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Metabolic and Auditory Implications of Fasting in Type 2 Diabetes Mellitus: Insights from Leptin and Ghrelin Profiles

Courtney Rynder [1,2*], Patrick Fan Sharpe [1,2], Georga Sallows [1,2], Julieann Coombes [3], Ray Mahoney [4]

[1] College of Medicine and Public Health, Flinders University, GPO Box 2100, Adelaide 5001, South Australia, Australia

[2] Flinders Health and Medical Research Institute, Flinders University, GPO Box 2100, Adelaide 5001, South Australia, Australia

[3] The George Institute for Global Health, University of New South Wales, UNSW Sydney, Sydney 2052, New South Wales, Australia

[4] Commonwealth Scientific Industrial Research Organisations, GPO Box 2583, Brisbane 4001, Queensland, Australia

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ABSTRACT

Type 2 Diabetes Mellitus (T2DM) is associated with systemic metabolic disturbances that may contribute to auditory dysfunction, potentially mediated by appetite-regulating hormones such as leptin and ghrelin. This study aimed to examine the association between fasting status, serum leptin and ghrelin levels, and the risk of hearing loss in adults with T2DM. A cross-sectional study was conducted involving 86 participants, categorized into fasting (n=46) and non-fasting (n=40) groups. Serum leptin and ghrelin levels were measured using enzyme-linked immunosorbent assay (ELISA) following overnight fasting, while hearing function was assessed using pure-tone audiometry at 500, 1000, 2000, and 4000 Hz, with hearing loss defined as a mean threshold >25 dB. The results showed that fasting participants had significantly lower leptin and ghrelin levels compared to non-fasting individuals ($p<0.05$). Although mean hearing thresholds were slightly lower in the fasting group, the difference was not statistically significant ($p>0.05$). However, the prevalence of hearing loss was significantly lower among fasting participants (21.7%) compared to non-fasting participants (37.5%, $p<0.05$). Logistic regression analysis indicated that higher leptin levels were associated with an increased risk of hearing loss, while fasting status showed a protective effect. In conclusion, fasting is associated with favorable hormonal profiles and a reduced risk of hearing loss in adults with T2DM, suggesting its potential role in supporting auditory health through metabolic regulation.

Corresponding Author:

Courtney Rynder,
College of Medicine and Public Health,
Flinders University,
Level 5, Room 5E209 Flinders Medical Centre, Bedford Park SA 5042, Australia,
Email: *courtney.rynder@flinders.edu.au*

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) has emerged as a major global public health challenge, with its prevalence increasing substantially over recent decades, particularly in low- and middle-income countries (Cuschieri, 2020). Epidemiological evidence indicates that T2DM is associated with a wide range of chronic complications affecting multiple organ systems. While classical complications such as nephropathy, neuropathy, and retinopathy have been extensively studied, growing attention has been directed toward less recognized manifestations, including auditory dysfunction (Gupta et al., 2019). Several previous studies have reported a higher prevalence of hearing impairment among individuals with T2DM compared to non-diabetic populations, which is commonly attributed to microvascular damage, oxidative stress, and diabetic neuropathy. Historically, auditory complications received limited attention in diabetes management; however, current trends highlight an increasing recognition of their clinical significance due to their impact on communication, social interaction, and overall quality of life (Moreda & Riberio, 2026); (Karishma et al., 2024); (Walia et al., 2023).

From a physiological perspective, metabolic dysregulation in T2DM extends beyond hyperglycemia and involves alterations in endocrine signaling, particularly in appetite-regulating hormones such as leptin and ghrelin. Leptin plays a critical role in energy homeostasis and is also implicated in inflammatory pathways and neuroprotective mechanisms, whereas ghrelin is involved in appetite regulation and has been reported to exert protective effects on neuronal tissues. Emerging evidence suggests that these hormones may influence cochlear function and auditory pathways, although the underlying mechanisms remain insufficiently understood (Novita, 2025); (Kharbanda et al., 2022). In parallel, fasting has gained increasing attention as a non-pharmacological intervention capable of improving metabolic profiles, including insulin sensitivity and hormonal balance. Several studies have demonstrated that fasting can modulate leptin and ghrelin levels; however, the extent to which these changes are associated with auditory outcomes in individuals with T2DM has not been adequately explored. Understanding this relationship is important not only for advancing scientific knowledge but also for informing preventive strategies aimed at mitigating diabetes-related complications through lifestyle modification (Dyńka et al., 2025).

Given the increasing burden of T2DM and the potential implications of metabolic and hormonal factors on auditory health, there remains a critical gap in the literature regarding the role of fasting in modulating appetite-regulating hormones and its association with hearing loss. Addressing this gap is essential to provide a more comprehensive understanding of the systemic effects of T2DM and to identify potential integrative approaches for complication management. Theoretically, this study contributes to the growing body of knowledge on the interaction between metabolic regulation and sensory function. Practically, it may offer insights into the potential benefits of structured fasting as a feasible and accessible intervention to reduce the risk of hearing impairment in individuals with T2DM. Therefore, this study aims to examine the association between fasting status, serum leptin and ghrelin levels, and the risk of hearing loss in adults with T2DM.

RESEARCH METHOD

Study Design

This study employed an analytical observational approach with a cross-sectional design and was conducted from November to December 2024 in Malang, Indonesia. Participants were recruited consecutively from community-based health screening programs organized in collaboration with the Department of Internal Medicine, Brawijaya Academic Hospital. Eligible participants were adults aged 18–65 years with a confirmed diagnosis of Type 2 Diabetes Mellitus (T2DM). The fasting group comprised individuals who, in addition to receiving standard antidiabetic therapy, regularly practiced voluntary fasting. These practices included Islamic sunnah fasting (e.g., Monday–Thursday fasting, Dawud fasting, and other routine religious fasts) as well as intermittent fasting. Intermittent fasting refers to dietary patterns involving repeated periods of reduced or absent caloric

intake, typically ranging from 16 to 48 hours, with variations such as alternate-day fasting, modified fasting, and time-restricted eating. In contrast, periodic fasting generally involves longer durations of dietary restriction, ranging from 2 to 21 days or more. Despite variability in fasting practices among participants, the operational definition of fasting in this study was standardized as abstinence from caloric intake for 8–16 consecutive hours prior to blood sampling and audiometric assessment to ensure consistency and reflect common fasting durations in both religious and dietary practices.

Population and Sample

The study population consisted of adult patients diagnosed with T2DM based on one or more of the following criteria: (1) ongoing use of antidiabetic medication; (2) fasting blood glucose ≥126 mg/dL; (3) random blood glucose ≥200 mg/dL; (4) a discharge diagnosis of diabetes mellitus during hospitalization; or (5) physician-confirmed outpatient diagnosis. A consecutive sampling technique was applied to recruit 86 eligible participants who met the inclusion criteria. Participants were subsequently categorized into two groups: those who routinely practiced fasting (n = 46) and those who did not engage in regular fasting (n = 40).

Data Collection

Demographic characteristics, including age and sex, were obtained through structured interviews. Venous blood samples were collected in the morning following a minimum fasting period of 8 hours to ensure the accuracy of hormonal measurements. Serum samples were separated and analyzed for leptin and ghrelin concentrations using validated enzyme-linked immunosorbent assay (ELISA) kits (Catalog No. ab100581 for leptin and ab100592 for ghrelin; Abcam, Cambridge, UK) in accordance with the manufacturer's protocols. Hearing function was evaluated using pure-tone audiometry with the Interacoustics Clinical Audiometer AD629. Both air- and bone-conduction thresholds were measured in a certified soundproof booth with ambient noise levels maintained below 40 dB. Hearing thresholds were assessed at frequencies of 500, 1000, 2000, and 4000 Hz, and the average threshold across these frequencies was calculated. Hearing status was classified as normal if the average threshold was <25 dB and as impaired if >25 dB, based on the World Health Organization criteria.

Data Analysis

Statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD) and compared between groups using the Mann–Whitney U test due to non-normal distribution. Categorical variables, including sex and the presence of hearing loss, were analyzed using Pearson's chi-square test. To determine the independent associations of leptin, ghrelin, age, sex, and fasting status with hearing loss, binary logistic regression analysis was conducted. The results were reported as odds ratios (ORs) with 95% confidence intervals (CIs). A p-value of <0.05 was considered statistically significant.

RESULTS AND DISCUSSIONS

The fasting and non-fasting groups were generally comparable in terms of demographic and baseline metabolic characteristics. A total of 86 individuals with Type 2 Diabetes Mellitus (T2DM) were included in this study, accounting for 172 ears (Table 1). Of these, 46 participants (92 ears) were in the fasting group, while 40 participants (80 ears) and 40 participants (80 ears) were in the non-fasting group. Table 1 summarizes the clinical and laboratory characteristics between the two groups. Participants in the fasting group had a significantly higher mean age (56.32 ± 5.85 years) than those in the non-fasting group (53.35 ± 6.32 years; p = 0.001). Serum leptin levels were significantly lower in the fasting group (32.85 ± 31.03 ng/mL) compared to the non-fasting group (40.89 ± 23.40 ng/mL; p = 0.012). Similarly, serum ghrelin levels were significantly lower in the fasting group (5.48 ± 3.37 ng/mL) than in the non-fasting group (7.32 ± 3.32 ng/mL; p < 0.001). Mean hearing threshold

was slightly lower in the fasting group (20.80 ± 8.10 dB) than in the non-fasting group (23.32 ± 11.13 dB); however, the difference was not statistically significant (p = 0.192).

Table 1. Comparison of age, hormonal markers, and hearing thresholds between fasting and non-fasting groups

Variable	Fasting (n=92 ears)		Non fasting (n=80 ears)		Total (n=172 ears)		p-value
	Mean	SD	Mean	SD	Mean	SD	
Age (years)	56.32	5.85	53.35	6.32	54.94	6.24	0.001*
Leptin (ng/mL)	32.85	31.03	40.89	23.40	36.59	27.96	0.012*
Ghrelin (ng/mL)	5.48	3.37	7.32	3.32	6.33	3.4	0.000*
Hearing Threshold (dB)	20.80	8.1	23.32	11.13	21.97	9.69	0.192

*Note: Mann-Whitney U test was used. *Statistically significant at $p < 0.05$.*

When examining sex distribution and hearing outcomes, we observed that fasting participants were less likely to have hearing loss than non-fasting participants. The distribution of sex and hearing loss status between the two groups is shown in Table 2. The fasting group consisted of 15 males and 31 females, while the non-fasting group included 6 males and 34 females. The difference in sex distribution was statistically significant (p = 0.007). Regarding hearing loss status, 10 participants in the fasting group had hearing impairment, compared to 15 in the non-fasting group. This difference was statistically significant (p = 0.015), indicating a lower frequency of hearing loss among fasting participants.

Table 2. Sex and hearing loss distribution between fasting and non-fasting groups

Variable	Fasting (n=46 people)	Non Fasting (n=40 people)	Total (n=86 people)	p-value
Female	31	34	65	
Total	46	40	86	
Hearing Loss Distribution				
Hearing Loss	10	15	25	0.015*
No Hearing Loss	36	25	61	
Total	46	40	86	

Note: Pearson chi-square test was used. *Statistically significant at p < 0.05.

Logistic regression analysis was conducted to evaluate the association between appetite-regulating hormones, demographic factors, and fasting status with the risk of hearing impairment in adults with T2DM. The overall model was statistically significant ($\chi^2 = 17.26$, df = 5, p = 0.004), explaining 9.5%-13.6% of the variance in hearing outcomes (Cox & Snell $R^2 = 0.095$; Nagelkerke $R^2 = 0.136$). Leptin levels were significantly associated with higher odds of hearing impairment (OR = 1.023; 95% CI = 1.004 - 1.042; p = 0.015), while fasting status was associated with reduced risk (OR = 0.429; 95% CI = 0.197 - 0.935; p = 0.033). Gender showed a borderline effect (OR = 2.567; 95% CI = 0.987 - 6.677; p = 0.053), whereas ghrelin and age were not significant predictors.

Table 3. Logistic Regression Analysis of Factors Associated with Hearing Impairment

Variable	B	SE	Wald	p-value	OR (Exp(B))	95% CI for OR
Leptin	0.022	0.009	5.878	0.015*	1.023	1.004 - 1.042
Ghrelin	-0.044	0.065	0.467	0.494	0.957	0.843 - 1.086
Age	0.008	0.029	0.085	0.771	1.008	0.953 - 1.068
Gender (Male vs Female)[a]	0.943	0.488	3.738	0.053	2.567	0.987 - 6.677
Fasting (Yes vs No)[a]	-0.846	0.397	4.535	0.033*	0.429	0.197 - 0.935
Constant	0.999	1.813	0.303	0.582	2.715	

DISCUSSION

This study demonstrated that fasting status was independently associated with a reduced risk of hearing loss in adults with T2DM, even after adjustment for age, sex, leptin, and ghrelin levels.

Notably, leptin emerged as a significant predictor of hearing outcomes, whereas ghrelin and age did not show independent associations. These findings suggest that fasting may confer protective effects on auditory function through metabolic and neuroendocrine mechanisms, particularly via leptin regulation. Leptin, an adipokine primarily involved in energy homeostasis, also plays a role in inflammatory modulation, vascular function, and neuroprotection. In physiological conditions, leptin supports neuronal survival and synaptic plasticity; however, in T2DM, chronic hyperleptinemia and leptin resistance impair these protective mechanisms. Dysfunctional leptin signaling has been linked to increased oxidative stress, endothelial dysfunction, and microvascular damage, all of which are critical contributors to cochlear degeneration. Therefore, the lower leptin levels observed in the fasting group may reflect improved metabolic balance and reduced inflammatory burden, ultimately contributing to better auditory outcomes.

In contrast, ghrelin, a hormone known for its role in appetite stimulation and neuroprotection, did not show a significant association with hearing loss in this study, despite being lower in the fasting group. This finding may reflect complex hormonal adaptations to habitual fasting, where long-term metabolic adjustments lead to a new equilibrium rather than acute fluctuations typically observed in short-term fasting studies. Beyond hormonal regulation, fasting is also known to activate key cellular maintenance mechanisms, particularly autophagy, which plays a crucial role in maintaining cellular integrity by removing damaged organelles and reducing oxidative stress. In the context of T2DM, impaired autophagy contributes to the accumulation of cellular damage in metabolically active tissues, including the cochlea. Fasting-induced autophagy may therefore enhance cochlear resilience by preserving mitochondrial function and preventing apoptosis of hair cells and auditory neurons. Additionally, fasting may influence telomere dynamics by reducing oxidative stress and systemic inflammation, thereby slowing cellular aging processes that contribute to neurodegeneration, including in auditory pathways. These combined mechanisms provide a plausible biological explanation for the lower prevalence of hearing loss observed among fasting participants.

From a clinical and public health perspective, the findings of this study highlight the potential of structured fasting as a complementary, non-pharmacological strategy in the management of T2DM and its complications, including hearing impairment. Given that hearing loss remains an under-recognized complication of diabetes, integrating routine auditory screening into diabetes care may facilitate early detection and intervention. However, several limitations should be acknowledged. The cross-sectional design precludes causal inference, and fasting status was self-reported, which may introduce recall bias. Additionally, important confounding variables such as duration of diabetes, glycemic control, and dietary patterns were not assessed. The relatively small sample size may also limit the generalizability of the findings. Despite these limitations, this study provides important preliminary evidence supporting the role of metabolic and hormonal pathways in auditory health. Future longitudinal and interventional studies are needed to clarify causal relationships, determine optimal fasting protocols, and further elucidate the underlying mechanisms linking fasting, hormonal regulation, and hearing function in individuals with T2DM.

CONCLUSION

This study suggests a potential link between regular fasting practices and decreased serum leptin and ghrelin levels, along with a lower prevalence of hearing loss among adults with T2DM. Although no significant differences were observed in mean hearing thresholds, the observed hormonal patterns and reduced incidence of auditory impairment in the fasting group indicate that improved metabolic regulation may contribute to the preservation of auditory function. These findings highlight the relevance of incorporating culturally appropriate lifestyle interventions, such as intermittent or religious fasting, into diabetes management strategies. In addition, they emphasize the importance of implementing routine hearing assessments as part of standard diabetes care, particularly in resource-constrained settings where early detection of sensory impairment is often limited. Further longitudinal research is needed to clarify the causal mechanisms underlying the relationship between fasting, hormonal regulation, and auditory health.

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