in MHR values, we believe that the MHR is not an independent risk factor in SHL patients. However, high MHR values may be correlated with a poor prognosis, which might be associated with microvascular damage and increased inflammation.

## CONCLUSION

Although the MHR value was not different between patients and controls, it was lower in patients with a good prognosis than in patients with a poor prognosis. Therefore, we propose that the MHR might a prognostic factor and not a predictive factor. As further elucidation of this finding may clarify the etiopathogenesis of SHL, studies with larger samples are required.

## REFERENCES


1. O'Malley M.R., Matthew R,. Haynes D.S.: Sudden hearing loss. Otolaryngologic Clinics of North America. 2008; 41 (3): 633–649.
2. Seo Y.J, Choi J.Y, Moon I.N.: Neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio: novel markers for diagnosis and prognosis in patients with idiopathic sudden sensorineural hearing loss. Disease Markers. 2014.
3. Ancuta P., Jianbin W., Gabuzda D.: CD16+ monocytes produce IL-6, CCL2 and matrix metalloproteinase-9 upon interaction with CX3CL1-expressing endothelial cells. Journal of leukocyte biology. 2006; 80 (5): 1156–1164.
4. Canpolat U., Çetin E.H., Cetin S., Aydin S., Akboga M.K., Yayla C., Turak O., Aras D., Aydogdu S.: Association of monocyte-to-HDL cholesterol ratio with slow coronary flow is linked to systemic inflammation. Clin. Appl. Thromb.Hemost. 2016; 22: 476–482.
5. Kanbay M., Solak,Y., Unal H.U., Kurt Y.G., Gok M., Cetinkaya H., Covic A.: Monocyte count/HDL cholesterol ratio and cardiovascular events in patients with chronic kidney disease. International urology and nephrology. 2014; 46 (8): 1619–1625.
6. Akboga M. K., Balci K. G., Maden O., Ertem A. G., Kirbas O., Yayla C., Aydogdu S.: Usefulness of monocyte to HDL-cholesterol ratio to predict high SYNTAX score in patients with stable coronary artery disease. Biomarkers in Medicine. 2016; 10 (4): 375–383.
7. Siegel L.G.: The treatment of idiopathic sudden sensorineural hearing loss. Otolaryngologic clinics of North America. 1975, 8 (2): 467.
8. O'Malley M.R., Haynes D.S.: Sudden hearing loss. Otolaryngol. Clin. North Am. 2008; 41: 633–649.
9. Lamm H., Müller-Kortkamp C., Warnecke A., Pohl F., Paasche G., Lenarz T., Stolle S.R.: Concurrent hyperbaric oxygen therapy and intratympanic steroid application as salvage therapy after severe sudden sensorineural hearing loss. Clinical Case Reports. 2016; 4 (3): 287–293.
10. Johnsen S.H., Fosse E., Joakimsen O. et al.: Monocyte count is a predictor of novel plaque formation: a 7-year follow-up study of 2610 persons without carotid plaque at baseline the Tromso Study. Stroke. 2005; 36 (4); 715–719.
11. Karabacak M., Kahraman F., Sert M., Celik E., Adali M.K., Varol E.: Increased plasma monocyte chemoattractant protein-1 levels in patients with isolated low high-density lipoprotein cholesterol. Scandinavian Journal of Clinical and Laboratory Investigation. 2015; 75 (4): 327–332.
12. Kuvin J.T., Rämet M.E., Patel A.R., Pandian N.G., Mendelsohn M.E., Karas R.H.: A novel mechanism for the beneficial vascular effects of high-density lipoprotein cholesterol: enhanced vasorelaxation and increased endothelial nitric oxide synthase expression. Am. Heart. J. 2002; 144 (1): 165–172.
13. Kundi H., Kiziltunc E., Cetin M., Cicekcioglu H., Cetin Z.G., Cicek G., Ornek E.: Association of monocyte/HDL-C ratio with SYNTAX scores in patients with stable coronary artery disease. Herz. 2015: 1–7.

Word count: 1700 Tables: 3 Figures: – References: 13

Access the article online: DOI:10.5604/00306657.1209435 Full-text PDF: www.otolaryngologypl.com/fulltxt.php?lCID=1209435

Corresponding author: Hasan Emre Koçak; Bakırköy Dr.Sadi Konuk Training and Research Hospital, Department of Otorhinolaryngology - Head and Neck Surgery, Turkey; e-mail: drhekbb@gmail.com



Competing interests: The authors declare that they have no competing interests.

Cite this article as: Koçak H. E., Acipayam H., Elbistanlı M. S., Yiğider A. P., Alakhras W., Kıral M. N., Kayhan F. T.: Is the Monocyte/HDL Ratio a Prognostic Marker of Idiopathic Sudden Hearing Loss?; Otolaryngol Pol 2016; 70 (5): 26-30