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ORIGINAL ARTICLE

Diabetes in rural individuals of different nutritional status and the alarming situation demands focus more on its under-nutrition association

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Abstract

Objective: To study the relationship of nutritional-status with diabetes. *Design*: The socio-economics/anthropometrics, blood-glucose/systemic-hypertension are evaluated in consecutively-selected diabetic-patients. *Setting*: Semi-urban/rural India. *Subjects*: Hyperglycaemic patients (total 90/male 37). *Results*: Blood-glucose (PP-mean ± SE) in individuals is overweight – 38.89% (226.94 ± 9.59), normal-weight – 50% (217.58 ± 1.34), underweight – 11.11% (305.50 ± 21.35) indicating most hyperglycaemia in undernourished-group ($F = 6.357$, $p < 0.003$). This group occupies higher glucose-groups in ≤140, 141–270, and ≥270 mg/dL. The blood-glucose negatively correlates with waist($r = -0.282$; $p < 0.01$) and hip ($r = -0.254$; $p < 0.05$) circumference indicating the under-nutrition association with glucose-homeostasis ($F = 7.6$–8.2, $p < 0.001$). The higher glucose is noticed in more number of individuals in lower (<40 years) age-group ($\chi^2 = 12.86$; $p < 0.002/\rho = -0.355$; $p < 0.001$). The prevalence of hypertension is 28% (underweight = 20%, overweight = 27%, normal = 30%). The group of 141–270 mg/dL glucose has 45% and rest groups together have 23% hypertensive individuals relating directly, hypertension and diabetic-onset. *Conclusions*: Diabetes, explored in <40 years group and even more in female should be extensively studied accounting WHO categorization (1985/TRS/727) of malnutrition related diabetes (MRDM). Further, different interactive risk-factors should be properly addressed and the global-malnutrition/gender-based inequities be eradicated.

Keywords

Body mass index, blood pressure, malnutrition related diabetes, semi-urban/rural community, socioeconomic status

History

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Introduction

Epidemiology of highly occurring metabolic syndrome like diabetes and associated conditions has been recognized. Socio-economic/demographic profiles, family health care setting, general education levels, nutrition/health consciousness, life style and psychological states have been implicated as the major risk factors of diabetes (Gary-Webb *et al*., 2013). In general, age factors, reduced physical activity and obesity result in high blood glucose, triglycerides and low high-density cholesterol (HDL-C) levels, which are regarded as the important markers of diabetes pathogenesis (Mahajan *et al*., 2013; Selvin & Parrinello, 2013). Worldwide, hypertension and/or obesity are common co-morbidities in adults with type-II diabetes mellitus (Colosia *et al*., 2013). Categorical estimation suggests that a robust volume of undiagnosed diabetes (pre-diabetic) co-exists beside the diagnosed individuals (Leong *et al*., 2013). Report suggests that diabetes now affects both high and low income countries (HIC and LIC), with particularly developing countries bearing the majority of this burden (Maruthur, 2013). In an investigation, 39.6% of diabetic patients are recognized as malnourished; one also encounters mainly hypertension, diabetes and cancer as common co-morbidity factors (Chakravarty *et al*., 2013). A major role of amenities, infrastructural facilities and pollution contributes to diabetes by impairing the physical ability and activity, and by increasing different stress factors (Pasala *et al*., 2010). A report reveals that lower financial security and higher level of depression are linked with diabetes (Logan *et al*., 2013). Ethnicity has been reported as being associated with diabetic prevalence which may be linked to the education-social and/or genetic factors (Logan *et al*., 2013). The proper management for the women with gestational diabetes mellitus (GDM) may control the manifestations of diabetes in adulthood of their children (Ali *et al*., 2013). The knowledge on metabolic syndrome are lacking in individuals living in slum and rural settings (Joshi *et al*.,

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2013). The estimated prevalence of diabetes in Chinese adults was 11.6% and the prevalence of pre-diabetes was 50.1% (Xu *et al*., 2013). The surge in the prevalence of type 2 diabetes in South America is appreciable. The forecast for diabetic prevalence in rapidly developing as well as developed countries are portentous (Steckel, 2013). An Expert Committee of WHO has elaborated on the classification of diabetes mellitus introducing a new classification as malnutrition-related diabetes (MRDM) observed in undernourished (BMI < 19) individual (WHO, 1985). Predictions for the first third of the twenty-first century suggest a huge surge of the prevalence of T2DM in the Middle East, Sub-Saharan Africa, India, China and in Latin America (Ginter & Simko, 2012). Epidemiological studies have revealed strong and reproducible links between indices of poor foetal growth and susceptibility to the development of glucose intolerance and insulin resistance syndrome in adult life (Lee *et al*., 2005). Pancreatic involvement and autoimmune influences are considered to be the predictors of MRDM (Kanungo *et al*., 2002; Saraya *et al*., 2003). Unlike in normal and overweight diabetic patients, infections of the skin and soft tissues and pulmonary tuberculosis are often seen in MRDM patients (Samal *et al.,* 2002). Protein-calorie malnutrition produces glucose intolerance and reduced insulin release in response to glucose which has also been shown in experimental animal model (de-Mello & Luciano, 1995).

The present objective is to study the nutritional status on the diabetes occurrence with emphasis on under-nutrition. The prevalence of diabetes is evident in the individuals of almost all categories of nutritional and socioeconomic status with diverse risk factors. The under-nutrition status is a significant risk factor in the settings of a developing country. The present study elucidates the occurrence of diabetes in a rural/semi urban locality in the eastern part of India. Present significance of WHO-described MRDM and its severity in hyperglycaemic status has been focused in this investigation.

Methods

Study location and human participants

The present study was conducted (August 2013 to October 2013) among individuals suffering from diabetes and inhabitants of the neighbourhood areas of the Pachim Medinipur districts. The study design was a community based cross-sectional type.

Ethical consideration

The study is approved by the Institutional Research Ethics Committee. The researcher explained the study to potential participants. The anonymity of the participants is absolutely conserved. The researchers also obtained permission from the administrative authority and before the study oral and written permission was obtained from the participants.

Inclusion/exclusion criteria

Randomly and consecutively selected total 90 (male 37) diabetic patients (screened and diagnosed by their family physicians/health care providers) who have no reported complications of chronic cardiac, nephritic, peripheral vascular or chronic infectious diseases. Those patients regularly use different anti-diabetic drugs. The socioeconomic status/related demographic profile of subjects are assessed by Kuppuswami's socioeconomic scale upgraded by Kumar *et al*. (2012).

Psychological assessment

All the participants were assessed using a Mental Status Examination (MSE) by a consultant neuro-psychiatrist, Medical College, Kolkata (Sadock & Sadock, 2007; Tombaugh, 2005). Only competent, responding consistently, psychiatrically healthy diabetic individuals are included.

Anthropometric measurements

All anthropometric measurements are made by trained professionals using the standard techniques (Lohman *et al*., 1998). Height was measured using Martin's anthropometer. Body weight was recorded digitally and with a weighing scale (Doctor Beliram and Sons, New Delhi, India). Errors of measurements were computed within acceptable limits (Ulijaszek & Kerr, 1999).

The body mass index (BMI) of the individuals were computed using the following standard equations; BMI (kg/m^2) = Weight (kg)/height (m^2). Nutritional status was evaluated using internationally accepted BMI guidelines (WHO, 1995). The following cut-off points were utilized; Grade III Thinness: BMI < 16.0, Grade II Thinness: BMI = 16.0–16.9, Grade I Thinness: BMI < 17.0–18.4, Normal: BMI = 18.5–24.9, Overweight: BMI ≥ 25.0.

Determination of blood glucose (pp) and haemoglobin level

Blood glucose of the participants is measured by glucose assay kit employing the glucose oxidase and peroxidase method. Serum haemoglobin is measured by the proper assay kit by Drabkin's reagent (Ranbaxy, India).

Statistical analysis

The statistical analyses are done using the SPSS for Windows statistical software package (SPSS Inc., Chicago, IL, USA, 2001). Normally distributed data are expressed as means ± standard error, the group means are tested using one way ANOVA with Tukey's post hoc test. Pearson's chi-square test is used to determine significant differences within categories. The p value < 0.05 is considered statistically significant. Blood glucose and BMI is the primary outcome variable. Secondary outcome measures included are mid upper arm circumference (MUAC) and weight height ratio (WHR). Baseline variables and outcome measures are compared by the Student's t test for continuous variables Spearman's rank coefficient or Spearman's ρ was calculated to evaluate the statistical dependence within age group, sex, two variables.

Results

The distribution and dispersion pattern of nutritional status represented by BMI of both sexes among the three groups of participants, classified as their blood glucose level (viz.

≤140, 141–270, ≥270 mg/dL) are shown in Figure 1(a). Nutritional status (BMI) and age wise distributions of male and female blood glucose data are shown in a typical scattered plot (Figure 1b). Of the total 90 patients, 53 (58.89 %) are males. The mean age is 49.78 years in males and 43.32 years in females ($p < 0.01$). When the studied group are divided into two age groups (≤40 and >40 years), it is found that the blood glucose is higher of the participants of ≤40 years than >40 years (mean ± SE 258.75 ± 10.18 and 212.48 ± 10.67 respectively, $p = 0.004$) (Figure 2b). Spearman correlation suggests a significant negative association between age groups and blood glucose groups ($\rho = -0.355$, $p < 0.001$) (Table 2). Present results indicate that the mean ± SE glucose levels (PP) are 305.50 ± 21.35, 217.58 ± 1.34 and 226.94 ± 9.59 mg/dL in underweight, normal weight or overweight categories respectively ($F = 6.357$, $p < 0.003$) (Figure 1a). While participants are grouped based on their diabetic severity (≤140, 141–270, ≥270 mg/dL PP), it is noticed that unlike normal or overweight groups, all malnourished individuals occupy 141–270 and ≥270 mg/dL glucose groups (Figure 3).

The distributions of participants in overweight and underweight groups are 38.89% and 11.11%. A trend of higher blood glucose level (>270 mm/dl) is seen among underweight participants (60%), while among the normal and overweight participant it is 26.67% and 31.43% respectively (Figure 1). The 83.02% of females had a waist circumference above the cut off value as compared with 27.03% in males ($\chi^2 = 29.427$, $p < 0.001$). It is also observed that there is a negative association of the blood glucose level with waist circumference ($r = -0.282$, $p = 0.007$) and that with hip circumference ($r = -0.254$, $p = 0.016$) of all the participants (Table 2). In females waist circumference is significantly associated to blood glucose ($r = -0.355$, $p = 0.009$), for hip circumference this value is $r = -0.260$ and $p = 0.06$. The waist and hip circumferences in sex combined group or in female are found to be higher in 141–270 mg/dL blood glucose group than the other two groups ($p < 0.01$) (Table 1). The ANOVA result also supports these correlations ($p < 0.005$) (Table 1).

Pearson Chi square statistics suggest that the distribution pattern of age groups in different blood glucose groups is highly significant ($p < 0.002$). The 30% of normal, 27% of overweight and 20% of underweight are found to be hypertensive and a significant number of total respondent manifest normotensive status. The group of 141–270 mg/dL glucose has 45% and other two groups together have 23% hypertensive individuals. The association between malnutrition and diabetes is noticed especially in < 40 years group ($t = 2.983$, $p < 0.004$ and $\chi^2 = 12.86$, $p < 0.002$) and even more in the female.

Discussion

An increasingly sedentary lifestyle and childhood obesity predispose to nutrition-related non-communicable diseases like metabolic syndrome, type 2 diabetes mellitus (T2DM), polycystic ovarian syndrome, hypertension, dyslipidemia, coronary artery diseases and other peripheral vascular disease

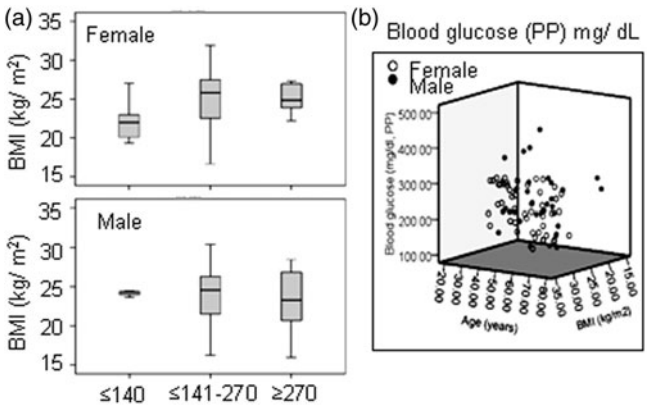

Figure 1. Nutritional status (BMI) wise distribution and dispersion pattern in female and male data from different groups of blood glucose level.

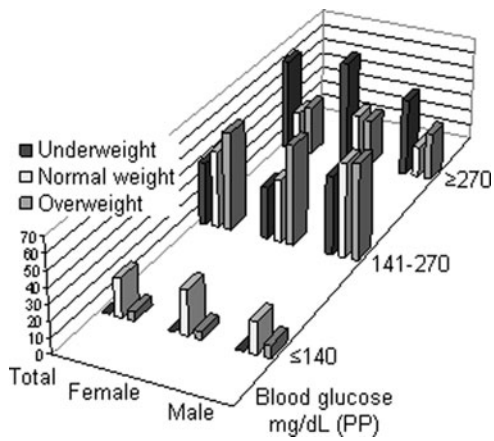

Figure 3. Nutritional status wise distribution patterns (%) of individuals from different groups of blood glucose level.

Figure 2. Comparison by Student's *t* test of underweight and overweight blood glucose levels with that of the participants of normal body weight group (a). Age wise comparison of blood glucose levels between >40 years and ≤40 years group (b). Bar represents the mean ± SE. Level of significance is denoted as a = $p < 0.05$ and b = $p < 0.01$.

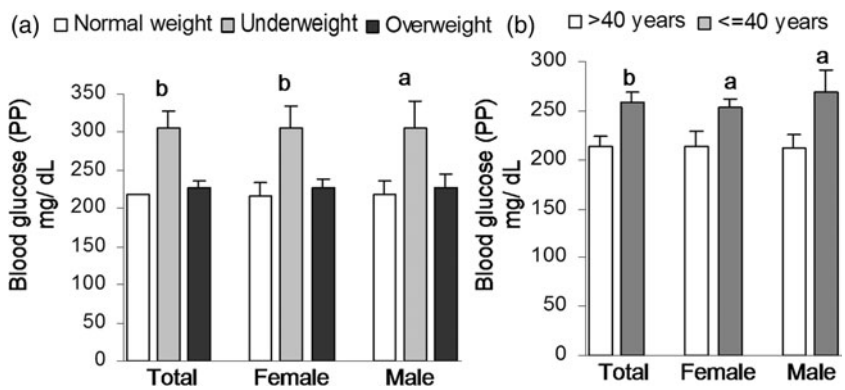

Table 1. ANOVA results on comparison between different anthropometric indices of individuals and their blood glucose levels.

	Blood glucose (mg/dl)				
	<=140	141–270	>270	Total	*F*
Female					
Number (%)	8 (15.09)	26 (49.06)	19 (35.85)	53 (100)	
Waist circumference (cm)	87.29 ± 6.19	90.58 ± 7.85	80.76 ± 9.60	86.56 ± 9.33	7.658**
Hip circumference (cm)	89.25 ± 6.86	94.34 ± 7.18	86.45 ± 5.33	90.74 ± 7.39	8.273**
Waist: hip ratio	0.98 ± 0.08	0.96 ± 0.07	0.93 ± 0.09	0.95 ± 0.08	1.396
Male					
Number (%)	5 (1.51)	22 (59.46)	10 (27.03)	37 (100)	
Waist circumference (cm)	92.70 ± 8.97	90.00 ± 9.17	88.85 ± 7.34	90.05 ± 8.53	0.328
Hip circumference (cm)	91.90 ± 7.56	91.85 ± 7.82	90.10 ± 5.53	91.38 ± 7.09	0.215
Waist: hip ratio	1.01 ± 0.08	0.98 ± 0.06	0.98 ± 0.05	0.99 ± 0.06	0.434
Combined					
Number (%)	13 (14.44)	48 (53.33)	29 (32.22)	90 (100)	
Waist circumference (cm)	89.37 ± 7.53	90.31 ± 8.39	83.55 ± 9.59	88.00 ± 9.13	5.66*
Hip circumference (cm)	90.27 ± 6.95	93.20 ± 7.51	87.71 ± 5.59	91.01 ± 7.23	5.87*
Waist: hip ratio	0.99 ± 0.08	0.97 ± 0.07	0.95 ± 0.08	0.97 ± 0.07	1.62

Significance of ANOVA are *$p<0.01$; **$p<0.001$.

Table 2. Correlation result between dependant variable blood glucose and several independent variables. MUAC and SBP represent for blood glucose, mid upper arm circumference and systolic blood pressure respectively.

Correlation between variables	*N*	*r*	*p* Value
Weight vs blood glucose	90	−0.193	0.069
MUAC vs blood glucose	90	−0.181	0.088
Waist vs blood glucose	90	−0.282	0.007*
Hip vs blood glucose	90	−0.254	0.016*
Age vs blood glucose	90	−0.201	0.058
Waist vs SBP	90	0.232	0.039*
Age vs SBP	90	0.208	0.064
Spearman's (ρ) age vs blood glucose	90	−0.355	0.001*

*Denotes statistically significant.

(Gupta *et al*., 2013). In the individuals from areas undergoing rapid economic development, some epigenetic phenomena are possibly modified by environmental, socioeconomic and nutritional factors, resulting in clinical consequences. In the present investigation more number of females is found to be diabetic in $\leq$ 40 years group. They are also noticed with higher hyperglycaemic status. Role of female steroids has been implicated in glucose homeostasis (Jana *et al*., 2014). Not only glycaemic state, these steroids have been shown to regulate the plasmin/plasminogen function and platelet role in a cardiac event of diabetic or non-diabetic origin (Jana *et al*., 2013).

Foetal metabolism associated with *in utero* exposure to maternal stress is assumed to alter gene expression resulting in the increased risk of cardiovascular, metabolic disorders and diabetes mellitus in adults (Kong *et al*., 2013). Unhygienic life style, pollution and malnutrition may generate a stressful condition in some of the rural/semi urban settings (Sinha *et al*., 2013). In addition, in some cases gender-based inequities synergize the stressful effects in female of reproductive age group (Ray *et al*., 2013). That may explain of diabetic more individuals in $\leq$40 year group in total and especially in female individuals. In the present study ~40% of individuals are found to be overweight who are diabetic. This is evident from our result that the waist and hip circumferences in sex combined group or in females are higher in the 141–270 mg/dL blood glucose group. In addition, waist circumference is found to be significantly and positively associated to the systolic blood pressure. Age is found to be markedly associated ($p<0.064$) with systemic hypertensive status. The association is found to be not significant possibly due to small sample size and higher inter-individual variability.

A report reveals that an efficient innate immune response can exaggerate obesity-associated inflammatory responses and several metabolic syndromes including diabetes (Kong *et al*., 2013). Severity of hyperglycaemia dependant higher c-reactive protein has been shown in the serum of diabetic individuals (data not shown). The increasingly young age at diagnosis of diabetes mellitus in developing countries results in prolonged exposure to gluco-lipotoxicity, sub-threshold inflammation and increased oxidative stress, which put enormous strain on pancreatic β-cells (Kong *et al*., 2013). In another project in our laboratory, it has been demonstrated that most of the diabetic patients irrespective to their nutritional status, show lower level of serum non-protein soluble thiol (NPSH) with higher level of oxidative-stress marker malondialdehyde and atherosclerotic lipid component (cholesterol and triglyceride) (unpublished data). This suggests that impaired glucose homeostasis significantly influence fat metabolism. The precise mechanism by which obesity leads to insulin resistance and to T2DM is not completely known but it may be related to several biochemical factors such as abnormalities in free fatty acids, adipokines, leptin and other substances (Ginter & Simko, 2012). One recent hypothesis from our research group has explained the fact of the translocation of glucose transporter-4 (GLUT-4) in the production of insulin in the hepatic tissues. And this translocation and synthesis mechanism has been shown to be up-regulated by the glucose induced activation of hepatocyte membrane nitric oxide synthase (NOS) (Bhattacharya *et al*., 2013). In case of fatty liver or other impairments in this organ, insulin resistance and hyperglycaemia may develop. This finding may suggest the role of extra-pancreatic insulin in glucose homeostasis. A certain

degree of impaired liver function may develop insulin resistance. The adiponectin gene variants and haplotype contribute to the genetic risk towards the development of type 2 diabetes, obesity and hypo-adiponectinemia, which has been demonstrated in a large number of population (Ramya *et al*., 2013). An increasing prevalence of diabetes and obesity in women of reproductive age in developing countries could be associated with a parallel increase in macrosomic births (Koyanagi *et al*., 2013). An extensive screening based study on 19,072 persons with diabetes suggest a trend toward more number of younger persons, particularly women being diabetic from the rural areas (Sridhar *et al*., 2010), which parallels with our present result ($t = 2.983$, $p < 0.004$ and $\chi^2 = 12.86$, $p < 0.002$). Report suggests that BMI is a strong predictor of fasting plasma glucose and glycaemic control (Sankhla *et al*., 2013) which is evident in our investigation (Figure 2). The negative association of steroids viz. oestrogen and progesterone in diabetic manifestation in female may be indicated. The control of hyperglycaemia by estriol and progesterone in alloxan-induced Type I diabetes mellitus has been demonstrated (Bhattacharya *et al*., 2014). Impaired steroid metabolism may be increasingly occurring in rural females, possibly due to malnutrition and environmental pollution.

Diabetes mellitus (DM), inflammation, and malnutrition are prevalent and regarded as contributing factors to peripheral vascular diseases (cardiac-renal) (Suliman *et al*., 2003). These vascular diseases are known to be associated with hypertension related disorder. A significant number (20–30%) of hypertensive participants are found in different nutritional categories. A report reveals that the increase in some allele in MRDM patients, and the immunogenetic basis, result in certain associations between inflammation and malnutrition in their diabetic manifestations in eastern India (Sanjeevi *et al*., 2002). The MRDM patients are typically young at onset with low body mass index and with an insulin-resistance (Kanungo *et al*., 2002). These reports are in agreement with our findings that unlike normal or overweight group, all malnourished individuals occupy 141–270 and $\geq$270 mg/dL glucose groups and those are mainly from $\leq$40 year age group. However, MRDM may co-exist with insulin dependent diabetes mellitus (IDDM) in these patients and that malnutrition could be one of the reasons for the slower onset in IDDM-affected individuals (Sanjeevi *et al*., 2002). The influence of HLA class II gene polymorphism in MRDM patients is also evident in Eastern India (Sanjeevi *et al*., 1999).

Endothelial dysfunction in malnourished individuals and a stronger influence of obesity on blood pressure have been suggested (Stanner *et al*., 1997). Anti-oxidant status, oxidative stress and DNA damage in the aetiology of malnutrition related diabetes mellitus have been proposed (McDonagh *et al*., 1997). This is in accordance with our laboratory findings (data not shown). Autoimmune responses may play a role in the aetiology of MRDM patients (Dabadghao *et al.,* 1996). The MRDM is reported to affect about 40–50% of young adult diabetics in the tropical and sub-tropical countries (Akanji, 1990). A trend of higher blood glucose level (> 270 mm/dl) is noticed among underweight participants (60%) in our present study. In the perspective of health and nutritional awareness, evidence of ingestion of cyanogens and in others consumption of coarse cereals containing some pancreatotoxins and hepatotoxins are noteworthy. It is important to recognize the etiogenesis of the entity as this may provide preventive public health measures. As discussed earlier, hepatic damage may also result in impairment of energy metabolism, insulin resistance, fatty liver and other metabolic syndrome. Malnutrition merely predisposes the islet cell to some diabetogenic agent(s) that damages pancreatic endogenous and exogeous function to varying degree. If this agent/s can be identified, preventive measures can be evolved.

Conclusion

To conclude, in the present study we have randomly covered a certain population of the community. Detailed longitudinal investigations on the role of nutrition in diabetes are required to comment on the possible association of different factors. Socio-economic up-gradation in developing countries necessitates the continuous monitoring of nutritional factors/pre-diabetic state and verify/validate the developmental indicators. The understanding of how several factors attributing to malnutrition, varying by geography, socio-demographic and economic profiles will make it easier to design global interventions that are more integrative and effective. Though some contentious parts have come from some investigators this is unequivocally recommended to focus on a large number of undiagnosed diabetic individuals and especially the younger people with a variety of risk factors both obesity and malnutrition. It may provide a better preventive measure for the development of community and public health.

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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