The associations between leukocyte, erythrocyte or platelet, and metabolic syndrome in different genders of Chinese

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Abstract
Leukocyte, erythrocyte or platelet and metabolic syndrome (MS) are closely correlated, and there exist gender differences. We aimed to explore the associations between the hematological parameters and MS in different genders of Chinese. This cross-sectional study included 32,900 participants (20,733 males, 12,167 females) who were enrolled in a health examination. Clinical data including anthropometric measurements and serum parameters were collected. The associations between hematological parameters and MS of both genders were analyzed separately. Odds ratio (OR) of MS was calculated by binary logistic regression models. All hematological parameters were related to MS. With leukocyte and erythrocyte counts rising, the risks of developing MS increased in both genders, which was more obvious in women. For instance, in model 3, the ORs of MS in leukocyte quartiles in females were from 1.333 to 2.045 ($P < 0.01$), while in males, from 1.238 to 1.675 ($P < 0.01$). Platelet seemed as a protective factor in males. Model 1 and model 3 in quartile 2 demonstrated ORs of 0.922 ($P < 0.05$) and 0.912 ($P < 0.05$). However, platelet acted as risk factor in female. For instance, the ORs were 1.253 ($P < 0.01$), 1.461 ($P < 0.01$), and 1.322 ($P < 0.01$) in platelet quartile 4 of all 3 models in female. Gender influences on the associations between leukocyte, erythrocyte or platelet, and MS. In both genders, higher levels of leukocyte and erythrocyte increased risks of MS. For men, platelet was a protective factor, but for women, platelet seemed as a risk factor.

Abbreviations: ALT = alanine amino transferase, AST = aspartate amino transferase, BMI = body mass index, BUN = blood urea nitrogen, Cr = creatinine, CVD = cardiovascular disease, DBP = diastolic blood pressure, DM = diabetes mellitus, FG = fasting glucose, HDL = high-density lipoprotein, LDL = low-density lipoprotein, MS = metabolic syndrome, OR = odds ratio, PLT = platelet, RBC = red blood cell, SBP = systolic blood pressure, SPSS = Statistical Product and Service Solutions, SUA = serum uric acid, TBIL = total bilirubin, TC = total cholesterol, TG = triglycerides, WBC = white blood cell, WC = waist circumference.

Keywords: erythrocyte, gender, leukocyte, metabolic syndrome (MS), platelet

1. Introduction
Metabolic syndrome (MS) is characterized by a constellation of interrelated metabolic disorder including abdominal obesity, hypertension, hypertriglyceridemia, hyperglycemia and decreased high-density lipoprotein (HDL).[1] MS was first defined in 1998 by the World Health Organization.[2] In 2001, the National Cholesterol Education Program Adult Treatment Panel III proposed alternative clinical criteria for defining the MS.[3] The definition for Chinese people was proposed by the Chinese Diabetes Society in 2004.[4] In 2005, the International Diabetes Federation updated Adult Treatment Panel III definition to meet fasting glucose (FG) standard, which was set by the American Diabetes Association and to tailor WC cut-points to specific ethnicity.[5] And in 2009, a consensus criterion was reached by a joint statement from the International Diabetes Federation and American Heart Association and National Heart, Lung and Blood Institute.[6] MS was diagnosed over 3 of 5 factors as following: increased waist circumference (WC) (indicating central obesity), elevated triglycerides (TG), reduced HDL, elevated blood pressure, and elevated FG. MS shows strong association with increased risk of cardiovascular disease (CVD) and predicts the CVD morbidity and mortality.[7] It is also reported as a risk factor for type 2 diabetes mellitus (DM).[8] MS seems to be an inflammatory state and the link between inflammation and insulin resistance plays an important role in a cluster complex of such disorders.[9]

The relationship between hematological parameters and MS remains controversial, and has not been discussed extensively. The major hematological parameters include leukocyte, white blood cell (WBC); erythrocyte, red blood cell (RBC); and platelet (PLT), and thrombocyte. For leukocyte, Wu et al.[10] found WBC was negatively correlated with HDL and positively with body mass index (BMI) in boys, yet no significance was found in girls. Hsieh et al.[11] reported higher level of WBC correlated with significantly higher BMI in both genders, and lower HDL in male subjects only. Kim et al.[12] stated that WBC was elevated in male MS subjects yet no association between WBC and MS in female MS subjects. Pei et al.[13] found WBC was significantly higher in the group with MS than without MS in both genders. In the case...
of erythrocyte, some reports demonstrated that in both men and women, RBC was positively associated with MS, while other studies found no such association in both genders. As far as thrombocyte is concerned, PLT counts were found to rise with higher PLT count was associated with increased prevalence and risk of MS in both genders.

The aforementioned inconsistencies raise the need for further research. This study was to illuminate the relationships between hematological parameters (WBC, RBC, and PLT) and MS and to investigate differences in both genders.

2. Methods

2.1. Design

In this cross-sectional study, we investigated 32,900 participants (20,733 males, 12,167 females) who were enrolled in the general health examination at the Tianjin Medical University General Hospital during the period from 2007 to 2013. Information on medical history, lifestyle, alcoholic intake, and smoking was obtained during interviews. All participants were ostensibly healthy as they reported. To avoid the influence of confounding factors, the exclusion criteria were determined as the followings: subjects with disease history of hematology, liver, kidney, gastrointestinal, or oncology; subjects with any diseases or taking any medicine that might affect hematological parameters or metabolism. Written consents were obtained, and the study was approved by the institutional review board and ethic committee of Tianjin Medical University General Hospital. The protocol has been reported in details in our previous publications.

2.2. Measurements

Routine physical examinations and fasting blood sample tests were performed when participants visited the hospital. Height, weight, and WC were measured. And BMI was calculated according to the equation: weight (kilograms) divided by the square of height (meters). Blood pressure was measured by using a standard mercury sphygmomanometer after a seated rest for at least 5 minutes. FG, total cholesterol (TC), TG, HDL, low-density lipoprotein (LDL), alanine aminotransferase (ALT), aspartate amino transferase (AST), total bilirubin (TBIL), blood urea nitrogen (BUN), serum uric acid (SUA), and creatinine (Cr) were determined enzymatically by an autoanalyzer (Hitachi Model 7600 analyzer, Hitachi, Tokyo, Japan). WBC, RBC, and PLT were measured on a hemocytometer analyzer (Sysmex Corporation, Kobe, Japan). The blood cells of the participants were all measured by the same method and equipment.

The followings were the laboratory reference ranges for the parameters:

- FG: 3.6 to 5.8 mmol/L
- TC: 3.59 to 5.18 mmol/L
- TG: 0.57 to 1.70 mmol/L
- LDL: 1.33 to 3.37 mmol/L
- HDL: 0.8 to 2.2 mmol/L
- ALT: 5 to 40 U/L
- AST: 4 to 40 U/L
- TBIL: 3.4 to 20 μmol/L
- BUN: 1.7 to 8.3 mmol/L
- SUA: 140 to 414 μmol/L
- Cr: 44 to 115 μmol/L
- WBC: 4.0 to 10.0 × 10^9/L
- RBC: 3.5 to 5.5 × 10^12/L
- PLT: 100 to 300 × 10^9/L

2.3. Definition

Diagnosis of MS required at least three of the followings: central obesity, WC more than 90 cm in men and more than 80 cm in women; hypertriglyceridemia, TG more than 1.7 mmol/L; low HDL cholesterol, LDL of 1.03 mmol/L or less in males or 1.29 mmol/L or less in females; hypertension, systolic blood pressure (SBP) of 130 mmHg or more, or diastolic blood pressure (DBP) of 85 mmHg or more; and hyperglycemia, FG 5.6 mmol/L or more.

WBC, RBC, and PLT were classified in 2 ways. The first grouping method was done according to medical reference ranges. WBC was divided into 3 subgroups. WBC of 4.0 × 10^9/L or less was considered as leukopenia, WBC more than 10.0 × 10^9/L as leucocytosis, and 4.0 × 10^9/L less than WBC of 10.0 × 10^9/L as normal. Likewise, in accordance with the lower and upper cutoff values of RBC and PLT; abnormalities were termed as erythropenia, erythrocytosis, thrombopenia, and thrombocytosis, respectively. The second grouping method was based on quartiles of the measurements.

2.4. Statistical analysis

The analysis was accomplished by using the Statistical Product and Service Solutions (SPSS version 17.0, Chicago, IL). All data were presented as mean ± standard deviation. Independent sample t test was used to analyze differences of indices between groups. Multiple comparisons among subgroups were analyzed by the least significant difference test. Chi-square test was used to compare intergroup prevalence differences. Pearson bivariate correlation was made among variables. The binary logistic regression models were used to calculate the odds ratio (OR) for MS with 95% confidence interval. P < 0.05 was regarded as significant.

3. Result

3.1. Characteristics of the participants in different genders

Table 1 revealed that all parameters had significant differences between opposite gender (P < 0.01). Males were younger than females. BMI, WC, SBP, DBP, FG, TG, ALT, AST, TBIL, BUN, Cr, and SUA in males were higher than in females. However, TC, HDL, and LDL in males were lower than in females. WBC and RBC in males were higher than in females, yet PLT was lower in males than in females.

3.2. Prevalence of MS in different genders

Of the 32,900 participants, 32.47% (10,684/32,900) had MS. The prevalence rates of MS in males and females were 37.67% (7811/20,733 cases) and 23.6% (2873/12,167 cases), respectively. It was significantly higher in males than in females, with a chi-square value of 363.387 (P < 0.01).

According to leukocyte subgroups, except for leucocytosis subgroup, males had significantly higher MS prevalence than females (P < 0.01). The prevalence of MS increased as WBC counts increased, which was more prominent in females than in males (for females, chi-square value = 130.640, P < 0.01; for males, chi-square value = 119.292, P < 0.01) (Fig. 1).

The prevalence of MS according to erythrocyte subgroups revealed different patterns (Fig. 2). Men had significantly higher MS prevalence than women in erythropenia subgroup (P = 0.033) and normal RBC subgroup (P < 0.01). Prevalence of MS showed an increasing tendency in females, the significantly sharp increase of MS prevalence started from the normal RBC subgroup to erythrocytosis subgroup (chi-square value = 6.809, P = 0.033). MS prevalence showed a zigzag pattern in different RBC subgroups in males (chi-square value = 87.916, P < 0.01).
As for thrombocyte subgroups, there were significant differences on the prevalence of MS (Fig. 3). The prevalence of MS in males was significantly higher than in females except for the thrombopenia subgroup ($P < 0.01$). However, in females, there was an obvious decreasing trend (chi-square value $= 9.628$, $P < 0.01$).

### 3.3. Correlations of key variables in different genders

WBC showed significantly positive correlations with BMI, WC, SBP, DBP, FG, TC, TG, LDL, ALT, BUN, and SUA, yet significantly negative relationships with age, HDL, and TBIL in both genders (Table 2).

It was revealed that RBC was positively correlated with BMI, WC, SBP, DBP, FG, TC, TG, LDL, ALT, AST, TBIL, and SUA, yet negatively correlated with HDL and BUN in both genders. Age showed negative correlation with RBC in males, yet positive correlation in females.

In both genders, PLT and BMI, WC, DBP, TC, TG, LDL, and SUA showed positive correlations, while PLT and age, HDL, AST, BUN, and Cr showed negative correlations.

### 3.4. Risks of developing MS in different genders

Binary logistic regression models were utilized to calculate the risks of developing MS in different blood cell quartiles (Table 3).
WBC, RBC, and PLT quartiles were designated as categorical variables, with the lowest quartile as the reference. Model 1 has no covariate, model 2 included age and BMI as covariates and model 3 included age, BMI, ALT, AST, TBL, BUN, Cr, and SUA as covariates. For leukocyte, significantly increased risk of developing MS was demonstrated from quartile 2 to 4 for both genders. In general, females had higher ORs than males. And for the same quartile, ORs decreased as covariates increased in both sexes. For erythrocyte, very similar results were demonstrated just like leukocyte. The ORs increased as RBC quartiles rose in both genders. Females had higher ORs than males. And for PLT, ORs decreased as covariates increased in both genders.

4. Discussion

The prevalence of MS was increasing not only in well-developed countries but also in developing countries. Multiple studies are necessary to investigate its risk factors. With the significant progress of science and the speedy development of economy, lifestyle of Chinese people has changed obviously. A more caloric diet, a rise of processed food, and a lack of exercise all result in metabolic abnormality, such as obesity, hypertension, and dyslipidemia, which can decrease the quality of life. People with MS are more likely to have heart disease and DM than those who do not have. Type 2 DM and CVDs morbidity are the explicit adverse outcomes of the MS and it is also related to elevated risk for CVDs mortality.[15,7,8]

This study showed that WBC count was closely related to MS, the risks of developing MS increased in both genders as the WBC count elevated. Similar performance was done in several previous reports.[22,23] Among women, the risk of MS increased across successive quartiles of WBC counts.[22] The baseline levels of WBC count were significantly higher among MS cases than those without in apparently healthy Korean adults.[23] The mechanisms explaining the association between WBC and MS are not fully elucidated, but several possibilities have been expounded. Insulin resistance, abdominal obesity and inflammation have been
Table 3

| Parameter values | Model 1 | Model 2 | Model 3 |
|------------------|---------|---------|---------|
| **Males**        |         |         |         |
| WBC quartiles    |         |         |         |
| Quartile 1       |         |         |         |
| WBC<4.90 (reference) | 1.467 (1.352–1.592) | 1.264 (1.155–1.383) | 1.238 (1.129–1.359) |
| Quartile 2       |         |         |         |
| WBC<5.70 (reference) | 1.809 (1.606–1.985) | 1.468 (1.300–1.998) | 1.393 (1.269–1.530) |
| Quartile 3       |         |         |         |
| WBC<6.60 (reference) | 2.419 (2.232–2.621) | 1.790 (1.638–1.962) | 1.675 (1.527–1.837) |
| Quartile 4       |         |         |         |
| **Females**      |         |         |         |
| WBC quartiles    |         |         |         |
| Quartile 1       |         |         |         |
| WBC<4.30 (reference) | 1.619 (1.420–1.845) | 1.407 (1.214–1.639) | 1.333 (1.148–1.548) |
| Quartile 2       |         |         |         |
| WBC<5.10 (reference) | 2.240 (1.936–2.554) | 2.053 (1.605–2.604) | 1.923 (1.565–2.314) |
| Quartile 3       |         |         |         |
| WBC<5.90 (reference) | 3.025 (2.667–3.432) | 2.517 (2.093–2.974) | 2.045 (1.673–2.573) |

**RBC quartiles**

| Parameter values | Model 1 | Model 2 | Model 3 |
|------------------|---------|---------|---------|
| Quartile 1       |         |         |         |
| RBC<1012/L (reference) | 1.009 (0.912–1.102) | 0.912 (0.822–1.000) | 0.912 (0.822–1.000) |
| Quartile 2       |         |         |         |
| RBC<1177/L (reference) | 1.061 (0.955–1.171) | 0.931 (0.835–1.030) | 0.931 (0.835–1.030) |
| Quartile 3       |         |         |         |
| RBC<205/L (reference) | 1.036 (0.959–1.122) | 0.917 (0.836–1.000) | 0.917 (0.836–1.000) |
| Quartile 4       |         |         |         |
| PLT quartiles    |         |         |         |
| Quartile 1       |         |         |         |
| PLT<177.00 (reference) | 1.038 (0.912–1.169) | 1.150 (0.982–1.325) | 1.088 (0.942–1.257) |
| Quartile 2       |         |         |         |
| PLT<205.00 (reference) | 1.111 (1.005–1.225) | 1.258 (1.092–1.448) | 1.182 (1.023–1.368) |
| Quartile 3       |         |         |         |
| PLT<238.00 (reference) | 1.220 (1.092–1.353) | 1.370 (1.162–1.613) | 1.288 (1.064–1.552) |
| Quartile 4       |         |         |         |
| PLT>238.00       |         |         |         |

**PLT quartiles**

| Parameter values | Model 1 | Model 2 | Model 3 |
|------------------|---------|---------|---------|
| Quartile 1       |         |         |         |
| PLT<177.00 (reference) | 1.038 (0.912–1.169) | 1.150 (0.982–1.325) | 1.088 (0.942–1.257) |
| Quartile 2       |         |         |         |
| PLT<205.00 (reference) | 1.111 (1.005–1.225) | 1.258 (1.092–1.448) | 1.182 (1.023–1.368) |
| Quartile 3       |         |         |         |
| PLT<238.00 (reference) | 1.220 (1.092–1.353) | 1.370 (1.162–1.613) | 1.288 (1.064–1.552) |
| Quartile 4       |         |         |         |
| PLT>238.00       |         |         |         |

**WBC** = white blood cell, **RBC** = red blood cell, **PLT** = platelet, **OR** = odds ratio, **CI** = confidence interval.

1 Logistic regression model included age and BMI as covariates.
2 Logistic regression model included age, BMI, ALT, AST, TBL1, BUN, Cr, and SUA as covariates.
3 P < 0.05.
4 P < 0.001.

The likelihood of MS in different genders.
hormone. Female sex hormone is generally believed to decrease the risk of MS. Nagata et al. suggested that autocrine estradiol secretion could increase PLT production by triggering pro-PLT formation. This study showed that PLT was positively related with MS developing in women. The role of PLT in female was due to the dominance of female sex hormone on PLT. We consider that the enhancing effect of female sex hormone to PLT might overcome its protective role for MS, resulting in gender disparity in this study. Third, as far as testosterone is concerned, it was reported that administration of testosterone replacement therapy could result in PLT increase. But in our study, we did not identify such an endangering effect of PLT on MS in male. So we figure that testosterone might not play as important role as female sex hormone. More researches need to be carried out for confirmation.

The present study has several limitations. First, it was a cross-sectional study, so a causal relationship cannot be pinpointed. Further prospective studies are necessary to explain the causality question. Second, sex hormones were not measured in this investigation due to budget shortage, so the real effects of sex hormones need to be confirmed in the future. Third, cytokines (like interleukin 6 and tumor necrosis factor α) were not measured in this study because of budget shortage as well. Forth, insulin resistance was not gauged, which shall be in our next stage investigations. Finally, detailed food recall and some other consumed drugs, which could influence hematologic parameters or metabolism, should be recorded in specific details for risk stratification in further research.

In conclusion, higher levels of WBC, RBC, and PLT are potential risks for developing MS in females. However, higher levels of WBC and RBC are risks in males, while higher PLT is a protective factor. Special attention should be paid when measuring these easily available hematologic parameters. Higher levels of these easily measured hematologic parameters may play important roles in MS.

Acknowledgments
This study was supported by the National Key Clinical Specialty Project (awarded to the Departments of Nuclear Medicine and Radiology). This study was supported by Tianjin Medical University General Hospital New Century Excellent Talent Program; Young and Middle-aged Innovative Talent Training Program from Tianjin Education Committee; and Talent Fostering Program (the 131 Project) from Tianjin Education Committee, Tianjin Human Resources and Social Security Bureau (awarded to ZM). This study was supported by China National Natural Science Foundation grant 81571709, Key Project of Tianjin Science and Technology Committee Foundation grant 16JCZDJC34300 (awarded to ZM). This study was also supported by Tianjin Science and Technology Committee Foundation grants 12ZCZDSY20400 and 13ZCZDSY20200 (awarded to QZ and KS).

The funders gave financial support, but did not design the investigation.

References
[1] Meng Z, Liu M, Zhang Q, et al. Gender and age impacts on the association between thyroid function and metabolic syndrome in Chinese. Medicine 2015;94:e2193.
[2] Alberti KG, Zimmer PZ. Definition diagnosis and classification of diabetes mellitus and its complications. Part I: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. Diabet Med 1999;15:539–53.
[3] National Cholesterol . Education Program Expert Panel on Detection, Treatment of High Blood Cholesterol in A. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation 2002;106:3143–421.
[4] Yu L, Zhang YH, Liu YY, et al. Comparison of three diagnosis criteria for metabolic syndrome in Mongolian people of agricultural and pastoral regions. J Endocrinol Invest 2009;32:420–5.
[5] Alberti KG, Zimmet P, Shaw J, et al. The metabolic syndrome—a new worldwide definition. Lancet 2005;366:1059–62.
[6] Alberti KG, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation 2009;120:1640–50.
[7] Butunierne J, Benucevics A, Saudargiene A, et al. Metabolic syndrome, major depression, generalized anxiety disorder, and ten-year all-cause and cardiovascular mortality in middle aged and elderly patients. Int J Cardiol 2015;190:360–6.
[8] Sattar N, McCannachie A, Shaper AG, et al. Can metabolic syndrome usefully predict cardiovascular disease and diabetes? Outcome data from two prospective studies. Lancet 2008;371:1927–35.
[9] Dandonna P, Aljada A, Chaudhuri A, et al. Metabolic syndrome: a comprehensive perspective based on interactions between obesity, diabetes, and inflam-mation. Circulation 2005;111:1448–54.
[10] Wu CZ, Lin JD, Li JC, et al. Association between white blood cell count and components of metabolic syndrome. Pediatr Int 2009;51:14–8.
[11] Hsieh CH, Pei D, Kuo SW, et al. Correlation between white blood cell count and metabolic syndrome in adolescence. Pediatr Int 2007;49:827–32.
[12] Kim JA, Choi YS, Hong JJ, et al. Association of metabolic syndrome with white blood cell subtype and red blood cells. Endocr J 2006;53:133–9.
[13] Pei C, Chang JB, Hsieh CH, et al. Using white blood cell counts to predict metabolic syndrome in the elderly: a combined cross-sectional and longitudinal study. Eur J Intern Med 2015;26:324–9.
[14] Nebeck K, Gelaye B, Lemma S, et al. Hematological parameters and metabolic syndrome: findings from an occupational cohort in Ethiopia. Diabetes Metab Syndr 2012;6:62–7.
[15] Lohsoonthorn V, Jamjarasungrung W, Williams MA. Association of hematological parameters with clustered components of metabolic syndrome among professional and office workers in Bangkok, Thailand. Diabetes Metab Syndr 2007;1:143–9.
[16] Park BJ, Shin JY, Lee HK, et al. The relationship of platelet count, mean platelet volume with metabolic syndrome according to the criteria of the American Association of Clinical Endocrinologists: a focus on gender differences. Platelets 2012;23:345–50.
[17] Lim HJ, Seo MS, Shim JY, et al. The association between platelet count and metabolic syndrome in children and adolescents. Platelets 2015;26: 758–63.
[18] Zhang Q, Lou S, Meng Z, et al. Gender and age impacts on the correlations between hyperuricemia and metabolic syndrome in Chinese. Clin Rheumatol 2011;30:777–87.
[19] Meng Z, Liu M, Zhang Q, et al. Gender and age impact on the association between thyroid-stimulating hormone and serum lipids. Medicine 2015;94:e2186.
[20] Liu L, Lou S, Xu K, et al. Relationship between lifestyle choices and hyperuricemia in Chinese men and women. Clin Rheumatol 2013;32: 233–9.
[21] Zhang J, Meng Z, Zhang Q, et al. Gender impact on the correlations between subclinical thyroid dysfunction and hyperuricemia in Chinese. Clin Rheumatol 2016;35:143–9.
[22] Lohsoonthorn V, Dhanamun B, Williams MA. Prevalence of metabolic syndrome and its relationship to white blood cell count in a population of Thai men and women receiving routine health examinations. Am J Hypertens 2006;19:339–45.
[23] Jung CH, Lee WY, Kim BY, et al. The risk of metabolic syndrome according to the white blood cell count in apparently healthy Korean adults. Yonsei Med J 2013;54:615–20.
[24] Romero GR, Lee J, Shoelson SE. Metabolic syndrome, insulin resistance, and roles of inflammation—mechanisms and therapeutic targets. Arterioscler Thromb Vasc Biol 2012;32:1771–6.
[25] Fjeldborg K, Pedersen SB, Møller HJ, et al. Human adipose tissue macrophages are enhanced but changed to an anti-inflammatory profile in obesity. J Immunol Res 2014;2014:390548.
[26] Lee YJ, Shin YH, Kim JK, et al. Metabolic syndrome and its association with white blood cell count in children and adolescents in Korea: the 2005 Korean National Health and Nutrition Examination Survey. Nutr Metab Cardiovasc Dis 2010;20:165–72.

[27] Pickup JC, Crook MA. Is type II diabetes mellitus a disease of the innate immune system? Diabetologia 1998;41:1241–8.

[28] Chou SK, Li JC, Tsai WC, et al. Correlations between white blood cell count and metabolic syndrome in middle-age Taiwanese. Endocr Res 2005;31:39–50.

[29] Hoogerbrugge N, Zillikens MC, Jansen H, et al. Estrogen replacement decreases the level of antibodies against oxidized low-density lipoprotein in postmenopausal women with coronary heart disease. Metabolism 1998;47:675–80.

[30] Frohlich M, Muhlberger N, Hanke H, et al. Markers of inflammation in women on different hormone replacement therapies. Ann Med 2003;35:53–61.

[31] Ren J, Kelley RO. Cardiac health in women with metabolic syndrome: clinical aspects and pathophysiology. Obesity 2009;17:1114–23.

[32] Tsilidis KK, Rohrmann S, McGlynn KA, et al. Association between endogenous sex steroid hormones and inflammatory biomarkers in US men. Andrology 2013;1:919–28.

[33] Barbieri M, Rago E, Benvenuti E, et al. New aspects of the insulin resistance syndrome: impact on haematological parameters. Diabetologia 2001;44:1232–7.

[34] Wang YY, Lin SY, Liu PH, et al. Association between hematological parameters and metabolic syndrome components in a Chinese population. J Diabetes Complications 2004;18:322–7.

[35] Hara N, Nishiyama T, Takizawa I, et al. Decline of the red blood cell count in patients receiving androgen deprivation therapy for localized prostate cancer: impact of ADT on insulin-like growth factor-1 and erythropoiesis. Urology 2010;75:1441–5.

[36] Rochira V, Zirilli L, Madeo B, et al. Testosterone action on erythropoiesis does not require its aromatization to estrogen: insights from the testosterone and estrogen treatment of two aromatase-deficient men. J Steroid Biochem Mol Biol 2009;113:189–94.

[37] Taylor SR, Meadowcroft LM, Williamson B. Prevalence, pathophysiology, and management of androgen deficiency in men with metabolic syndrome, type 2 diabetes mellitus, or both. Pharmacotherapy 2015;35:780–92.

[38] Jesri A, Okonofua EC, Egan BM. Platelet and white blood cell counts are elevated in patients with the metabolic syndrome. J Clin Hypertens 2005;7:705–11; quiz 703–712.

[39] Chen YL, Hung YJ, He CT, et al. Platelet count can predict metabolic syndrome in older women. Platelets 2015;26:31–7.

[40] Baatout S. Interleukin-6 and megakaryocytopoiesis: an update. Ann Hematol 1996;73:157–62.

[41] Ayapak C, Turdi O, Bircan MA, et al. Could mean platelet volume among complete blood count parameters be a surrogate marker of metabolic syndrome in pre-pubertal children? Platelets 2014;25:393–8.

[42] Nagata Y, Yoshikawa J, Hashimoto A, et al. Proplatelet formation of megakaryocytes is triggered by autocrine-synthesized estradiol. Genes Dev 2003;17:2864–9.

[43] Badawi MA, Salih F, Al-Humaidi AA, et al. Bone marrow hypoplasia responsive to testosterone therapy in a patient with panhypopituitarism: need for adherence to androgen replacement. Endocr Pract 2008;14:229–32.

[44] Iijima M, Shihehara K, Sugimoto K, et al. Myelodysplastic syndrome treated effectively with testosterone enanthate. Int J Urol 2011;18:469–71.

[45] Severo CB, Ribeiro JP, Umpierre D, et al. Increased atherothrombotic markers and endothelial dysfunction in steroid users. Eur J Prev Cardiol 2013;20:195–201.