Impairment of extra-high frequency auditory thresholds in subjects with elevated levels of fasting blood glucose

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Abstract

This study was performed to assess whether there is an association between elevated Fasting Blood Glucose (FBG) and hearing impairment in Bangladeshi population. A total of 142 subjects (72 with elevated FBG; 70 control) were included in the study. The mean auditory thresholds of the control subjects at 1, 4, 8 and 12 kHz frequencies were 6.35 ± 0.35, 10.07 ± 0.91, 27.57 ± 1.82, 51.28 ± 3.01 dB SPL (decibel sound pressure level), respectively and that of the subjects with elevated FBG were 8.33 ± 0.66, 14.37 ± 1.14, 38.96 ± 2.23, and 71.11 ± 2.96 dB, respectively. The auditory thresholds of the subjects with elevated FBG were significantly (p < 0.05) higher than the control subjects at all the above frequencies, although hearing impairment was most evidently observed at an extra-high (12 kHz) frequency. Subjects with a long duration of diabetes (>10 years) showed significantly (p < 0.05) higher level of auditory thresholds at 8 and 12 kHz, but not at 1 and 4 kHz frequencies, compared to subjects with shorter duration of diabetes (<10 years). In addition, based on the data of odds ratio, more acute impairment of hearing at the extra-high frequency was observed in diabetic subjects of both older (>40 years) and younger (<40 years) age groups compared to the respective controls. The binary logistic regression analysis showed a 5.79-fold increase in the odds of extra-high frequency hearing impairment in diabetic subjects after adjustment for age, gender and BMI. This study provides conclusive evidence that auditory threshold at an extra-high frequency could be a sensitive marker for hearing impairment in diabetic subjects.

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1. Introduction

Diabetes mellitus, commonly known as diabetes, is a group of metabolic diseases that affect insulin production or impair the sensitivity of cells to insulin leading to an increase in blood sugar (Gardner and Shoback, 2011). A nationwide survey in Bangladesh estimates that around a tenth of the adult population suffer from this chronic disease (Akter et al., 2014). Diabetes is perhaps the single most important metabolic disease that can affect almost every organ system in the body. Diabetes-mediated complications related to organ dysfunction include heart and blood vessels, eyes, kidneys, nerves, pancreases, limbs etc (Martins, 2015). Despite enormous progress in research on diabetes-related complications, the relationship between diabetes and hearing impairment still remains controversial.

Hearing loss is regarded as a communication disorder, which is not directly life threatening, but may impair quality of life due
to social withdrawal, loss of confidence, and increased frustration and anxiety (Huang and Tang, 2010). Hearing organs generally undergo aging-associated degenerative changes and the process of aging is considered as the most frequent cause of hearing loss in adults worldwide (Wilson et al., 1999; Cruickshanks et al., 1998; Smith et al., 2011). In addition to aging, a variety of environmental factors including noise exposure, lifestyle, use of MP3 player, medication, cigarette smoking may also cause hearing impairment (Kim et al., 2009; Mohammadi et al., 2010; Kim, 2010; Ohgami et al., 2011; Sumit et al., 2015). Numerous studies have evaluated the relationship between diabetes and hearing loss; however, the findings are not always consistent. Several studies showed a positive correlation between diabetes and hearing impairment (Kurien et al., 1989; Ferrer et al., 1991; Mitchell et al., 2009; Diniz and Guida, 2009; Bainbridge et al., 2010; Jang et al., 2011; Forogh et al., 2013), while others failed to confirm such association (Sieger et al., 1983; de Espana et al., 1995; Dalton et al., 1998).

It is worth mentioning that most research showing a relation between diabetes and hearing loss are limited to older people. In addition, most previous studies suggest that persons with diabetes undergo hearing impairment at low/mild or high frequencies (Kakarlapudi et al., 2003; Bainbridge et al., 2010; Rajendran et al., 2011; Jang et al., 2011; Lin et al., 2012; Agarwal et al., 2013; Oh et al., 2014), but not at an extra-high-frequency. More research is therefore necessary to examine whether or not hearing at extra-high-frequency auditory thresholds is impaired in a wider age group of people with diabetes. This study was conducted for the first time to examine a relationship between elevated Fastin Blood Glucose (FBG) and hearing impairment among Bangladeshi population. For this purpose, 142 subjects of different ages were included in this study, among them 72 had elevated FBG levels and the remaining 70 were control. The audiometric measurement was done in three frequency groups: low frequency (1 kHz), high frequency (4 and 8 kHz), and extra-high-frequency (12 kHz). The correlation between diabetes and hearing impairment was analyzed using blood sugar level and the mean ± S.D values of auditory thresholds of the subjects. The study also attempted to find if there was any association between hearing impairment with duration of diabetes, age, gender and body mass index (BMI).

2. Materials and methods

2.1. Study subjects

This study was conducted among 142 subjects who agreed in writing to participate in this study. The subjects with elevated FBG (≥7.0 mmol/L or ≥126 mg/dL) were considered as diabetic and 72 of them were included in this study. The FBG levels of the participants were measured at a local diagnostic center in Dhaka, Bangladesh. Subjects were selected randomly and their ages were between 21 and 64 years. We excluded those subjects who had a previous history of ear diseases or deafness and suffered from other illnesses at the time of conducting this study. Age and sex matched non-diabetic apparently healthy subjects were included as controls (FBG <6.1 mmol/L or <110 mg/dL). Furthermore, there was no specific predilection for race, religion or socioeconomic status. Ethical issues were considered for all of the experiments. The study was approved by the Ethical Review Committee of the Faculty of Biological Sciences, University of Dhaka (Ref. no. 02/BioSci/2015–2016). Data were collected using a self-reporting questionnaire including duration of diabetes as well as demographic information such as age, gender, height and weight of the participants.

2.2. Measurement of hearing level

Hearing levels of all the participating subjects were measured at 1, 4, 8 and 12 kHz frequencies. The audiometric examination was performed in a sound-proof room using a sophisticated iPod with earphones as described previously (Van Tasell and Folkard, 2013; Sumit et al., 2015). Sound signals at 1, 4, 8 and 12 kHz frequencies were presented to each subject until the threshold of sound that the subjects were just able to perceive was identified. Hearing levels of the subjects were measured by providing an initial 5 dB stimulus followed by a stepwise increase in the sound level by 5 dB. To confirm the reproducibility of the results, examinations were repeated for each of the subjects. The subjects were classified as having low/mild frequency hearing loss if the average of the pure-tone thresholds at 1, 4 and 8 kHz frequencies exceeded 25 dB SPL. Extra high frequency hearing loss was considered if the average of the pure-tone thresholds at 12 kHz frequencies exceeded 40 dB SPL (Ohgami et al., 2011, 2016).

2.3. Analysis of data

Data were statistically analyzed using SPSS program version 22 software (SPSS Inc., Chicago, USA). As the data did not show normal distribution, the difference between each group was analyzed using Pearson’s χ2 (chi-square) method. Descriptive statistics have been presented in the results section. The p-value and odds ratio were measured for each characteristic of the subjects. For further confirmation, binary logistic regression analysis was performed to determine adjusted odds ratio at 95% confidence interval (CI). The regression analysis made use of different predictor variables in the categorical form. Hearing level was taken as a dependent variable, and diabetes (reference: control), age (reference: ≤40 years), gender (reference: male) and BMI (reference: normal weight) were considered as independent variables. The significance of the results was set at p < 0.05.

3. Results

3.1. Characteristics of the study participants

Among 142 subjects analyzed in this study, 70 (49.3%) were control and 72 (50.7%) were diabetic with elevated FBG (Table 1). Of the 142 subjects, male and female participants were equal in numbers (71 for each case). The number of male
and female participants in the diabetic group was 34 (47.2%) and 38 (52.8%), while that of the control was 37 (52.9%) and 33 (47.1%), respectively. The mean age of the diabetic group was 45.48 ± 1.06 years and that of the control was 41.72 ± 1.38 years. Of the diabetic (n = 72) subjects, 24 (33.3%) were ≤40 years and the remaining 48 (66.7%) were >40 years. The participating subjects were further categorized as under-, normal- and over-weight based on their BMI value of <18.5, 18.5–25 and > 25 kg/m², respectively. The number of diabetic subjects belonging to under-, normal- and over-weight was 2 (2.8%), 31 (43.1%) and 39 (54.2%), respectively, while that of the control subjects was 4 (5.7%), 42 (60.0%) and 24 (34.3%), respectively. For control subjects the major portion was of normal weight (60.0%); while for the diabetic subjects it was overweight (54.2%). However, in both the cases, the least number of subjects was found to be underweight (diabetic: 2 (2.8%) and control: 4 (5.7%)). Among the 72 diabetic subjects, 46 (63.9%) had diabetes for ≤10 years and the remaining 26 (36.1%) had diabetes for >10 years.

3.2. Comparison of auditory thresholds between diabetic and control subjects

The average auditory thresholds of the non-diabetic control subjects at 1, 4, 8 and 12 kHz frequencies were 6.35 ± 0.35, 10.07 ± 0.91, 27.57 ± 1.82 and 51.28 ± 3.01 dB SPL, respectively (Fig. 1). When the average auditory thresholds of the diabetic subjects with elevated FBG were measured at all of the frequencies mentioned above, the values found as 8.33 ± 0.66, 14.37 ± 1.14, 38.96 ± 2.23, and 71.11 ± 2.96 dB, respectively. The threshold of hearing is known to be frequency-dependent. In our study, we observed an increase in mean thresholds with increasing sound frequency in both cases of control and diabetic subjects. The hearing level is measured in dB; and higher values of dB indicate a higher degree of hearing impairment. Normal hearing, in this study, was defined as 0–25 dB range and hearing loss as ≥26 dB. When compared with the control subjects, the average auditory thresholds of the subjects with elevated FBG at all the frequencies tested were significantly higher (p < 0.05). These results suggest that the control subjects had better hearing overall, whereas the diabetic subjects experienced deterioration of hearing at all the frequencies tested. Hearing loss, observed in diabetic subjects, was most evident at an extra-high (12 kHz) frequency (hearing thresholds of 71.11 dB at 12 kHz frequency).

3.3. Longer duration of diabetes impaired hearing mostly at higher frequencies

Diabetic subjects were divided into two subgroups (Table 2): diabetes for ≤10 years and diabetes for >10 years according to earlier reports (Forogh et al., 2013). The average auditory thresholds of the subjects having diabetes for ≤10 years were 7.82 ± 0.84, 13.47 ± 1.39, 34.67 ± 2.63 and 65.00 ± 3.87 dB at 1, 4, 8 and 12 kHz, respectively. However,
these values for the other group of diabetic subjects (>10 years) were altered and the values became 9.23 ± 1.02, 15.96 ± 1.94, 46.53 ± 3.67 and 81.92 ± 3.68 dB at 1, 4, 8 and 12 kHz, respectively (Table 2). The average auditory thresholds of the subjects having diabetes for >10 years were significantly higher than those having diabetes for ≤10 years at 8 and 12 kHz frequencies (p values 0.01 and 0.005, respectively). However, the difference in auditory thresholds between the two diabetic groups at lower frequencies such as 1 and 4 kHz was not statistically significant (p > 0.05). Based on the data of odds ratio, more profound impairment of hearing at an extra-high (12 kHz) frequency was observed in subjects with longer duration (>10 years) of diabetes in comparison with those with shorter (≤10 years) diabetes duration (OR: 6.94, CI: 0.83–57.74). In addition, the odds ratio was higher in subjects with longer diabetes duration at 12 kHz than in those at 8 kHz (OR: 6.94 and 2.96). These results indicate that longer duration of diabetes deteriorates hearing mostly at higher frequencies (8 and 12 kHz); however, statistically stronger impairment occurs at an extra-high frequency (12 kHz).

### 3.4. Variation in hearing thresholds of younger and older diabetic subjects compared to controls

Aging is among the most known risk factors that causes hearing deterioration. The average auditory thresholds of the control subjects aged ≤40 years at 1, 4, 8 and 12 kHz frequency were 5.64 ± 0.30, 7.2 ± 0.97, 18.54 ± 1.75 and 34.67 ± 2.96 dB, respectively; whereas for those aged >40 years the thresholds were 6.92 ± 0.56, 12.3 ± 1.34, 34.74 ± 2.42 and 64.48 ± 3.70 dB, respectively (Table 3). An increase in hearing threshold, at all the above frequencies, was observed in older non-diabetic subjects (>40 years) than younger subjects (≤40 years). This result clearly indicated that subjects older than 40 years are more likely to experience additional hearing loss than subjects younger than 40 years. The average auditory thresholds of the diabetic subjects aged ≤40 years were 7.70 ± 1.24, 10.62 ± 1.45, 27.29 ± 2.97 and 51.66 ± 5.05 dB at 1, 4, 8 and 12 kHz frequencies, respectively. When these auditory values were compared with the values of the non-diabetic control subjects of the same age group (≤40 years), significant differences were found at 8 and 12 kHz frequencies with p values 0.01 and 0.004, respectively. On the other hand, the average auditory thresholds of the diabetic subjects older than 40 years were 8.64 ± 0.76, 16.25 ± 1.47, 44.79 ± 2.63 and 80.83 ± 2.74 dB at 1, 4, 8 and 12 kHz frequencies, respectively. Again, significant differences were observed at higher frequencies such as 8 and 12 kHz (p-value 0.007 and 0.001, respectively), but not at lower frequencies such as 1 and 4 kHz (p-values >0.05) when compared with the control subjects of the same age group (>40 years). It can, therefore, be concluded that hearing impairment in diabetes is gradually progressive involving high-frequency thresholds. Moreover, based on the data of odds ratio provided in Table 3, the risk of hearing loss was found more acute in diabetic subjects at higher frequencies compared to control subjects of both age groups. The odds of hearing loss in the subjects (≤40 years) with diabetes at extra-high (12 kHz) frequency were 5.71 times higher (OR: 5.71, CI: 1.75–18.59) than the odds of hearing loss in the control subjects. Again, the odds of hearing loss in the subjects (>40 years) with diabetes at 12 kHz frequency were 6.89 times higher (OR: 6.89, CI: 1.39–34.17) than the odds of hearing loss in the control subjects. Relatively less effect in hearing loss was observed at 8 kHz, in which the odds of hearing loss in subjects aged ≤40 and > 40 years with diabetes were 3.81 and 3.30 times the odds of hearing loss in control subjects aged ≤40 years (OR: 3.81, 95% CI: 0.67–21.72) and >40 years (OR: 3.30, 95% CI: 1.25–8.58), respectively. Therefore, no noticeable variation in the extent of hearing loss was observed in older and younger diabetic subjects. These results indicate a possible association between diabetes and hearing impairment in subjects of both younger and older age groups, although the strength of this association was not noticeably influenced by the subjects’ age.

### 3.5. Binary logistic regression analysis

Logistic regression analysis was also performed to evaluate the association of hearing loss with diabetes. Here, the hearing loss (>40 dB for extra-high 12 kHz frequency and ≥26 dB for other frequencies) was taken as a dependent variable and diabetes, age, gender and BMI of the participants were considered as independent variables. The independent variables were categorized considering control (non-diabetic group), age ≤40 years, BMI (normal weight) and gender (male) as the reference group. After adjusting all these factors, only diabetes and age were found to affect the hearing level more profoundly than the reference group (Table 4). The results suggest that controlling for differences in age, gender and BMI of the participants; diabetes increased the likelihood of hearing loss by 3.44, 4.23 and 5.79 fold than the control group at 4, 8 and 12 kHz frequencies, respectively (p < 0.05). Although age played a positive role on hearing impairment at higher frequencies, however, we did not find any statistically significant association between hearing impairment and higher BMI or gender.

### Table 3

Comparison of hearing thresholds in younger and older diabetic subjects compared to controls.

| Frequency (kHz) | Age category (years) | Hearing thresholds (dB SPL) (Mean ± S.E) | p-value | OR (95% CI) |
|-----------------|----------------------|------------------------------------------|---------|-------------|
|                 |                      | Control                                   |         |             |
| 12              | ≤40                  | 34.67 ± 2.96                              | 0.004*  | 5.71 (1.75–18.59) |
|                 | >40                  | 64.48 ± 3.70                              | 0.001*  | 6.89 (1.39–34.17) |
| 8               | ≤40                  | 18.54 ± 1.75                              | 0.010*  | 3.81 (0.67–21.72) |
|                 | >40                  | 34.74 ± 2.42                              | 0.007*  | 3.30 (1.25–8.58) |
| 4               | ≤40                  | 12.3 ± 1.34                               | 0.057   | 2.77 (0.23–32.00) |
|                 | >40                  | 7.2 ± 0.97                                | 0.052   | 2.77 (0.23–32.00) |
| 1               | ≤40                  | 5.64 ± 0.30                               | 0.07    | 2.3 (0.15–99.97) |
|                 | >40                  | 6.92 ± 0.56                               | 0.08    | 1.04 (0.28–91.12) |

*Significant association < 0.05.

Abbreviation: OR: Odds Ratio, CI: Confidence Interval.
Diabetes status
Hearing level (n = 142)

| Hearing level (n = 142) | 1 kHz | 4 kHz | 8 kHz | 12 kHz |
|------------------------|-------|-------|-------|--------|
|                        | OR (95% CI) | p-value | OR (95% CI) | p-value | OR (95% CI) | p-value | OR (95% CI) | p-value |
| Diabetes               | 1.40 (1.1–7.7) | 0.03a  | 4.23 (1.7–10.3) | 0.002b  | 5.79 (2.2–15.2) | 0.001b |
| Age ≤40 years          | 1.03 (0.1–12.3) | 0.06   | 4.05 (1.5–11.0) | 0.006b  | 10.93 (4.2–28.1) | 0.001b |
| Age ≥40 years          | 1.03 (0.1–12.3) | 0.06   | 4.05 (1.5–11.0) | 0.006b  | 10.93 (4.2–28.1) | 0.001b |
| BMI                    |                  |       |       |        |
| Normal weight          | 1 (0.21–1.3)     | 1     | 1     | 1      |
| Underweight            | 1.46 (0.3–2.9)   | 1     | 1     | 1      |
| Overweight             | 1.46 (0.3–2.9)   | 0.76  | 0.60  | 0.41   |
| Male                   | 1.59 (0.1–19.7)  | 0.39  | 0.64  | 0.55   |
| Female                 | 1.59 (0.1–19.7)  | 0.39  | 0.64  | 0.55   |

Abbreviation: OR: Odds ratio, CI: Confidence interval.
a Adjusted for diabetes, age, BMI and gender.
b Statistically significant.

4. Discussion

Diabetes is known to affect multiple organ systems and people with diabetes, therefore, experience a variety of serious medical complications. It is, hence, reasonable to investigate whether the auditory system among them is affected. Till date there are no reports on investigation of association between diabetes and hearing impairment among Bangladeshi population. This study, for the first time, demonstrated that hearing impairment in subjects with diabetes was several-fold more prevalent than those without diabetes among Bangladeshi population. We observed significant differences in hearing thresholds of the diabetic subjects at all the frequencies, and the most marked difference was obtained at an extra-high (12 kHz) frequency.

So far researches carried out to find a causal relationship between diabetes and hearing function, have failed to bring adequate consensus on this matter. A positive correlation between diabetes and hearing loss has been demonstrated by some studies (Kurien et al., 1989; Ferrer et al., 1991; Mitchell et al., 2009; Diniz and Guida, 2009; Bainbridge et al., 2010; Jiang et al., 2011; Forogh et al., 2013); however, others failed to find this correlation (Sieger et al., 1983; Dalton et al., 1998; de Espana et al., 1995). Analysis of the audiometric data revealed that hearing thresholds of the subjects with elevated FBG were significantly different from the controls at all the frequencies tested (Fig. 1). Consequently, the most noticeable difference was observed at higher frequencies including the extra-high frequency, which is not clinically tested in audiograms. Existence of a possible association between hearing loss and diabetes at low/mild or high frequencies were demonstrated earlier (Kakarlapudi et al., 2003; Bainbridge et al., 2010; Rajendran et al., 2011; Jiang et al., 2011; Lin et al., 2012; Agarwal et al., 2013; Oh et al., 2014), but existence of this association at the extra-high-frequencies is rarely known.

As diabetes affects most of the organ systems in the body, increase in duration of diabetes can consequently lead to higher prevalence of complications. In this study, average auditory thresholds were higher in subjects with longer duration of diabetes (>10 years) than those with relative shorter duration (<10 years) in all tested frequencies. However, the differences were statistically significant only at higher, but not at lower, frequencies (Table 2). We observed 2.96 times greater risk of hearing impairment at 8 kHz frequency (OR: 2.96, CI: 1.08–8.07) and 6.94 times greater risk at 12 kHz frequency (OR: 6.94, CI: 0.83–57.74) in subjects with diabetes for a longer duration. These results signify that longer duration of diabetes affects hearing acuity at the extra-high frequency more profoundly. Some earlier reports also demonstrated that longer duration of diabetes is associated with increasing hearing impairment predominantly at higher frequencies (Ma et al., 1998; Tay et al., 1995; Çelik et al., 1996); however, in most cases the effect at extra-high frequency was not explored.

Aging is considered a common risk factor for both hearing loss and diabetes. It has been reported that progressive aging leads to an increase in the prevalence of hearing loss as well as diabetes (Oh et al., 2014). As a result, it is sometimes difficult for many researchers to interpret whether hearing loss in diabetes is due to the normal process of aging or due to various physiological/biochemical abnormalities associated with diabetes. Hence, it is reasonable to think that the significant relationship observed between hearing impairment and diabetes, in our study, is merely a phenomenon of aging. However, hearing impairment in both younger and older diabetic subjects was found to be more acute at higher frequencies compared to non-diabetic age-matched controls, and the extent of hearing impairment did not noticeably vary among the older and younger diabetic subjects. This result, therefore, argues that incidence of diabetes, not particularly age, plays an important role in hearing loss. This argument is supported by
an earlier report, in which an independent association of diabetes with hearing loss has been demonstrated, although the possibility of residual confounding effects of age could not be ruled out (Horikawa et al., 2012). In our study, when differences in age, BMI and gender of the subjects were controlled, logistic regression analysis showed several fold increase in hearing loss among diabetic subjects compared to non-diabetic controls (OR: 3.44, 4.23 and 5.79 at 4, 8 and 12 kHz frequencies, respectively; p < 0.05 in all cases). When OR values at different frequencies were compared, an accelerated loss of hearing at the extra-high 12 kHz frequency was again evident. We did not find any statistically significant correlation between hearing loss and higher/lower BMI or gender. Contrary to the results presented here, some studies reported positive correlation of higher BMI with hearing impairment (Fransen et al., 2008; Bainbridge et al., 2010; Dabrowski et al., 2013). On the other hand, no correlation between higher BMI and hearing loss among diabetic subjects was also shown (Sakuta et al., 2007; Bhaskar et al., 2014), providing support to our observation. In most cases like that of ours, the influence of sex on hearing thresholds in diabetic subjects has been shown to be statistically insignificant (Bainbridge et al., 2010). However, contrasting results of hearing impairment among male and female diabetic subjects are also known, where hearing in males were found to be worse than females (Cullen and Cinnamond, 1993) and vice versa (Taylor and Irwin, 1978).

We acknowledge some of the limitations associated with this study. Amongst those limitations, the most important seem to be the relatively small number of participants. Data were collected using a self-reporting questionnaire regarding diabetes status as well as demographic information. Also, diabetic subjects were not classified between type 1 and type 2 diabetes, although most of them are believed to have type 2 diabetes. In addition, the current FBG level of the subjects was mainly considered as a measure of diabetes in our study population, although we know that slight variation in FBG values may occur on a daily basis. For assessing long term complications of diabetes, we admit that HbA1c is a better parameter than FBG. However, reports of some studies that showed significant positive correlation of HbA1c and FBG levels in diabetics, made us to consider FBG as an equally effective alternative to HbA1c in the assessment of chronic glycaemia (Peter et al., 2006; Ghazanfari et al., 2010; Goud et al., 2011). Moreover, the involvement of various confounding factors in hearing mechanism, in fact, creates complexity in designing a single study to examine the relationship between hearing impairment and diabetes. Nonetheless, these limitations do not prevent us to conclude that diabetes impaired hearing level on selected Bangladeshi subjects with a wider age range.

5. Conclusions

In conclusion, the study shows progressive high frequency hearing impairment in subjects with elevated FBG, and impairment of hearing at the extra-high (12 kHz) frequency was more profound. Therefore, auditory thresholds at 12 kHz could be a good marker for diabetes-associated hearing loss. We recommend the testing of hearing at 12 kHz as a useful measure of preclinical hearing loss among diabetic subjects.

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Conflicts of interest

All authors declare no competing interests.

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