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Association of Hematological Parameters with Clustered Components of Metabolic Syndrome among Professional and Office Workers in Bangkok, Thailand

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Abstract

Background—Accumulating evidence documents associations between alterations in hematological parameters, indicative of prothrombotic and proinflammatory states, and risk of metabolic syndrome (MetS). We investigated associations of hematological parameters with MetS and individual criteria of the syndrome among Thai professional and office workers.

Methods—Study subjects were 1,314 patients (531 men and 783 women) who participated in annual health examinations during the period of August through December 2001. MetS was defined using the modified ATP III criteria. Multivariable logistic regression procedures were used to estimate odds ratios (OR) and 95% confidence intervals (95% CI) of MetS risk according to quartiles of each hematological parameter with the lowest quartile specified as the referent group.

Results—WBC counts increased with increasing numbers of MetS components in both men and women. Among women, platelet counts, hemoglobin and hematocrit concentrations increased with increasing numbers of MetS components ($p < 0.05$). No similar trends were observed for men. Of the hematological parameters studied, elevated platelet and WBC were statistically significantly associated with MetS among men (OR=1.86, 95% CI: 1.03–3.36; OR=2.26, 95% CI: 1.27–4.02), respectively. Among women, MetS risk increased across successive quartiles of hemoglobin (1.00, 2.63, 3.59 and 4.36; p for trend = 0.002), hematocrit (1.00, 2.35, 3.04 and 5.70; p -for trend < 0.001), platelet (1.00, 2.37, 2.83 and 3.11; p -for trend = 0.014) and WBC counts (1.00, 2.97, 4.09 and 5.41; p -for trend < 0.001).

Conclusions—Our data are consistent with an emerging literature demonstrating altered hematological status in patients at high risk of MetS.

Keywords

Metabolic Syndrome; Hematological Parameters; Thailand

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Introduction

Metabolic syndrome (MetS), an increasingly important and prevalent predisposing risk factor for incident type 2 diabetes mellitus and cardiovascular disease [1,2], has recently been associated with increased erythropoiesis, and increased white blood cell (WBC) counts [3–8]. For instance, Wang et al noted that subjects in the highest quartile of WBC or RBC counts demonstrated a three- and two-fold increase, respectively, in the odds ratio for MetS compared to subjects in the lowest quartile of WBC or RBC counts [8]. Additionally, Jesri et al reported that platelet and WBC counts significantly increased with increasing numbers of MetS components ($p < 0.01$). Mean platelet and WBC counts were 22.0% and 14.8% greater for subjects with ≥ 3 MetS components as compared to those with none of the MetS components [9].

Collectively, these emergent data suggest that alterations in hematological parameters such as increased platelet and WBC counts may serve as markers of a prothrombotic and proinflammatory state that may predispose to MetS and arterothromboembolic complications [9]. Little information exists on the epidemiological characteristics of the MetS in Thailand. We, therefore, conducted the present study to investigate the association of hematological parameters with metabolic syndrome among Thai professional and office workers who participated in an annual health examination program conducted by the Mobile Health Checkup Unit of King Chulalongkorn Memorial Hospital in Bangkok.

Methods

Study Population and Data Collection

We conducted a cross-sectional study of 1,339 patients who participated in annual health examinations at the Mobile Health Checkup Unit of King Chulalongkorn Memorial Hospital in Bangkok, Thailand during the period of August through December 2001. Because hematological parameters may be influenced by multiple medical conditions including pulmonary, hepatic, renal, infectious disorders, and malignancies, we excluded subjects with WBC counts greater than $15,000/\text{mm}^3$ and subjects with platelet counts greater than $500,000/\mu\text{l}$. Also excluded were subjects with hemoglobin concentrations greater than 18 and those with concentrations less than 10 g/dl. After making these exclusions, a total number of 1,314 subjects (531 men and 783 women) remained for analysis.

During routine clinic visits, participants were asked to provide information about their age, marital status, occupation, educational attainment, medical history, smoking status, alcohol consumption habits, and regular weekly physical exercise. Participants underwent routine physical examinations which included collection of venous blood samples after an overnight fast, and measurement of height, weight, and resting blood pressure. Standing height was measured to the nearest 0.5 centimeter without shoes. Weight was determined without shoes and with participants lightly clothed. Weight was measured using an automatic electronic scale (Seca, Inc., Hamburg, Germany) to the nearest 100 grams. Blood pressure, measured using an automatic sphygmomanometer (UDEX-IIa, UEDA, Corp., Tokyo, Japan), was taken in the seated position after each subject rested for at least 5 minutes.

Laboratory Analyses

Serum triglyceride (TG) concentrations were determined by standardized enzymatic procedures using glycerol phosphate oxidase assay. High density lipoprotein-cholesterol (HDL-C) was measured by a chemical precipitation technique using dextran sulfate. Fasting plasma glucose (FPG) concentrations were determined using the hexokinase method. Hemoglobin, hematocrit, platelet and white blood cell (WBC) counts were determined on the

automated hematology analyzer SE 9500 (Sysmex Corporation, Kobe, Japan). All laboratory assays were completed without knowledge of participants' medical history. Lipid, lipoprotein and FPG concentrations were reported as mg/dl. Hemoglobin and hematocrit were reported as g/dl and percent, respectively. Platelet and WBC counts were reported as cells per μl .

All participants provided informed consent and the research protocol was reviewed and approved by the Ethical Committee of Faculty of Medicine, Chulalongkorn University, and the Division of Human Subjects Research, University of Washington.

Analytical Variable Specification

MetS was defined using a modified version of the ATP III criteria [10]. Briefly, four of the five MetS components were defined using the following ATP III categorizations: 1) high blood pressure $\geq 130/85$ mmHg; 2) hypertriglyceridemia ≥ 150 mg/dl; 3) low high-density lipoprotein-cholesterol (HDL-C) < 40 mg/dl in men and < 50 mg/dl in women; 4) hyperglycemia or high fasting glucose ≥ 110 mg/dl. The fifth component was defined based on body mass index (BMI). Measures of participants' waist and hip circumferences are not routinely measured in our study setting, thus we were not able to categorize subjects according to measures of central adiposity [11]. Subjects with a BMI ≥ 25 kg/m² were classified as having a high central obesity in this study population. Consistent with the ATP III diagnostic criteria for MetS, participants with three of any of the five components were classified as having MetS.

Next, we classified subjects according to categories of hemoglobin, hematocrit, platelet and WBC counts. Each hematological parameter was categorized into approximate quartiles for men and women separately. Among men, the interquartile cut off points were 14.1, 15.0, 15.7 g/dl for hemoglobin level; 42.4, 44.5, 46.5% for hematocrit; 226, 257, 295 $\times 10^3/\mu\text{l}$ for platelet counts; and 5.72, 6.74, 8.03 $\times 10^3$ cells/ μl for WBC counts. The corresponding interquartile cut off points for women were 12.4, 13.1, 13.7 g/dl for hemoglobin level; 37.3, 39.1, 40.7% for hematocrit; 238, 275, 316 $\times 10^3/\mu\text{l}$ for platelet counts; and 5.40, 6.41, 7.51 $\times 10^3$ cells/ μl for WBC counts.

Statistical Analyses

We first explored frequency distributions of socio-demographic, behavioral and clinical characteristics. All data were summarized and displayed as number of subjects plus the percentage in each group for categorical variables and as mean $\pm$ SD for the continuous variables. Participants were divided into four groups according to the number of components of the MetS: 0, 1, 2, and 3 or more components. Means of each hematological parameter were then calculated for each subgroup. Significance for monotonic trends was assessed by linear regression analysis. Statistical analysis was performed separately for men and women. We examined the correlation between hemoglobin, hematocrit, platelet or WBC counts and each component of MetS using partial correlation coefficient adjusted for age. Univariate and multivariable logistic regression procedures were employed to calculate unadjusted odd ratios (OR) of potential risk factors associated with MetS. Confounding factors were evaluated on the basis of their hypothesized relationship with the covariates of interest and with MetS. Confounding was assessed by entering potential covariates into a logistic regression model one at a time, and by comparing the adjusted and unadjusted ORs [12]. Final logistic regression models included covariates that altered unadjusted ORs by at least 10%. All analyses were completed separately for male and female patients. Statistical analyses were performed using SPSS (version 13.0, SPSS Inc. Chicago, IL, USA) software. All reported p-values are two tailed, and confidence intervals were calculated at the 95% level.

Results

Socio-demographic and clinical characteristics of male and female study participants are summarized in Table 1. As expected for this Thai population, a history of smoking and alcohol consumption was higher among men as compared with women. Women were more likely to report regular participation in exercise than their male counterparts. The age distributions were similar for male and female participants.

As seen in Table 2, there is no evidence of a linear trend of increased mean concentrations of hemoglobin or hematocrit with increasing numbers of MetS components among men. There was, however, some suggestive evidence of increased platelet (trend $P = 0.003$) and WBC counts (trend $P < 0.001$) with increasing numbers of MetS components among men. Mean platelet and WBC counts were 7.0% and 12.1% greater for male subjects with ≥ 3 MetS components as compared to those with none of the MetS components.

Among women, all hematological parameters of interest were strongly and positively related with increasing numbers of MetS components (Table 2). Mean platelet and WBC counts were 9.5% and 14.1% greater for female subjects with ≥ 3 components as compared to those with none of the MetS components.

After adjusting for age, we noted statistically significant positive associations of WBC counts with body mass index, serum triglyceride, fasting blood sugar, and systolic blood pressure ($P < 0.05$) among men (Table 3). Platelet counts were positively associated with body mass index and serum triglyceride ($P < 0.05$). A statistically significant inverse association was noted between platelet count and serum HDL concentrations ($P < 0.05$). Hemoglobin concentrations were not associated with any of the MetS components among men. In women however, we noted positive associations of hemoglobin and hematocrit concentrations with triglyceride concentrations, as well as systolic and diastolic blood pressures. Platelet counts were positively associated with body mass index, triglyceride concentrations, fasting blood sugar and diastolic blood pressure. A weak, though statistical inverse association, was noted between platelet count and serum HDL-C concentrations. Similar patterns of associations were observed for WBC counts.

We next estimated multivariable logistic regression models to identify risk of hemoglobin, hematocrit, platelet or WBC counts for MetS in our study population. The results of these analyses are summarized in Table 4. Among men, elevated platelet and WBC counts in the highest quartile were statistically significantly associated with MetS. Those with elevated platelet counts (upper quartile: $\geq 295 \times 10^3/\mu\text{l}$) had a 1.86-fold increased risk (OR=1.86, 95% CI: 1.03–3.36) of MetS as compared with men who had platelet counts in the lowest quartile ($< 226 \times 10^3/\mu\text{l}$). Elevated WBC counts were associated with a 2.26-fold (OR=2.26, 95% CI: 1.27–4.02) increased risk of MetS. Among women, the risk of MetS increased across successive quartiles of hemoglobin (1.00, 2.63, 3.59 and 4.36), hematocrit (1.00, 2.35, 3.04 and 5.70), platelet (1.00, 2.37, 2.83 and 3.11) and WBC counts (1.00, 2.97, 4.09 and 5.41) with the lowest quartile as the referent group.

Discussion

In this study, we found that hematological parameters, particularly, WBC counts and platelet were associated with an increased risk of MetS. Platelets are the cell fragments circulating in the blood that involve in the cellular mechanisms of primary haemostasis leading to the formation of blood clots [13]. Dysfunction or low platelet counts (thrombocytopenia) predisposes to bleeding [14], while high platelet counts (thrombocytosis), although usually asymptomatic, may increase the risk of thrombosis [15]. Recent studies have provided insight into platelet functions in inflammation and arterogenesis [16,17]. White blood cells help to

defend the body against infectious disease and foreign materials as part of the immune system. White blood cells involve systemic chronic low-grade inflammation and associated with components of MetS [6,18].

Our data are consistent with emerging literature demonstrating altered hematological status in patients at high risk of MetS [5,8,9,19]. For instance, Jesri A et al reported that patients with MetS had higher platelet and WBC counts than controls [9]. Platelet counts were increased from 226 to 257 and $276 \times 10^3/\mu\text{l}$ among subjects with 0, 1–2, and ≥ 3 MetS components, respectively. Platelet counts were increased 22% among group of three to five MetS components as compared to those with none of the MetS components, while WBC counts were also increased significantly across the three groups (5.4 , 6.2 and $6.6 \times 10^3/\mu\text{l}$). Additionally, Nagasawa et al reported that WBC counts were statistically significantly higher in subjects with MetS as compared with controls (P for trend <0.001) [19]. In the present study, we also observed that the platelet and WBC counts increased with increasing numbers of MetS components. Mean platelet and WBC counts were 9.5% and 14.1% greater for female subjects with ≥ 3 MetS components as compared to those with none of the MetS components.

Our results are largely consistent with reports by Wang et al who reported that subjects in the highest quartile of WBC counts ($>7.57 \times 10^3\text{cells}/\mu\text{l}$) had a 3-fold increase in the risk of MetS as compared with subjects in the lowest quartile of WBC counts ($<5.41 \times 10^3\text{cells}/\mu\text{l}$) [8]. In the present study, men with highest quartile of WBC counts ($>8.03 \times 10^3\text{cells}/\mu\text{l}$) had a 2.26-fold increased in risk for MetS as compared with men with lowest quartile of WBC counts ($<5.72 \times 10^3\text{cells}/\mu\text{l}$). For platelet, there was a similar 1.86-fold increased in risk for MetS. Among women, the risk of MetS increased across successive quartiles of platelet (1.00, 2.37, 2.83 and 3.11) and WBC counts (1.00, 2.97, 4.09 and 5.41) with the lowest quartile as the referent group. Both platelet and WBC counts enhanced the risk for MetS. Arteaga et al demonstrated increased formation of platelet-leukocyte conjugates in patients with MetS [20].

Despite mounting evidence suggestive of associations between hematological parameters and risk of MetS, explanatory biological mechanisms for these associations remain to be elucidated. Several investigators have hypothesized plausible biological mechanisms that will have to be evaluated in future studies. Some investigators have noted that vascular endothelial cells are activated by the presence of atherosclerotic risk factors, such as hypertension, hyperlipidemia and hyperglycemia, thus promoting the increased synthesis and release of cytokines and chemokines into circulation. An increased pro-inflammatory state is then thought to further enhance activation of WBC and endothelial cells, thereby promoting platelet aggregation and thrombus formation [21]. Alternatively, some investigators speculate that increased cell mass, increased platelet number and activation of platelet and leukocytes promote the formation of platelet leukocyte aggregates which then contributes to the pathophysiological processes leading to increased risk for atherosclerotic disorders [15].

Regardless of underlying mechanisms, MetS is known to be associated with an increased risk of diabetes and cardiovascular disease morbidity and mortality, resulting in an enormous economic burden to society [22]. Men with four or five features of MetS have a 3.70-fold increase in risk for CHD and a 24.50-fold increase for diabetes as compare with men with none of the abnormalities (both $P<0.0001$) [23]. On the basis of these and other similar observations, it remains prudent to encourage patients to adopt healthful behaviors include increasing physical activity, maintain stable adult weight, increase dietary intake of complex carbohydrates while reducing total and saturated fat intake, limit alcohol consumption, and refrain from cigarette smoking [24].

Several limitation of our study merits consideration here. First, this study was cross-sectional study in design, and thus did not permit the identification of causal relationship between hematological parameters and MetS. Second, our study population included professional and office workers who received annual health examinations. Some characteristics of the present study population may be substantially different from other populations that do not access available medical services. Therefore, the generalizability of our study may be limited. Third, misclassification of MetS status may have occurred in our study because we did not have direct measurements of waist circumference and thus had to use BMI as a measure of central adiposity. In sensitivity analyses, we noted that excluding BMI from the criteria for MetS did not alter the association between hematological parameters and the risk of MetS (data were not shown).

In conclusion, we noted that hematological parameters, particularly, WBC and platelet counts were associated with clustered components of MetS among Thai professional and office workers who received annual health examinations in Bangkok.

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Table 1
Socio-demographic and clinical characteristics of study population of Thai professional and office workers (number and percent/mean $\pm$ standard deviation)

Characteristics	Men (N=531)		Women (N=783)	
	n ^a	%	n ^a	%
Age (Years)				
<30	59	11.1	73	9.3
30–39	149	28.1	196	25.0
40–49	211	39.7	328	41.9
≥ 50	112	21.1	186	23.8
Mean $\pm$ SD	42.0 $\pm$ 9.0		42.8 $\pm$ 8.9	
Education				
less than Bachelor degree	193	37.3	169	21.7
Bachelor degree	253	48.9	485	62.3
higher than Bachelor degree	71	13.7	124	15.9
Ever smoker	118	22.3	7	0.9
Ever drinker	308	58.7	54	7.0
No Exercise	237	45.2	478	61.4
Components of MetS				
Body Mass Index (kg/m ²)	24.5 $\pm$ 3.4		22.8 $\pm$ 3.8	
Systolic blood pressure (mmHg)	123.4 $\pm$ 14.7		115.4 $\pm$ 14.1	
Diastolic blood pressure (mmHg)	80.8 $\pm$ 10.4		75.3 $\pm$ 9.9	
HDL-Cholesterol (mg/dl)	51.7 $\pm$ 12.7		62.6 $\pm$ 14.5	
Triglyceride (mg/dl)	152.2 $\pm$ 112.3		95.8 $\pm$ 58.3	
Fasting plasma glucose (mg/dl)	96.5 $\pm$ 26.5		89.4 $\pm$ 16.6	
Hematological Parameters				
Hemoglobin (g/dl)	14.9 $\pm$ 1.2		13.0 $\pm$ 0.9	
Hematocrit (%)	44.4 $\pm$ 3.2		39.0 $\pm$ 2.7	
Platelet ($\times 10^3/\mu\text{l}$)	262.4 $\pm$ 52.0		278.5 $\pm$ 58.3	
WBC ($\times 10^3$ cells/ μl)	7.0 $\pm$ 1.8		6.6 $\pm$ 1.6	

^aNumber may not be added up to the total number due to missing data

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

Number of components	0	1	2	≥3	p for trend
Men (n = 531)	n = 164	n = 139	n = 91	n = 137	
Hemoglobin (g/dl)	14.9 ± 1.2	14.9 ± 1.2	15.0 ± 1.1	15.0 ± 1.3	0.259
Hematocrit (%)	44.3 ± 3.1	44.3 ± 3.4	44.5 ± 2.7	44.6 ± 3.3	0.374
Platelet (×10 ³ /μl)	251.3 ± 47.2	263.9 ± 53.5	270.7 ± 55.1	268.8 ± 58.2	0.003
WBC (×10 ³ cells/μl)	6.6 ± 1.7	6.8 ± 1.5	7.5 ± 2.0	7.4 ± 1.8	<0.001
Women (n = 783)	n = 411	n = 202	n = 106	n = 64	
Hemoglobin (g/dl)	13.0 ± 0.9	13.1 ± 0.9	13.0 ± 1.1	13.5 ± 0.9	0.004
Hematocrit (%)	38.8 ± 2.7	39.0 ± 2.5	39.0 ± 3.0	40.3 ± 2.5	0.001
Platelet (×10 ³ /μl)	269.3 ± 56.7	283.6 ± 56.6	294.9 ± 58.9	295.0 ± 62.5	<0.001
WBC (×10 ³ cells/μl)	6.4 ± 1.5	6.7 ± 1.6	6.9 ± 1.5	7.3 ± 2.0	<0.001

Results of the age adjusted Pearson partial correlation coefficients between the hemoglobin, hematocrit, platelet and white blood cell to the individual components of the metabolic syndrome for men and women.

Table 3

Hematological parameters	BMI	HDL	TG	FBS	SBP	DBP
Men (N = 531)						
Hemoglobin	-0.018	-0.028	0.046	0.024	0.068	0.084
Hematocrit	0.020	-0.024	0.047	0.042	0.094 ^a	0.104 ^a
Platelet	0.116 ^a	-0.135 ^a	0.120 ^a	-0.051	0.008	0.008
WBC	0.148 ^b	-0.127 ^a	0.182 ^b	0.099 ^a	0.137 ^a	0.083
Women (N = 783)						
Hemoglobin	0.011	-0.006	0.127 ^b	0.055	0.131 ^b	0.137 ^b
Hematocrit	0.011	0.024	0.154 ^b	0.063	0.146 ^b	0.107 ^a
Platelet	0.207 ^b	-0.101 ^a	0.137 ^b	0.088 ^a	0.043	0.108 ^a
WBC	0.236 ^b	-0.092 ^a	0.153 ^b	0.146 ^b	0.107 ^a	0.109 ^a

^a p < 0.05,
^b p < 0.001

BMI = body mass index; HDL = high-density lipoprotein; TG = triglyceride; FBS = fasting blood sugar; SBP = systolic blood pressure; DBP = diastolic blood pressure

Table 4

Odds ratio (OR) and 95% Confidence interval (CI) for hemoglobin, hematocrit, platelets and WBC counts among Thai professional and office workers.

Hematological parameters	Men		Women	
	OR ^a	95%CI	OR ^a	95%CI
Hemoglobin (g/dl)				
<14.1	1.00	Reference	1.00	Reference
14.1–14.9	1.22	(0.67–2.23)	2.63	(0.92–7.49)
15.0–15.6	1.05	(0.58–1.90)	3.59	(1.28–10.04)
≥15.7	1.67	(0.94–2.99)	4.36	(1.61–11.81)
	p for trend = 0.122		p for trend = 0.002	
Hematocrit (%)				
<42.4	1.00	Reference	1.00	Reference
42.4–44.4	0.94	(0.52–1.70)	2.35	(0.80–6.87)
44.5–46.4	1.41	(0.80–2.48)	3.04	(1.08–8.58)
≥46.5	1.55	(0.87–2.74)	5.70	(2.14–15.21)
	p for trend = 0.065		p for trend < 0.001	
Platelet (×10 ³ /μl)				
<226	1.00	Reference	1.00	Reference
226–256	1.77	(0.97–3.21)	2.37	(0.94–6.00)
257–294	1.24	(0.67–2.27)	2.83	(1.14–7.06)
≥295	1.86	(1.03–3.36)	3.11	(1.27–7.61)
	p for trend = 0.123		p for trend = 0.014	
WBC Counts (×10 ³ cells/μl)				
<5.72	1.00	Reference	1.00	Reference
5.72–6.73	0.85	(0.45–1.60)	2.97	(1.11–7.97)
6.74–8.02	1.74	(0.97–3.12)	4.09	(1.56–10.74)
≥8.03	2.26	(1.27–4.02)	5.41	(2.08–14.07)
	p for trend = 0.001		p for trend < 0.001	

^a Adjusted for age (<30, 30–39, 40–49, ≥50 years), and smoking status (never smoker/ever smoker) Separate models were estimated for men and women