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Hematological Parameters and Metabolic Syndrome: Findings from an Occupational Cohort in Ethiopia

K Nebeck[a], **B Gelaye**[a,d,*], **S Lemma**[b], **Y Berhane**[b], **T Bekele**[c], **A Khali**[c], **Y Haddis**[c], and **MA Williams**[a,d]

[a]Department of Epidemiology, Multidisciplinary International Research Training Program, University of Washington School of Public Health, Seattle, Washington, USA

[b]Addis Continental Institute of Public Health, Addis Ababa, ETHIOPIA

[c]International Clinical Laboratories, Addis Ababa, ETHIOPIA

[d]Departmet of Epidemiology, Harvard School of Public Health, Boston, Massachusetts, USA

Abstract

Objective—To examine associations between hematological parameters (i.e., hemoglobin, hematocrit, platelet counts, red blood cell (RBC), and white blood cell (WBC) counts) and components of metabolic syndrome (MetS) among working adults in Addis Ababa, Ethiopia.

Methods—Participants were 1,868 (1,131 men and 737 women) working Ethiopian adults. MetS was classified according to the International Diabetes Federation criterion. Odds ratios (OR) and 95% confidence intervals (95% CI) of MetS were calculated using logistic regression procedures.

Results—Hematologic parameters (hemoglobin, hematocrit, and RBC) were positively associated with MetS components (P_{trend}<0.05).In both men and women, white blood cell (WBC) counts were positively associated with BMI and waist circumference (P<0.05). RBC counts were associated with diastolic blood pressure in men (P<0.05) and women (P<0.001). Men in the third quartile of hemoglobin concentrations had 2-fold increased odds (OR=1.99; 95% CI) of MetS compared with the lowest reference quartile (P_{trend} = 0.031) while women in the fourth hemoglobin quartile had 2.37-fold increased odds of having MetS compared with the reference group (p_{trend} = 0.003). Both men and women in the fourth quartiles of RBC counts had2.26-fold and 3.44-foldincreased odds of MetS (P=0.002 in men, P <0.001 in women). Among women, those in the fourth quartiles of hematocrit and platelet counts had2.53-fold and 2.01-foldincreased odds of MetS as compared with those in the reference group (P_{trend} = 0.004 and 0.065 respectively).

Conclusions—Our study findings provide evidence in support of using hematological markers for early detection of individuals at risk for cardiovascular disease.

*Corresponding author Mr. BizuGelaye Department of Epidemiology Harvard School of Public Health 677 Huntington Ave, Fifth Floor Boston, MA02115 USA Telephone: 617-432-6477 Facsimile: 617-566-7805 bgelaye@hsph.harvard.edu.

Conflict of Interest: NIL

Introduction

Cardiovascular disease (CVD) is the leading cause of non-communicable disease mortality worldwide. In 2008, CVD accounted for roughly 30% of global deaths [1]. A constellation of risk factors collectively referred to as metabolic syndrome (MetS) is known to precede the onset of CVD and type 2 diabetes (T2DM)[2]. These risk factors include abdominal obesity, hypertension, reduced high density lipoprotein cholesterol, elevated triglycerides, and high fasting glucose concentrations [2, 3].

A growing body of epidemiologic evidence shows that incidence of MetS, CVD and T2DM areincreasing in Sub-Saharan Africa where behavioral and lifestyle changes, commonly associated with increasing urbanization, are having detrimental effects on health. Such changes include increased tobacco and alcohol use, poor diet (e.g., increased calorie dense foods and low dietary fiber intake), and physical inactivity[4–8]. A recent study conducted among adults in Addis Ababa, Ethiopia revealed unexpectedly high prevalence estimates of hypertension: 31.5% among men and 28.9% among women [6]. Furthermore, Tran et al reported the prevalence of MetS to be 14.0% in men and 24.0% in women in their study of adults in Addis Ababa, Ethiopia [7].

A complete blood count is an inexpensive, frequently obtained test of hematological status recorded during routine health examinations [9]. Increasingly investigators have noted that hematological parameters commonly available from routine clinical examinations may provide important information indicative of increased risk for MetS. Consequently, some investigators have argued that hematological parameters may be used in early detection and evaluation of cardiovascular disease prevention and control programs. Of note, investigators have reported that elevated hemoglobin, hematocrit, white blood cell (WBC), red blood cell (RBC), and blood platelet counts are correlated with MetS and its components [10–23]. For example, in Thailand Lohsoonthorn et al reported that men in the highest quartiles of WBC counts ($>8.03\times10^3$cells/μl) had a 2.26- fold (95% CI: 1.27–4.02) increased odds of MetS as compared with those whose WBC counts were in the lowest quartile ($<5.72 \times 10^3$cells/μl) [16]. The odds of MetS were particularly elevated for women with high WBC counts (OR for highestvs. lowest quartile = 5.41; 95% CI:2.08–14.07)[16].

Currently, no published research has investigated relationships between hematological parameters and MetS in Sub-Saharan African populations. We, therefore, sought to evaluate the relationship between hematological parameters and MetS among working adults in Ethiopia. Elucidation of the relationship between hematological parameters and MetS may provide evidence in support of using low cost, readily available, routinely collected clinical hematological parameters for the early detection of individuals at risk for MetS and CVD.

Methods

This study was conducted in Addis Ababa, the capital city of Ethiopia, during the months of December 2009 and January 2010. Study participants were current permanent employees of the Commercial Bank of Ethiopia and teachers in government and public schools of Addis Ababa. Details of the study setting, sampling strategy and data collection procedures have been described in detail elsewhere [7, 8]. For the present study, a total of 1,858 (1,131 men and 737 women) participants were included.

We employed the World Health Organization's (WHO) STEP-wise (STEPS) approach for non-communicable diseases surveillance approach to collect data[24]. This approach consists three levels of risk factor assessment including collecting socio-demographic and behavioralinformation using questionnaires (step 1), physical measurements (step 2), and taking blood samples for biomedical assessment, (step 3). Study subjects were current

permanent employees of the Commercial Bank of Ethiopia and teachers in public and government schools of Addis Ababa. Blood specimens were collected from each participant by research nurses and processed at the Internal Clinical Laboratories. The collected blood samples were processed according to standard operating procedures to determine participants' complete blood counts including white blood cells, red blood cells, platelets, hemoglobin, and hematocrit. All subjects gave informed consent and research protocols were approved by the Addis Continental Institute of Public Health in Addis Ababa, Ethiopia and the Human Subjects Division at the University of Washington, USA.

Analytical variable specification

In this study, characterization of MetS was in accordance with the International Diabetes Federation(IDF) definition[3]. MetS was defined as a presence of central obesity (defined as waist circumference of ≥94cm for men and ≥80cm for women) and at least two of the following factors: [1] raised triglycerides (≥150mg/dL) or specific treatment for this lipid abnormality, [2] reduced HDL cholesterol (≤40mg/dL for men and ≤50mg/dL for women) or specific treatment for this lipid abnormality, [3] raised systolic (≥130mmHg) or diastolic (≥85mmHg) blood pressure or treatment of previously diagnosed hypertension, [4] raised fasting plasma glucose levels (≥100mg/dL) or previously diagnosed with type 2 diabetes.

Statistical analysis

Frequency distributions of socio-demographic characteristics of the study population were determined by performing cross-tabulations of covariates across gender and were expressed in percentage (%). Continuous variables were expressed as mean ± standard error of mean values. For skewed variables median [interquartile range] were provided. Chi-Square tests were used to evaluate the differences in the distribution of categorical variables for study groups. Student's T-tests were used to evaluate differences in mean values for study groups. Pearson's partial correlation coefficients were calculated between hematologic parameters (i.e., hematocrit, hemoglobin, platelet counts, RBC, WBC) and components of MetS (fasting blood glucose, triglyceride concentrations, HDL-C concentrations, systolic BP and diastolic BP). Participants were divided into three groups according to the number of components of the MetS: no MetS, abdominal obesity, abdominal obesity and 1 component of MetS, and abdominal obesity and ≥ 2 components of MetS. Means of each hematological parameter were then calculated for each subgroup. Significance for monotonic trends was assessed by linear regression analysis.

Logistic regression procedures were used to examine the relative odds of having MetS. Univariate and multivariate logistic regression procedures were used to calculate unadjusted odds ratios (ORs) and 95% confidence intervals (95% CIs) of MetS in relation to varying categories of each hematological parameter. Hematological parameters were categorized into quartiles and the lowest quartile was specified as the reference group. Potential confounding variables were considered a priori on the basis of their hypothesized relationship with MetS and each hematologic parameter. Confounding was also assessed by entering potential covariates into a logistic regression model one at a time, and by comparing the adjusted and unadjusted OR. Final logistic regression models included covariates that altered unadjusted ORs by at least 10%[25]. In multivariate analysis, tests for linear trend acrossincreasing categories of hematological parameters were conducted by treatingthe four-level hematological quartiles as an ordinalvariable. Separate analyses were performed for men and women. Statistical analyses were performed using SPSS (version 19.0, IBM, Chicago, IL, USA) software. Confidence intervals were calculated at 95% level and all reported P-values are two tailed.

Results

Socio-demographic, lifestyle and clinical characteristics of study participants are summarized in Table 1. More than two third of participants reported a “moderate” level of alcohol consumption (70.7% of men and 68.5% of women) whilst only 11.8% of men and 0.1% of women reported heavy alcohol use. Current khat use (an evergreen plant with amphetamine-like effects commonly used as a mild stimulant for social recreation and improve work performance in Ethiopia)[26, 27] was 13.7% among men and 0.5% among women. In addition, 7.2% of men and 0.1% of women reported being current cigarette smokers.

As shown in Table 2, there were substantial differences in mean values for cardiometabolic and hematological parameters between men and women in this cohort. Mean RBC counts were higher in men (mean±standard deviation:5.5±0.7 vs. 4.8±0.6, P-values < 0.001) than women (mean=, SD: 0.6). Similarly mean percentages of hematocrit and waist circumference were higher among men compared to women. However, mean plateletcounts were higher in women(mean± standard deviation: 229.3±62.7) compared with men (85.7±11.3) WBC count and fasting glucose levels remained similar between men and women.

We next sought to evaluate the extent to which, if at all, hematological parameters were associated with successively increasing number of MetS components (Table 3). Mean platelet counts decreased with increasing MetS components among men (P<0.05). No similar trends were observed among women. WBC counts, however, increased with increasing numbers of MetS components in both men and women although statistical significance was not achieved. Among women, we found that levels of hemoglobin, hematocritand red blood cells increased with increasing components of MetS.

As shown in Table 4, after adjusting for age, hemoglobin counts were positively associated with BMI and waist circumference in men (P <0.001). Positive association was observed between hemoglobin and triglycerides concentrations among men and women (men: P<0.001, women: P<0.05). WBC counts were also positively associated with BMI and waist circumference in men (P<0.05) and in women (P<0.05). In addition, a statistically significant association between RBC counts and diastolic blood pressure was noted in both genders (men: P<0.05; women: P<0.001). RBC counts were significantly positively associated with waist circumference in men at a P-value of <0.001 whereas no such associations were found in women.

The odds of MetS risk according to each quartile of hemoglobin, hematocrit, platelet, WBC and RBC counts are shown in Table 5. After adjusting for potential confounders, men within the third quartile of hemoglobin (16.4–17.2 g/dL) had a 1.99-fold increased odds of MetS as compared with the reference group (quartile 1: hemoglobin <15.8 g/dL) (95% CI: 1.2–3.3) (P_{trend} = 0.031). Statistically significant increases in risk of MetS were found across successive quartiles of hemoglobin (P_{trend} = 0.003) and hematocrit (P_{trend} = 0.004) levels in women. Those in the highest quartile of hemoglobin had a 2.37-fold increased odds of MetS(95% CI: 1.36–4.12). There was also a 2.53-fold increased odds of MetS for women in the highest compared to lowest quartiles of hematocrit (95% CI: 1.43–4.50). The odds ratio of developing MetS for women in the highest quartile of blood platelets was 2.01 (95% CI: 1.12–3.63) however, no significance was found across increasing quartiles of platelet counts (P_{trend} = 0.065).

The odds of MetS increased across quartiles of RBC counts in both genders (men: P_{trend} = 0.002; women: P_{trend} = <0.001). Men in the highest quartiles of RBC counts (>5.81×10^6) had a 2.26-fold increased odds of having MetS than those in the reference group (OR=2.26,

95% CI: 1.29–3.94). Women also had a 3.44-fold increased odds of having MetS when in the highest quartile group (>5.11×10^6) for RBC count (OR=3.44, 95% CI: 1.93–6.13) compared with the reference group.

Discussion

We found levels of hemoglobin, hematocrit and RBC counts to be significantly associated with accumulating components of MetS in women while no statically significant associations between hematological parameters and components of MetS were found among men. In addition,we found that elevated WBC counts were significantly associated with BMI and waist circumference in both men and women.

Our findings are in general agreement with previous reports[12, 16, 17, 20, 22]. For instance, in a Brazilian study Ellinger et al. found significant correlations between hematologic parameters (RBC, WBC, hemoglobin concentrations and hematocrit) and insulin resistance syndrome[12]. In 2005, Mardi et al, in Israel,found a significant correlation between increased erythropoiesis and the number of components of MetS in both men (p= 0.003) and women (p= 0.016). Erythropoiesis and waist circumference were also correlated in both men and women (p<0.005) [17]. While significant associations between platelet and WBC counts and increasing features of MetS was not observed in our study, some investigators have noted such associations [11–13, 15, 16, 18, 22, 23]. For example, Lohsoonthorn et al in their study among Thai men and women found mean WBC and platelet counts were 14.1% and 9.5% greater for women with 3 or more features of MetScompared with those lacking any features of MetS. Hemoglobin and hematocrit values were also significantly associated with MetS components in women but not in the men of their study (Hemoglobin P_{trend}= 0.004; Hematocrit P_{trend} = 0.001) [16]. Similar findings were reported by Wang et al[22]. On the contrary, Taniguchi et al, in their study of study of non-obese Japanese T2DM patients, found platelets to be an independent predictor of insulin resistance (P<0.0001) [20]. A study by Tamariz et al found adults in the highest hematocrit quartiles (>44.3%)were 60% more likely to develop diabetes compared with theircounterparts in the lowest quartiles (<39%)[19]. In our study, women in the highest quartiles of hematocrit (>50.4%) had a 2.53-fold increased odds of having MetS compared with the reference quartile (<45.6%)

Differences in study design, operational definitions of cardiovascular disease risk, as well as ethnic and racial differences across study populations may account for the absence of consistency across studies. Despite these variations, the concordance of our results with many other studies [10, 12, 16, 17, 19, 21, 22] suggests that observed associationsofhematologic parameters with MetS may provide some important opportunities for CVD risk prediction and for understanding the pathophysiology of cardiometabolic risk. It is important to note, however, thatbiological pathways linking cardiometabolicdisordersand hematologic parameters are not yetfully understood. Investigators have proposed a mechanism in which components of MetS, particularly raised LDL cholesterol, hypertension and insulin resistance trigger endothelial dysfunction and an inflammatory response[28]. Prolonged inflammation increases activation of WBC and endothelial cellswhich in turn leads to platelet and thrombus formation[28]. As mentioned previously, increased RBC and glycated hemoglobin concentrations can result from elevated insulin and glucose levels in the blood [17, 29–31]. High levels of RBC's, glycated hemoglobin and hematocrit can lead to reduced blood flow (via increased blood viscosity) and subsequent decreased circulation of oxygen, insulin and glucose to essential tissues. Therefore, slowed blood viscosity due to accumulation of hematological components can be a catalyst when it comes to the progression of type 2 diabetes[19, 32].

Some caveats should be considered when interpreting the results of our study. Social desirability bias to survey questions is a potential problem in our study where participants are likely to report low khat use and current smoking status especially among the women in our study population (0.5% and 0.1% respectively). The cross sectional nature of our study design does not allow us to determine the causal relationship between hematological parameters and MetS. Longitudinal studies, with serial measurements of hematologic parameters and the onset of conditions that define MetS, are needed.

MetS has been associated with an increased risk for CVD and T2DM[2]. A growing body of evidence shows that MetS is currently an important and prevalent risk factor in many Sub-Saharan African countries including Ethiopia [4–8]. Elucidating the changes in hematological parameters indicative of MetS could lead to new standards of early detection and potentially reduce CVD morbidity and mortality. Use of simple, inexpensive and widely available hematological paramaters as biological markers for MetS and CVD may be useful in low income countries such as Ethiopia where a physician's limited resources often prevent proper diagnosis. A recent study conducted by Gelaye et al has established reference values of hematological parameters in healthy Ethiopian adults [33]. These values could provide a baseline standard by which other Ethiopians may be compared when assessing for increased risk of MetS.

In summary, we found elevated levels of hemoglobin, hematocrit and RBCl counts to be significantly associated with clustered components of metabolic syndrome in working adults in Ethiopia. Regardless of the mechanisms, available evidence suggests that hematological parameters are potentially important biological markers of cardiometabolic risk. Inferences can be enhanced by future studies that aim to identify the relationships between incident cardiometabolic cases and hematologic parameters.

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Table 1

Characteristics of the study population by gender

Characteristic	Men N=1,131		Women N=737		p-value
	n	%	n	%	
Age (years)					
≤24	195	17.2	167	22.6	<0.001
25–34	425	37.6	234	31.8	
35–44	185	16.4	123	16.7	
45–54	204	18.0	160	21.7	
≥55	122	10.8	53	7.2	
Education					
≤ High school	238	21.0	307	41.7	<0.001
≥ Bachelors	893	79.0	430	58.3	
Current Smoker					
Yes	81	7.2	1	0.1	<0.001
Alcohol consumption in past year					
Non-Drinker	197	17.4	231	31.3	<0.001
Moderate	800	70.7	505	68.6	
Heavy	134	11.9	1	0.1	
Khat chewing					
No	976	86.3	732	99.5	<0.001
Yes	155	13.7	4	0.5	
Self reported health status					
Poor/Fair	413	36.5	323	43.8	0.0015
Excellent	718	63.5	414	56.2	
Body mass index (kg/m^2)					
Underweight (<18.5)	147	13.3	90	12.5	<0.001
Normal (18.5–24.9)	655	59.4	368	51.0	
Overweight (25.0–29.9)	275	24.9	187	25.8	
Obese (≥30.0)	26	2.4	77	10.7	

Table 2

Hematological and cardiometabolic characteristics of study population according to gender

Characteristic	Gender		P-value
	Men N=1,125	Women N=728	
	Mean(SD)	Mean(SD)	
WBC ($\times 10^3$)	5.9 (1.9)	5.9 (2.0)	0.539
RBC ($\times 10^6$)	5.5 (0.7)	4.8 (0.6)	<0.001
Hemoglobin (g/dl)	16.5 (1.3)	14.3 (2.2)	<0.001
Hematocrit (%)	43.6 (14.3)	39.1 (12.3)	<0.001
Platelet Count ($\times 10^3$)	209.6 (62.7)	229.3 (66.6)	<0.001
Waist Circumference	85.7 (11.3)	80.6 (12.9)	<0.001
Diastolic blood pressure (mmHg)	80.1 (14.7)	76.3 (10.3)	<0.001
Systolic blood pressure (mmHg)	124.4 (16.1)	116.4 (17.0)	<0.001
Mean Arterial Pressure	94.9 (13.5)	89.6 (11.8)	<0.001
Fasting glucose (mg/dL)	94.6 (29.0)	93.6 (27.0)	0.479
HDL cholesterol (mg/dL)	45.6 (8.7)	50.6 (10.6)	<0.001
LDL cholesterol (mg/dL)	115.7 (45.3)	120.1 (35.8)	0.028
	Median [IQ]	Median [IQ]	
Triglycerides (mg/dL)†	113.0 [81.0–173.0]	95.0 [72.0–126.5]	<0.001

A significance test was performed for log-transformed values.

† Data reported as median and interquartile range due to a skewed distribution.

Table 3

Hemoglobin, hematocrit, platelets, and white blood cell counts (mean and SD) for men and women in relation to the number of the components of the metabolic syndrome.

*Number of Mets Components	0	1	≥2	p-value for trend
	Mean (SD)	Mean (SD)	Mean (SD)	
Men	**n=873**	**n=95**	**n=162**	
Hemoglobin	16.4 (1.3)	16.5 (1.1)	16.5 (1.3)	0.322
Hematocrit (%)	43.8 (14.1	41.4 (16.2)	44.1 (14.1)	0.825
Platelet ($\times 10^3$)	211.9 (64.1)	202.8 (50.7)	201.2 (60.8)	0.028
WBC ($\times 10^3$)	5.9 (1.9)	5.9 (2.1)	6.0 (2.1)	0.248
RBC ($\times 10^6$)	5.4 (0.6)	5.4 (0.7)	5.5 (0.8)	0.685
Women	**n=426**	**n=155**	**n=102**	
Hemoglobin	14.2 (2.0)	14.3 (2.9)	14.6 (1.2)	0.070
Hematocrit (%)	38.3 (12.8)	39.9 (10.4)	40.1 (12.6)	0.086
Platelet ($\times 10^3$)	235.8 (69.9)	217.9 (57.7)	222.5 (63.5)	0.831
WBC ($\times 10^3$)	5.9 (2.1)	5.9 (1.8)	6.1 (2.0)	0.151
RBC ($\times 10^6$)	4.8 (0.6)	4.8 (0.5)	4.9 (0.7)	0.022

*Number of MetS components in addition to abdominal obesity

Table 4

Age adjusted Pearson partial correlation coefficients between selected hematological parameters with individual components of the metabolic syndrome for men and women

Hematological Parameters	BMI	HDL	TG	FG	SBP	DBP	WC
Men(N=1120)							
Hemoglobin	0.146[b]	−0.021	0.160[b]	0.051	0.069[a]	0.085[a]	0.142[b]
Hematocrit	0.031	0.002	−0.020	0.023	0.067[a]	0.040	0.018
Platelet	0.059[a]	0.003	0.044	0.026	0.001	0.018	0.039
WBC	0.079[a]	−0.019	0.057	0.036	0.035	0.041	0.065[a]
RBC	0.074[a]	−0.026	0.073	0.041	0.053	0.061[a]	0.101[b]
Women(N=730)							
Hemoglobin	0.023	−0.086[a]	0.101[a]	0.074[a]	−0.027	−0.006	0.041
Hematocrit	0.088[a]	−0.007	<0.001	0.082[a]	0.045	0.060	0.055
Platelet	0.015	0.045	0.062	0.043	0.058	0.036	0.008
WBC	0.135[b]	−0.080[a]	0.038	0.075[a]	0.062	0.027	0.089[a]
RBC	0.067	−0.059	0.073[a]	−0.005	0.084[a]	0.124[b]	0.043

[a] $p<0.05$

[b] $p<0.001$

Table 5

Odds ratio (OR) and 95% Confidence interval (CI) for hemoglobin, hematocrit, platelets and WBC counts among study participants

Hematological Parameters	Men	Hematological Parameters	Women
	OR* (95% CI)		OR* (95% CI)
Hemoglobin (g/dl)			
<15.8	Reference	<13.6	Reference
15.8–16.4	1.28 (0.77–2.14)	13.6–14.2	0.89 (0.49–1.59)
16.4–17.2	**1.99 (1.21–3.27)**	14.2–15	0.78 (0.42–1.44)
>17.2	1.55 (0.90–2.66)	>15	**2.37 (1.36–4.12)**
p-value for trend	0.031		0.003
Hematocrit (%)			
<45.6	Reference	<40.0	Reference
45.6–48.0	1.02 (0.62–1.69)	40.0–42.4	1.25 (0.68–2.28)
48.0–50.4	1.46 (0.86–2.46)	42.4–45.0	1.17 (0.66–2.05)
>50.4	1.48 (0.88–2.46)	>45.0	**2.53 (1.43–4.50)**
p-value for trend	0.068		0.004
Platelet Count (All) ($\times 10^3$)			
<171	Reference	<187	Reference
171–206	0.79 (0.48–1.31)	187–224	1.69 (0.97–2.96)
206–243	0.88 (0.54–1.47)	224–263	1.22 (0.68–2.19)
>243	1.08 (0.66–1.76)	>263	**2.01 (1.12–3.63)**
p-value for trend	0.767		0.065
WBC ($\times 10^3$)			
<4.6	Reference	<4.5	Reference
4.6–5.8	0.87 (0.52–1.47)	4.5–5.9	0.96 (0.54–1.71)
5.8–7.1	1.20 (0.73–1.98)	5.9–7.4	1.31 (0.74–2.32)
>7.1	1.05 (0.63–1.74)	>7.4	1.64 (0.91–2.94)
p-value for trend	0.579		0.058
RBC ($\times 10^6$)			
<5.2	Reference	<4.6	Reference
5.21–5.5	1.36 (0.82–2.24)	4.61–4.85	1.57 (0.83–2.97)
5.51–5.8	**1.84 (1.10–3.09)**	4.86–5.1	**2.17 (1.22–3.87)**
>5.81	**2.26 (1.29–3.94)**	>5.11	**3.44 (1.93–6.13)**
p-value for trend	0.002		<0.001

Separate models were estimated for men and women

*Adjusted for age (continuous), alcohol (never, moderate, heavy) and smoking (none, past, current).