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Review Article

Metabolic Syndrome and its Relationship with Hearing Loss: Review of Literature

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Abstract

Metabolic syndrome (Met S) is a serious health problem that is becoming increasingly common all over the world. This almost pandemic condition includes a variety of abnormalities such as obesity, hypertension, impaired glucose tolerance, high triglycerides levels, and low high-density lipoprotein (HDL) levels. Although the exact etiopathogenesis is not known, insulin resistance seems to play the most important role. The presence of Met S is important because it is associated with the risk of stroke, heart disease, and the development of diabetes mellitus. In addition to cardiometabolic complications, it is a disorder that can cause multysistemic problems, including hearing loss. There are many studies supporting the relationship between Met S and hearing loss in the literature. The precise mechanism behind this association are not yet fully understood, but it is thought that the metabolic changes (insulin resistance, inflammation, oxidative stress) that occure in Met S may damage the blood vessels and nerves of inner ear, which can lead to hearing loss. In particular, high blood pressure and high blood sugar levels are thought to be major contributors to this process.

Hearing loss is a problem that increases with aging and can develop due to various environmental factors such as noise exposure and infections as well as genetic reasons. It is a common a major problem that the quality of life directly affects negatively.

Treatment for Met S usually involves lifestyle changes, such as increasing physical activity and improving diet, as well as medications to manage the individual risk factors. Diagnosing and managing Met S may therefore be important for preventing or managing hearing loss. The aim of this review is to try to explain the relationship between Met S and hearing loss and to provide detailed literature support. In addition, new treatment approaches targeting risk factors will be mentioned.

Keywords: Metabolic Syndrome; Hearing Loss; Risk Factors; Therapy

Metabolic syndrome is one of the most researched and scanned topics in PubMed pages recently. What is the reason of this? We decided to write a review together with our teammates to solve this issue deeply and to find out what this MetS has to do with any diseases that harm general health, and how it can trigger. In particular, we wanted to examine how much the MetS has an effect on hearing loss, what factors, and the worldwide studies on this subject, and share the theories we found as a result of the review.

Type 2 diabetes mellitus, which is thought to play a role in insulin resistance on the basis of MetS, is a combination of risk

factors that can lead to the development of DM and coronary artery disease (CAD) [1]. MetS is also defined with different terms such as insulin resistance syndrome, syndrome X, polymetabolic syndrome, fatal quartet, and civilization syndrome. This syndrome; It includes components of obesity, hypertension (HT), impaired glucose tolerance, high triglyceride (TG) and low high-density lipoprotein (HDL) components, and its frequency is increasing all over the world [2].

The diagnosis of metabolic syndrome is made when all 3 of the risk factors are present. MetS leads to vascular endothelial dysfunction, increased body inflammation, and adipose tissue deposition, which is a risk factor for cardiovascular and cerebrovascular disease (such as diabetes, hypertension, chronic kidney disease, stroke, myocardial infarction, and angina pectoris). MetS has been found to be associated with a variety of clinical conditions, including stroke, myocardial infarction, death from cardiovascular disease, and diabetes [3].

It has been reported that the incidence of MetS and the associated ischemic heart disease frequency have increased in many developing countries, especially in the last three decades, due to industrialization, excessive calorie diet, insufficient physical activity, and adoption of a sedentary lifestyle [4]. The MetS is defined by different organizations, including the World Health Organization (WHO), the International Diabetes Federation (IDF), and the National Cholesterol Education Program-Adult Treatment Panel (NCEPATP) III. However, the variables considered for the diagnosis of MetS by all these institutions are blood pressure, plasma TG level, HDL cholesterol level, plasma glucose level, and waist circumference [5]. The prevalence of MetS is increasing worldwide at a rate that varies widely by demographic factors such as age, gender, and ethnicity. The significant increase in MetS in the last decade in Western countries has become a very serious public health problem [6,7].

The metabolic syndrome is important because of its association with an increased prevalence of diabetes and a higher risk of cardiovascular events such as heart disease and stroke, which have become major public health problems [8]. Dysregulation of certain adipokines may promote pathogenic conditions associated with obesity, lipid accumulation and insulin resistance. These increase the risk of atherosclerosis [9].

MetS, a constellation of various metabolic components, including abdominal obesity, high blood pressure, high fasting glucose, and dyslipidemia, has been suggested as an independent risk factor for HL [5,6].

Central obesity is the main cause of the etiological cascade of the metabolic syndrome. Abnormal fat distribution, rather than adiposity itself, is a more important risk factor for obesity-related disorders [10,11]. Recent research has shown that visceral adipose tissue is 'ectopic fat' originating from subcutaneous adipose tissue as fat that overflows beyond its extra energy storage capacity [12,13]. In 'ectopic fat', visceral adipose tissue is associated with insulin resistance, lipoprotein metabolism and high blood pressure [14]. Adipose tissue is an endocrine organ that expresses and secretes a variety of adipokines [15]. Adipose tissue includes adipocytes, anterior adipocytes, adipose tissue macrophages, other immune cells, and vascular components. Many factors, mainly secreted from adipocytes and adipose tissue macrophages, contribute to the development of metabolic syndrome [16,17].

More recently, the chronic inflammatory state accompanying central obesity has been shown to be an important factor in both the metabolic syndrome and its development, with associated pathophysiological consequences [18]. In this context, the role of factors originating from adipose tissue in the etiology of metabolic syndrome and the mechanisms suggested to be related are discussed.

Hearing loss is one of the many complications associated with metabolic syndrome. In the recent years, it has been showed by different studies that metabolic syndrome and its components are associated with gradual sensorineural hearing loss [19-23]. Sensorineural hearing loss is an important public health problem with an increasing prevalence as life expectancy increases [24]. For example, the Global Burden of Disease Study reported that the prevalence of hearing loss rose from 14.33% in 1990 to 18.06% in 2015, making it the fifth most common cause of disability in both developed and developing countries [25]. About 50% of people over the age of 70 and 80% of people over the age of 85 have hearing loss that affects their communication skills and social life [24]. Although various risk factors such as genetic factors, inflammatory processes, systemic diseases, noise, drugs, oxidative stress and aging have been reported to contribute to hearing loss, the pathophysiological mechanisms of hearing loss are complex [26].

Hearing loss (HL) results in reduced quality of life and limited communication with others, which can lead to impaired social connectivity and have adverse effects on the behavioral and social psychological state of those affected by HL. As a result, HL can reduce self-esteem and lead to decreased social activities, feelings of isolation, depression and anxiety, and poor quality of life [27,28].

As the prevalence of HL is expected to increase further due to the progressive aging of the world population, it is important to identify modifiable risk factors. of HL. It has been suggested that many factors are associated with the risk of HL. In addition to age, it is known that disease risk factors such as cardiovascular hypertension, hyperglycemia, obesity, smoking and exposure to noise are associated with hearing impairment [29].

The pathophysiological reasons underlying hearing loss are very complicated. Various risk factors such as inflammatory processes, systemic diseases, genetic factors and oxidative stress have been blamed [31]. The relationship between inflammatory diseases such as diabetes and cardiovascular disease and hearing loss has been demonstrated [30,33]. Some components of MetS are risk factors associated with sensorineural hearing loss. These factors are HT, hyperlipidemia and low HDL level. Hyperlipidemia is thought to impair the morphology and function of the cochlear [30,32]. It is also known that; Presence of MetS increases the risk of cardiovascular events and Type 2 DM development [33]. Interestingly, there is a relationship between high frequency sensorineural hearing loss and DM. MetS; HT consists of hypertriglyceridemia, glucose intolerance, central obesity and low HDL components. This situation is associated with cardiovascular disease, increased risk of CAD and DM, and all kinds of mortality [30]. To date, very few studies have investigated a direct relationship between hearing loss and MetS: Zhao., *et al*. in their study with 165 cases, found a relationship between TG elevation, one of the MetS components, and age-related hearing loss.

In addition, among all combinations of MetS components, the combination of TG and HDL cholesterol, the combination of TG and blood sugar, and the combination of TG and blood pressure were correlated with age-related hearing loss [32]. In another Korean study, 16,799 men (19 years, 7,170 men and 9,629 women) were included. Data were obtained from the Fifth Korea National Health and Nutrition Examination Questionnaire (2010-2012), and hearing impairment was reported in 47% of cases with MetS. In addition, fasting plasma glucose increase was found to be independently associated with hearing loss [34]. According to the results of another study published in 2017, which included 11,114 professional drivers, there was no significant relationship between obesity, HT, hypertriglyceridemia, high fasting glucose level, waist circumference and sensorineural hearing loss, which are among the MetS components. relationship is available [35]. According to another literature data, it has been reported that Type 2 DM is associated with microvascular complications that may affect hearing. The duration of diabetes and poor glycemic control were found to be associated with sensorineural hearing loss after adjusting for age [36].

In the study by Anuja Bhargava., *et al*. [37] the mean age of the patients examined was 37.06 ± 7.13 years, mostly female (65%). Majority of the patients were women (65%). The majority of patients (62%) had hearing loss. Regarding the severity of the hearing loss, mild hearing loss was the highest (35%), followed by moderate hearing loss (23%). Only 4 (4%) cases had severe hearing loss. With respect to severity of hearing loss, maximum (35%) had mild hearing loss, followed by moderate hearing loss (23%). And as a result of univariate analysis in this study, patients with hearing loss revealed significantly higher mean age, waist circumference, and fasting blood glucose levels, and patients with normal hearing had significantly higher systolic and diastolic blood pressures compared to those with normal hearing. Although, there are no Indian studies evaluating the prevalence of sensorineural hearing loss in metabolic syndrome patients, however, at component level, there are studies that have reported results similar to present study. In one such study, Srinivas., *et al*. [38] and Dadhich., *et al*. [39] also found prevalence of sensorineural hearing loss to be 66% and 73% in type 2 diabetes mellitus patients. In another study, Parmar., *et al*. [40] reported a prevalence of sensorineural hearing loss to the tune of 62% among diabetic and/or hyperlipidemia patients. Thus prevalence of hearing loss in metabolic syndrome patients in present study is in accordance with contemporary similar studies. In present study, maximum mild hearing loss was seen in 35%, moderate in 23% and severe hearing loss in 4% cases. Similar to present study, Dadhich., *et al*. [39] also reported a dominance of mild (48%), followed by moderate (21%) hearing loss and reported severe hearing loss in only 1% case. Swaminathan., *et al*. [41] too in their study reported the nature of hearing loss among diabetics and hyperlipidemic patients to be of mild to moderate order.

Alessandra G. Samelli., *et al*. 2017 published "Diabetes mellitus and sensorineural hearing loss: is there an association? He tried to prove that hearing loss is related to diabetes in his clinical studies called Baseline of the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil). 901 adult and elderly brazilian citizens participated in this study, and in their study, hearing loss and speech test results were significantly worse in the diabetic group than in the nondiabetic group. However, no significant differences were found between participants with and without diabetes after adjusting for age, gender, and presence of hypertension. Hearing loss was not affected by occupational noise exposure in the diabetic and nondiabetic groups. In addition, no association was observed between duration of diabetes and hearing loss after adjusting for age, gender, and hypertension. There are many studies that have worked on the same subject and come to the same conclusion [42].

Published in 2022, Dongye Guo., *et al*. in their comprehensive published review, emphasizes that Metabolic syndrome (MetS) is a risk factor for age-related hearing loss (ARHL). Diabetes is an important chronic disease with an increasing prevalence worldwide. It is estimated that the number of people with type 2 diabetes (T2DM) in the world will reach 700 million by 2045 and constitute 10.9% of the world population induced type 1 diabetes (T1DM) and T2DM in CBA/CaJ mice and found that the ABR threshold increased in each group in line with the characteristic performance of ARHL. Two months after diabetes induction, both the T1DM group and the T2DM group exhibited a significant reduction in distortion product otoacoustic emission amplitude at higher frequencies, while the control group did not show any significant change. This suggests that induction of diabetes in adult CBA/CaJ mice may exacerbate ARHL [43].

Moreover, not only DM but MetS affect hearing loss, other components: dyslipidemia, obesity, hypertension can cause age-related hearing loss, and the adverse impact of Metabolic syndrome (MetS) on hearing is related to the number of diagnostic components met. Dyslipidemia: MetS-associated dyslipidemia manifests primarily as high triglyceride (TG) levels and low high-density lipoprotein cholesterol (HDL-C) levels, both of which contribute to ARHL. Hyperlipidemia usually leads to atherosclerosis manifesting as spiral modular artery (SMA) stenosis and endothelial dysfunction in the cochlea. Atherosclerosis can disrupt the blood supply to the cochlea and lead to ischemia and hypoxia injury. As a result, hairy cell (HC) loss and spiral ganglion neuron (SGN) damage are exacerbated, and progression of ARHL is therefore accelerated. Obesity itself and its accompanying diseases have very important effects on hearing loss. Body mass index (BMI), an important indicator of obesity, is a risk factor for, researchers found that subjects with higher BMIs had more severe hearing loss, after adjusting for other influencing factors. Hypertension may exacerbate age-related hearing loss. In this regard. Hypertension is not only a common disease in the elderly, but also a component of MetS, and they have shown a significant association with the incidence and progression of ARHL [44].

Original article published by Hlologelo Ramatsoma and Sean Mark Patrick published in 2022. In this article, 106 (54.7% female) hypertensive adults and 92 (52.2% female) non-hypertensive, sex- and age-matched adults, aged 18-55, residing in South Africa, in a tertiary care hospital in South Africa. A cross-sectional study was carried out. And the result was a 37.4% prevalence of hearing loss among hypertensive adults compared to 14.1% in the non-hypertensive group ($P = 0.000$, $\chi 2 = 14.00$). The mean EHF pure tone was 44.1 ± 19.2 dB HL in the hypertensive group and 20.0 ± 18.3 dB HL in the control group. Bilateral mild sensorineural hearing loss was the most common type of hearing loss among hypertensive adults. A higher prevalence of tinnitus (41.5%) was found in the hypertensive group compared to the control group (22.8%) ($P = 0.008$, $\chi 2 = 7.09$). In this study, 30.3% of hypertensive patients had tinnitus without hearing loss in adults compared to 17.7% of non-hypertensive adults [45].

After a study in the article "The Association between Duration of Noise Exposure in the Workplace and Glucose Metabolism Status: Evidence from the Korea National Health and Nutrition Examination Survey"- published in the Korean Journal of Family Medicine in 2022 [46], HbA1c levels were found in exposure to noise. was significantly higher in the no-noise group than in the no-noise group. HbA1c levels were significantly higher in those exposed to occupational noise for more than 20 years. In a subgroup analysis among those exposed to noise for more than 20 years, the non-aerobic physical activity group had significantly higher HbA1c levels than the physical activity group. They also found evidence that among those exposed to noise for more than 20 years, the non-hearing protection group had significantly higher HbA1c levels than those who wore hearing protection.

In the study of Federico Maria Gioacchini., *et al*. individuals with DM are at high risk for hearing impairment, but this particular population can often have confounding comorbidities. We believe it is important to include a detailed assessment of hearing threshold in the diagnostic investigations of diabetic patients, as the severity, course, and consequences of hearing damage may be affected by the medical treatment of DM and the medical and rehabilitative management of HL. Interventions aimed at controlling factors that can cause morphological and functional changes in the cochlea are of critical importance in the management of diabetic hearing damage [47].

Jerremy Chee., *et al*. in a retrospective, cross-sectional study of 1787 adults aged 60-100 years who had undergone a comprehensive audiological evaluation at a community-based audiology clinic, also found that DM is an independent risk factor for the presence of at least moderate hearing in the community-dwelling elderly, and It emphasizes that individuals with DM <70 years of age should be screened for hearing loss to ensure early intervention [48].

The first step in treatment; Lifestyle changes and while teaching this, it should be emphasized that smoking and alcohol use, which are certain to increase cardiovascular, metabolic and hepatic complications, should also be stopped. If lifestyle changes are insufficient, pharmacological treatment should be initiated. In terms of hyperlipidemia, the first goal is to lower low-density lipoprotein (LDL) cholesterol.

For this purpose, statins are used. Fibrates can be started in the treatment for high TG and low HDL cholesterol. Metformin and Thiazolidinediones have positive effects. However, since thiazolidinediones can cause weight gain, their use in MetS seems unlikely. Therefore, metformin may be suitable for insulin resistance [49].

Studies with rimonabant directed at endogenous cannabinoid receptors have shown weight loss and improvement in metabolic parameters. However, this drug was withdrawn from clinical use due to its psychiatric side effects. While treating blood pressure in patients with MetS, the effects of the drug to be chosen on metabolic parameters should also be considered. While antihypertensive treatment is controlling blood pressure, it is expected to prevent target organ damage, to positively affect metabolic parameters or at least not negatively. In order to prevent atherothrombotic complications in risky patients, low-dose aspirin 75-100 mg daily is recommended. As for the treatment approaches related to hearing loss; If the underlying etiologic cause is MetS, all its components should be addressed separately, specific treatments should be planned, and regular follow-up and treatment should be continued. In addition to conventional treatments with hearing aids, stem cell treatment seems to be a new and different alternative [50].

Conclusion

In conclusion, it is important to treat each of the parameters that make up the metabolic syndrome - both lifestyle changes and pharmacologically. Here we summarize several studies from the current literature to show the relationship between MetS and hearing loss. Thus, we think that if Met S can be prevented, the risk of both Dm and atherosclerosis and hearing loss can be reduced.

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