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Association between night blindness history and risk of diabetes in the Chinese population: a multi-center, cross sectional study

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Abstract

Aims Night blindness (NB), an important manifestation of VA deficiency, may be associated with the odds of diabetes. The aim of this study was to explore the probable association between NB history and diabetes in Chinese community-dwelling adults.

Methods This multi-center, cross-sectional study enrolled a total of 5664 participants aged 18–82 years from eight sites in China. Information on demographics and medical history was collected using a standardized questionnaire. Diabetes was diagnosed based on the oral glucose tolerance test or a self-reported history. NB history was ascertained by a face-to-face interview with reference to the recommendation by the World Health Organization. Logistic regression analysis was used to evaluate the association between NB history and the odds of diabetes.

Results A total of 5049 participants were finally included, with 252 ascertained with NB history and 1076 with diabetes. The mean age of included participants was 52.9 years, and the percentage of participants with NB history was significantly higher in participants with diabetes than those without (7.0% vs. 4.5%). The multivariable adjusted odds ratio for diabetes was 1.41 (95% confidence interval 1.06, 1.89) in participants with NB history compared with those without. Furthermore, mediation analysis showed that obesity, as assessed by waist-height ratio, partially mediated the relationship between NB history and increased odds of diabetes.

Conclusions The results suggest that NB history might be associated with increased odds of diabetes in Chinese community-dwelling adults.

Keywords Night blindness, Diabetes mellitus, Risk, Waist-height ratio

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Introduction

Micronutrients (like vitamins) are important environmental factors affecting the development of diabetes [1]. Vitamin A (VA) is a dietary and fat-soluble vitamin that is involved in embryonic development, vision, immunity, and reproduction [2]. Moreover, recent studies have demonstrated that VA is closely related to diabetes [3–5]. This lies in the evidence that VA plays a key role in islet cell development [6], while VA deficiency may lead to β cell apoptosis, loss of β cell mass and activation of islet stellate cell [7, 8]. Moreover, VA has a regulatory effect on insulin sensitivity [9, 10]. In addition to diabetes, studies have also shown that VA deficiency is associated with obesity and metabolic syndrome [11, 12].

Night blindness (NB), characterized by impaired vision at nighttime, is an important manifestation of VA deficiency. And it could be easily identified by a questionnaire interview based on the recommendation from the World Health Organization [13–15]. NB is a problem of enormous magnitude worldwide, particularly in the underdeveloped regions [14, 16]. However, few studies have been conducted to explore the association between NB history and diabetes to date, although as aforementioned there is an increasing number of studies exploring the mechanism between VA and diabetes [17–19].

Obesity, as indicated by waist-to-height ratio (WHtR), is a well-identified risk factor for diabetes [20, 21]. WHtR is more indicative of abdominal fat accumulation when compared to other obesity indicators (like BMI or waist circumference) [22]. Research also shows that WHtR is more closely related to diabetes than BMI in the Chinese population [23]. Besides, several lines of evidence have supported the relevance of VA deficiency to the development of obesity [24–27]. In animal studies, VA supplementation is shown to effectively regulate adipose tissue mass [28, 29]. These observations suggest a potential role of obesity in linking NB history to diabetes, intriguing us to examine whether obesity (WHtR) could mediate the association between NB history and diabetes in the real-world setting.

Given these, the primary aim of this study was to investigate the association between NB history and diabetes in Chinese community-dwelling adults. The secondary aim was to assess whether this association could be mediated by obesity, as evaluated by WHtR.

Methods

Study design and population

Participants in this study were from the first follow-up survey of the SENSIBLE-cohort study, which was designed to determine the optimal cut-off value of advanced glycation end-products and HbA1c for diagnosing T2D in China [30, 31]. This first follow-up survey was started in July 2018 and a total of 5664 participants completed the survey. The survey included a face-to-face interview, physical examination and laboratory examination. Upon the exclusion of 460 and 155 subjects due to the lack of data to confirm the presence or absence of NB history and diabetes, respectively, a total of 5049 participants were included in the final data analysis (Fig. 1).

The study protocol was approved by the ethics committee of Zhongda Hospital, Southeast University and other sub-center hospitals involved, and written informed consent was signed by each participant prior to their participation.

Data collection

A standardized questionnaire was used to collect information on demographics (including sex, age, ethnicity, education level, annual household income and family history of diabetes) and medical history (including hypertension, dyslipidemia, diabetes, heart disease, and medication use) by trained doctors and nurses using a face-to-face interview. Anthropometric parameters including body weight, height, waist and hip circumference (WC) were measured based on standard protocols.

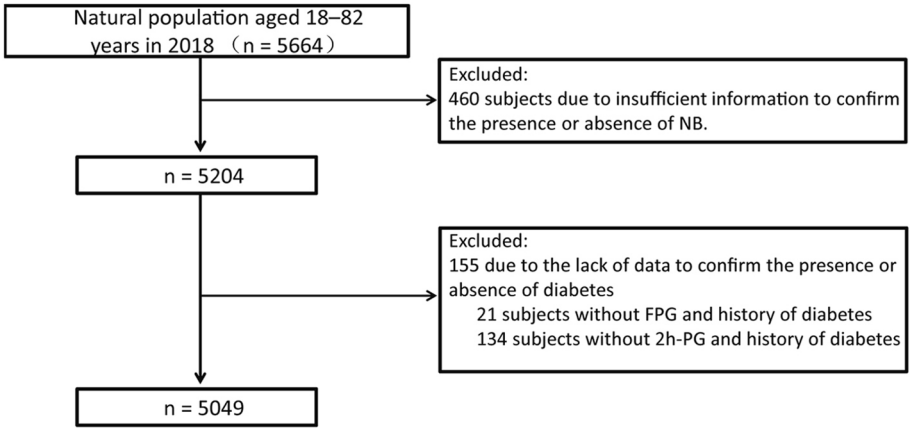

Fig. 1 Flow chart of this study. FPG, fasting plasma glucose; PG, plasma glucose

BMI (kg/m^2) was calculated as body weight/(height^2), WHR was as WC/hip and WHtR was as WC/height. Obesity was defined as BMI≥28 kg/m^2. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were also measured. Fasting blood samples were collected for measurements of fasting plasma glucose (FPG), glycosylated hemoglobin A1c (HbA1c), total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), uric acid. Oral glucose tolerance test was performed in participants without a prior history of diabetes, and venous blood samples were obtained for the measurement of 2 h plasma glucose (2 h-PG) at 120 min after the 75 g oral glucose load.

Ascertainment of night blindness history and diabetes

NB history was ascertained by trained doctors and nurses during the face-to-face interview. With reference to the questionnaire recommended by the World Health Organization, the questionnaire interview includes: (1) When you were a child (≤9 years old), did you have any problem seeing at nighttime, such as difficulty spotting food or toys? (2) Do you have any problem seeing at nighttime now? (3) Do you have any problem seeing in daytime now? (Shortsightedness, longsightedness, blurred or impaired vision)? (4) Have you ever suffered from night blindness? (Use local term that describes the symptom)? The detailed questionnaire can be found in Supplementary Materials.

Participants were considered with NB history if they answered "Yes" to question (4). The reasons to employ the first three questions were mainly designed to get a more accurate answer or enable the participants to better understand what NB is when they were asked the fourth question.

Diabetes was defined as FPG≥7.0 mmol/l, or 2 h PG≥11.1 mmol/l, or a self-reported history of diabetes (including diabetes medication use) [32].

Statistical analysis

Continuous data are presented as means and standard deviations (SDs), and categorical variables are as numbers and percentages. Missing data in covariates including age, heart rate, systolic blood pressure, Tc, HDL-C, Cr, and uric acid (UA), WHR and BMI were imputed using multiple imputation methods. The difference between participants with and without diabetes was assessed using the $\chi 2$ and student-t test where appropriate. Odds ratio (OR) and 95% confidence intervals (CI) were estimated using logistic regression analysis to examine the association between NB history and diabetes. Four different models were constructed, with model 1 including only the study variable, model 2 controlled for age and sex, model 3 additionally controlled for HR, SBP, TC, HDL-C, Cr, and UA based on model 2, and model 4 additionally controlled for BMI based on model 3.

Sensitivity analyses were performed by excluding participants with missing data in covariates including age, sex, HR, SBP, Tc, HDL-C, Cr, UA and BMI. Subgroup analyses stratified by sex (male vs. female), age (≥45 vs.<45 years), BMI (≥28 vs.<28 kg/m^2), WHR (Female, >0.80 vs.≤0.80; male >0.85 vs.≤0.85) and WHtR (≥0.5 vs.<0.5) were performed, with their interaction effects being tested. Mediation analysis was performed to assess the total, direct and indirect effects of NB history on diabetes in relation to BMI, WHR and WHtR. Data analyses were conducted using SPSS 25.0 (SPSS Inc., Chicago, IL, USA). Mediation analyses were conducted by RStudio with BruceR package, with the mediation effect being calculated as indirect effect/total effect × 100%. Statistical significance was defined as a two-sided p value of <0.05.

Results

Characteristics of study population

The baseline characteristics of the included 5049 participants based on the presence of NB history are shown in Table 1. Compared with participants without NB history, those with NB history were more likely to be females (64.2% vs. 71.2%) and had higher age, BMI, WHtR, HbA1c, TC and LDL-C. Moreover, compared with participants without diabetes, those with was more likely had NB history (4.5% vs. 7.0%, Supplementary Table 1).

Odds of diabetes in relation to NB history

As shown in Table 2, participants with NB history were more likely to have diabetes than those without (29.8% vs. 20.9%). Logistic regression analysis showed that the crude OR of diabetes was 1.61 (95% CI 1.22, 2.12) in participants with NB history compared with those without NB history. After multivariable adjustment, the association between NB history and diabetes remained significant (OR 1.41; 95% CI 1.06, 1.89; P=0.02; model 4). Sensitivity analyses upon the exclusion of participants with missing information in covariates showed similar outcomes (Table 2).

Subgroup analysis

As shown in Table 3, subgroup analysis showed that sex, age, BMI, WHR and WHtR had no significant interaction effect on the association between NB history and diabetes ($P_{interaction}$ = 0.498, 0.884, 0.402, 0.250 and 0.790 respectively).

Mediation analysis

Figure 2 and Supplementary Fig. 1 show the results of the mediation analysis on the relationship between NB history and diabetes. The association between NB history and diabetes was found to be mediated by BMI, waist-hip

Table 1 Baseline characteristics of included participants

	overall (5049)	Non-NB history (4797)	NB history (252)	*p*
Age	52.94 ± 9.89	52.77 ± 9.95	56.29 ± 8.00	< 0.001
Male, n (%)	1788 (35.4%)	1716(35.8%)	72 (28.8%)	< 0.001
BMI, kg/m2	25.35 ± 4.89	25.30 ± 4.93	26.15 ± 3.99	0.008
Diabetes				< 0.001
YES	1076 (21.3%)	1001 (20.9%)	75 (29.8%)	
NO	3973 (78.7%)	3796 (79.1%)	177 (70.2%)	
Waist height ratio, WHtR	0.53 ± 0.07	0.53 ± 0.07	0.56 ± 0.07	< 0.001
Waist hip ratio, WHR	0.89 ± 0.07	0.89 ± 0.07	0.91 ± 0.06	< 0.001
Heart Rate, bpm	78.18 ± 11.45	78.22 ± 11.48	79.40 ± 10.91	0.270
SBP, mmHg	131.79 ± 19.34	131.68 ± 19.30	133.81 ± 20.01	0.089
DBP, mmHg	81.01 ± 11.75	80.99 ± 11.75	81.32 ± 11.61	0.663
FPG, mmol/L	5.76 ± 1.48	5.76 ± 1.49	5.83 ± 1.37	0.447
2hPG, mmol/L	7.10 ± 2.44	7.10 ± 2.46	7.17 ± 2.14	0.712
HbA1c	5.59 ± 0.95	5.58 ± 0.95	5.71 ± 1.02	0.034
TC, mmol/L	4.76 ± 1.03	4.75 ± 1.03	4.91 ± 1.05	0.021
TG, mmol/L	1.81 ± 2.05	1.80 ± 1.99	1.90 ± 2.86	0.468
HDL-C, mmol/L	1.37 ± 0.38	1.37 ± 0.38	1.40 ± 0.38	0.262
LDL-C, mmol/L	2.72 ± 0.74	2.71 ± 0.74	2.83 ± 0.76	0.011
Cr, umol/L	67.80 ± 16.92	67.88 ± 17.03	66.16 ± 14.63	0.116
UA, umol/L	310.81 ± 87.09	311.02 ± 86.15	306.83 ± 86.15	0.547

There were 3 and 9 participants with missing information for UA and BMI respectively; and 50 participants without HR, 24 participants without SBP, 2 participants without age, HDL-C and Cr at baseline

Continuous data are presented as means and standard deviations and were analyzed by the student's t test. Categorical data are presented as n and %, and were analyzed by the χ2 test

BMI body mass index, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *FPG* fasting plasma glucose, *2 h-PG* 2-hour plasma glucose, *HbA1c* hemoglobin A1c, *TC* total cholesterol, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *TG* triglyceride, *Cr* creatinine, *UA* uric acid

ratio (WHR) and WHtR, with their mediation effect being 7.9%, 21.1% and 27.0% (bootstrap 95% CI: 0.014, 0.034, $p<0.001$) respectively.

Discussion

In this multicenter, cross-sectional study of Chinese community-dwelling adults, we found that: (1) participants with diabetes were more likely to present with NB history than those without; (2) NB history was associated with increased odds of diabetes, even after multivariable adjustment; and (3) the association of NB history with diabetes was partially mediated by WHtR.

To the best of our knowledge, this is the first study to examine the relationship between NB history and diabetes in a Chinese population. NB, which is a specific and sensitive clinical manifestation of VA deficiency [33], could be easily and quickly ascertained via the questionnaire interview. In our study, about 5.0% of the Chinese

Table 2 Odds of diabetes in relation to night blindness (NB) history in Chinese adults

	Non-NB cases (4797)	NB cases (252)	*p*
Diabetes	1001	75	
Rate (%)	20.9	29.8	
Model 1	1 (Ref.)	1.61 (1.22–2.12)	0.001
Model 2	1 (Ref.)	1.45 (1.26–1.68)	0.010
Model 3	1 (Ref.)	1.44 (1.24–1.67)	0.014
Model 4	1 (Ref.)	1.41 (1.06–1.89)	0.021
Sensitivity analysis*	Non-NB cases (4744)	NB cases (250)	
Diabetes	990	75	
Rate (%)	20.9	29.8	
Model 1	1 (Ref.)	1.59 (1.20–2.11)	0.001
Model 2	1 (Ref.)	1.45 (1.09–1.92)	0.012
Model 3	1 (Ref.)	1.43 (1.06–1.91)	0.018
Model 4	1 (Ref.)	1.40 (1.04–1.87)	0.026

Model 1 crude model includes only NB history

Model 2 adjusted for age, sex

Model 3 adjusted for all factors in model 2 plus HR, SBP, TC, HDL-C, Cr, UA

Model 4 adjusted for all factors in model 3 plus BMI

* Sensitivity analyses were performed by excluding participants with missing data in covariates including age, sex, HR, SBP, Tc, HDL-C, Cr, UA and BMI.

NB night blindness, *HR* heart rate, *SBP* systolic blood pressure, *TC* total cholesterol, *HDL-C* high-density lipoprotein cholesterol, *Cr* creatinine, *UA* uric acid, *BMI* body mass index

adults had a history of NB. This is generally comparable to the VA deficiency data from the World Health Organization and several other Chinese studies, which were reported to be 0.25-5.16% [34–39]. Our study showed a positive association between NB history and the odds of diabetes. This is consistent with several prior studies that observed a lowered VA intake in subjects with diabetes [40, 41]. Our study also showed that sex, age, BMI, WHR and WHtR had no interaction effect on the association between NB history and diabetes. These may due to insufficient statistical power, especially the small number of diabetic patients with NB history after grouping. So, more data validation is needed.

Our mediation analysis showed that WHtR, an indicator of obesity, significantly mediated the association between NB history and diabetes. This could be supported by the relevance of VA deficiency to the development of obesity [24–27, 42, 43], and the evidence that VA deficiency may influence the expression of the hepatic genes for fuel metabolism, adipocyte differentiation and adipogenesis [44–47]. Moreover, obesity is associated with occurrence of type 2 diabetes [48–50]. Compared with BMI and WHR, WHtR has a greater mediated effect, which may be because it is a better indicator of central obesity. Previous study also showed body adiposity, especially visceral fat, is correlated with reduced serum concentrations of vitamin A [51]. Considering these, it seems likely that obesity, especially central obesity, could be a therapeutic target for the prevention of

Table 3 Interactive effect of NB history on the risk of diabetes (odds ratios and 95% confidence intervals)

	Non-NB		NB				
	Diabetes (1001)	Total (%)	Diabetes (75)	Total (%)	OR	95% CI	*p*
Sex							
Male (1788)	434	1716 (25.3)	27	72 (37.5)	1.57	0.95–2.60	0.080
Female (3261)	567	3081 (18.4)	48	180 (26.7)	1.34	0.93–1.93	0.114
$P_{interaction}$							0.498
Age (years)							
<45 (897)	78	883 (8.8)	2	14 (14.3)	1.28	0.24–6.71	0.774
≥45 (4152)	923	3914 (23.6)	73	238 (30.7)	1.47	1.10–1.97	0.010
$P_{interaction}$							0.884
BMI (kg/m2)							
<28 (3981)	705	3802 (18.5)	50	179 (27.9)	1.54	1.09–2.19	0.016
≥28 (1068)	296	995 (29.7)	25	73 (34.2)	1.17	0.69–1.98	0.570
$P_{interaction}$							0.402
WHR							
≤0.80(F)or ≤0.85 (M) (627)	59	611(9.7)	1	16(6.3)	0.40	0.05–3.31	0.399
>0.80(F)or > 0.85 (M) (4422)	942	4186 (22.5)	74	236(31.4)	1.45	1.08–1.94	0.014
$P_{interaction}$							0.250
WHtR							
<0.5 (1519)	185	1464 (12.6)	12	55 (21.8)	1.62	0.82–3.22	0.167
≥0.5 (3530)	816	3333 (24.5)	63	197 (31.2)	1.36	0.98–1.87	0.064
$P_{interaction}$							0.790

Adjusted for all other confounding factors (age, sex, heart rate, systolic blood pressure, total cholesterol, high-density lipoprotein, creatinine, uric acid, body mass index). *F* female, *M* male

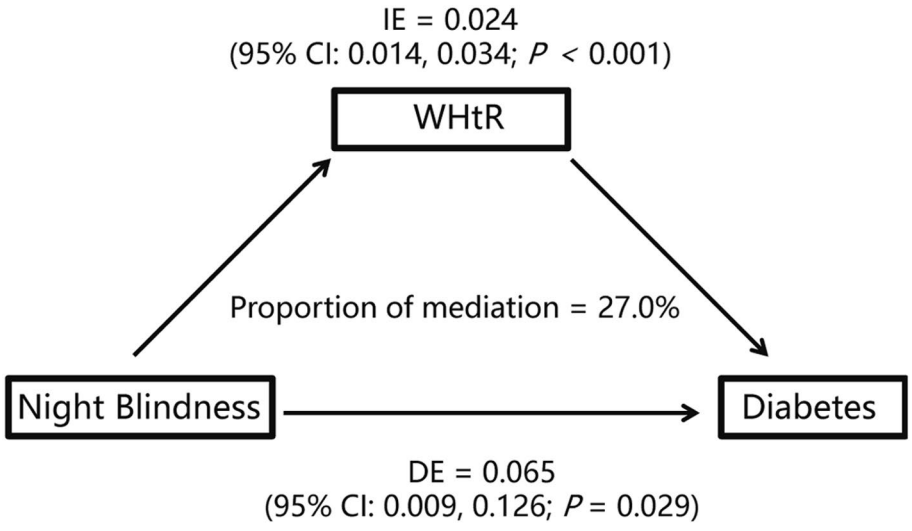

Fig. 2 Mediation analysis on the relationship between night blindness history and diabetes. IE, indirect effect; DE, direct effect; WHtR, waist-to-height ratio

diabetes in participants with NB history; however, this speculation needs to be verified by interventional studies.

Several limitations should be noted when interpreting our findings. First, NB history was ascertained subjectively using a self-reported questionnaire. This may lead to an increased risk of recall bias. Future studies might benefit from the objective assessment for NB history by measuring serum retinol, performing electroretinography or collecting medical records. Second, our study could not address the issue whether the severity of NB history was associated with the odds of diabetes, since such information was not obtained. Third, despite the adjustments for multivariable, residual confounding cannot be excluded from unmeasured factors, such as the status of other micronutrients [52]. Fourth, the cross-sectional nature of our study cannot determine

the causal relationship between NB history and diabetes, which requires to be confirmed by future prospective studies. Finally, our present study enrolled only Chinese population, the generalization of our findings to other populations (e.g., Americans) might be limited.

In conclusion, our study shows that NB, a clinical manifestation of VA deficiency, might be associated with increased odds of diabetes in Chinese adults. Moreover, this association was likely to be mediated by obesity. Further perspective cohort studies that enrolled populations from different ethnics are needed to confirm our findings.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12902-024-01721-2.

Supplementary Material 1.

Acknowledgements
Not applicable.

Research involving human participants and/or animals
This study involved human participants to evaluate the relationships of night blindness with odds of diabetes and test whether obesity mediate these associations in Chinese population.

Informed consent
Informed consent was obtained from all individuals included in the study.

Author contributions
JB.W., YT.Z., Y.L., and MM.S. were responsible for study conception and design. YZ.D., TT.L., XH.W., V.C., Q.W., Y.C., Z.S., ZS.C., H.W. and CM.N. contributed to data collection. D.W., S.Q., and Z.S. contributed to analysis and interpretation of results. JB.W. and V.C. drafted the manuscript. All authors reviewed the results and approved the final version of the manuscript.

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Availability of data and materials
The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study protocol was approved by the ethics committee of Zhongda Hospital, Southeast University and other sub-center hospitals involved, and written informed consent was signed by each participant prior to their participation. We ensured that the techniques in this study complied with the relevant guidelines and ethical principles, including the Declaration of Helsinki.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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