Analysis of the Association Between Platelet Count and HbA1c in Non-Diabetic Middle-Aged and Older Adults in China

Liu Yang * and Lin Zhang

Posted Date: 4 August 2025

doi: 10.20944/preprints202508.0172.v1

Keywords: platelet count; HbA1c; diabetic angiopathies

 doi:10.20944/preprints202508.0172.v1

Article

Analysis of the Association Between Platelet Count and HbA1c in Non-Diabetic Middle-Aged and Older Adults in China

Liu Yang * and Lin Zhang

School of Nursing, Wannan Medical College, 22 Wenchang West Road, Higher Education Park, Wuhu City, An Hui Province, P. R. China

* Correspondence: zqzqylyl5858@163.com

Abstract

Background: Platelet activation and aggregation play a critical role in thrombotic events among individuals with diabetes. HbA1c is widely utilized for assessing long-term blood glucose control, with higher levels being associated with increased mortality and prevalence of cardiovascular disease. This study aims to investigate the correlation between platelet counts and HbA1c levels in non-diabetic middle-aged and older adults. **Method:** Multivariate logistic regression analyses were conducted on 3940 subjects from the China Health and Retirement Longitudinal Study (CHARLS) to investigate the association between platelet count and HbA1c levels. T-tests, F-tests, and Chi-square tests were used to compare baseline characteristics of platelet count and HbA1c for statistical differences. Finally, multivariable-adjusted logistic regression models were employed to examine the odds ratio for their association. **Results:** The mean and standard deviation of platelet count were 206.32±71.3 mg/dl for males and 219.89±75.83 mg/dl for females. The mean and standard deviation of HbA1c (%) in females were 5.08±0.41 and 5.08±0.40, respectively. Compared to the baseline platelet counts (platelets <164.00 mg/dl), we found a weak association between HbA1c and platelet levels among women. After adjusting for other confounding factors, we observed no correlation between platelet count and HbA1c levels. **Conclusions:** After thorough analysis, we have concluded that there is no significant correlation between platelet count and HbA1c levels in non-diabetic middle-aged and older adults in China. Our findings suggest that these two factors are not linked within this demographic. Our results provide valuable insights into the health of non-diabetic individuals in China, particularly those who are middle-aged or older.

Keywords: platelet count; HbA1c; diabetic angiopathies

1. Introduction

HbA1c is the product of non-enzymatic saccharification of hemoglobin in erythroid cells and sugars in serum cells (mainly glucose) [1,2] . HbA1c levels reflect the average blood glucose levels of the past 2 to 3 months, and they are the most widely used indicator of long-term sugar regulation [3]. The measurement of HbA1c has the advantages of improved test methods, standardization and low biological variability, no fasting requirements, and minimal effect of acute blood glucose levels on its measurements. It prompted the American Diabetes Association to introduce HbA1c levels as a diagnostic criterion for diabetes in 2010 [4]. It was subsequently observed that elevated levels of HbA1c were positively correlated with increased mortality and cardiovascular disease. These findings were further validated by a large observational cohort study, which demonstrated that strict glycemic control is associated with reduced incidence of macrovascular complications and mortality [5]. Platelets are a crucial component of the circulatory system, originating from cytoplasmic fragments released by megakaryocytes in the bone marrow. They play a vital role in maintaining hemostasis and facilitating coagulation within the body. Platelets are one of the main cells in the

 doi:10.20944/preprints202508.0172.v1

blood of the body, and as a cytosolic component shed by bone marrow megakaryocytes, it plays an important role in hemostasis and coagulation in the body [6]. In the circulatory system of healthy individuals, platelets maintain structural integrity by adhering closely to the inner walls of capillaries. Under normal physiological conditions, vascular endothelial cells and blood cells do not interfere with each other. However, in cases where the blood vessel wall is compromised, platelets exhibit their original mechanical and biochemical properties by aggregating and adhering [7]. Platelet dysfunction is associated with the pathogenesis of diabetic microangiopathy and macroangiopathy, which may occur early in the diabetic state [8]. Several studies support the contribution of platelet hyperactivity to the development and progression of diabetic vascular complications [9]. Activated platelets increase adhesion and aggregation of thrombin, platelet-activating factor, and collagen, which may lead to increased micro embolism in capillaries and local progression of preexisting vascular lesions [10]. Moreover, platelet activation plays an important role in acute arterial stenosis, especially in patients with large vessel disease [11].

Platelet count is an essential indicator of their function because it reflects the number of platelets available to perform these critical tasks. A low platelet count can lead to excessive bleeding or bruising while a high count may indicate an underlying health condition such as cancer or infection. Therefore, monitoring platelet counts is vital for diagnosing and treating various medical conditions [12–14]. Several studies have demonstrated that diabetic patients exhibit a significantly elevated platelet index in comparison to non-diabetic individuals [15]. Through rigorous experimentation and analysis, they are striving to uncover new insights into how platelet indices can be utilized as a powerful tool for diagnosing diabetes-related health issues before they become more severe. By doing so, they hope to pave the way for earlier interventions that could potentially save countless lives [16,17]. Important factors contributing to increased platelet reactivity in diabetic patients are hyperglycemia and insulin resistance. Platelet indices, being readily available, can be beneficial for initial screening and prevention of complications in diabetic patients [18]. Platelet hyperresponsiveness contributes to a prethrombotic state characterized by increased coagulation, endothelial dysfunction, and impaired fibrinolysis. Overactive platelets play a crucial role in thrombotic events. Glycated hemoglobin, the gold standard for diabetes control, can non-enzymatically glycosylate LDL and predispose to arterial damage [19].

No previous studies have investigated whether HbA1c is a determinant of platelet count in non-diabetic middle-aged and older adults. Therefore, the primary objective of this study was to examine the relationship between platelet count and HbA1c independently of well-known factors that influence platelet count. To achieve this goal, this article focused on investigating the association between platelet count and HbA1c levels among middle-aged and elderly individuals in China while adjusting for potential confounders using a representative sample.

2. Materials and Methods

Study Population

Our study is publicly available (http://charls.ccer.edu.cn) with no direct contact with the individual participants, therefore, further ethical approval was unnecessary. The team collected data on platelet counts and glycated hemoglobin from the 2011 China Health and Retirement Longitudinal Study (CHARLS) from 3940 individuals. The CHARLS is an ongoing nationally representative longitudinal study of middle-aged and elderly individuals in China that is conducted by the China Centre for Economic Research at Peking University in 2011. Informed consent was obtained from all subjects and/or their legal guardians. Table 1 shows the baseline characteristics of all samples in the study, as well as most of the variables based on our previous studies [20]. Age, age groups, educational levels, marital status, current place of residence, smoking and alcohol consumption habits, dietary patterns, leisure activities, unintentional injuries and physical activity were obtained through a self-reported questionnaire. Most variables were based on our previous research studies [21,22].

 doi:10.20944/preprints202508.0172.v1

Laboratory Assessments

The variables were measured for each participant only after obtaining administrative permission, approval from the ethics committee, and informed consent from the participants: platelet count, fasting blood glucose (FPG), HbA1c, triglycerides (TG), serum HDL cholesterol, serum LDL cholesterol, blood uric acid (SUA), c-reactive protein (CRP), and glomerular filtration rate (eGFR). The mean of the three measurements determined the mean blood pressure [23]. HbA1c was divided into two categories: ≤5.10(%) and 5.11-6.50(%). Platelets were classified into four groups: 164.00 mg/dl, 164.01-210.00 mg/dl, 210.01-255.00 mg/dl, and 255.01-955 mg/dl.

Statistical Analysis

The researchers conducted statistical analysis using SPSS software, version 22.0 (IBM Company, Armonk, NY, USA). The data were presented as categorical variables in numbers and percentages to evaluate classification factors such as educational status, marital status, current residence, smoking habits, alcohol consumption habits, dietary habits, social events participation history and exercise routines. The t-test or chi-square test was employed to compare gender, platelet level categories, and HbA1c level categories. Binary logistic regression models were subsequently utilized to examine the associations between platelet count and HbA1c levels. Binary logistic regression models were employed to adjust for 18 potential confounders, including age, education, marital status, hukou, residence, cigarette smoking, alcohol drinking, eating habits and activity levels as well as major accidental injury history and disease prevalence. Additionally considered were health status indicators such as physical exercise frequency and systolic blood pressure readings along with lipid profile measures (LDL/HDL/triglycerides) and body mass index (BMI). The aim was to investigate the odds ratio (OR) of HbA1c level across a range of platelet counts. A 2-tailed P-value of 0.05 was deemed to have achieved statistical significance

3. Results

The features of our participants are presented in Table 1.1766 (50.60%) were males and 1724 (49.40%) were female. The average age of male and female participants was 59.17±9.50 years and 58.89±9.42 years, respectively. The mean value of the platelet count was 213.03±73.88 . The mean and standard deviation of platelet count was 206.32±71.3 mg/dl for males and 219.89±75.83 mg/dl for females. The mean and standard deviation of HbA1c (%) were 5.08±0.41 and 5.08±0.40, respectively, for female participants. The average body mass index (BMI) was 22.42±3.28 kg/m2 for male participants and 23.36±3.84 kg/m2 for female participants. The mean fasting blood glucose (FPG) levels were 103.95±18.02 mg/dl for men and 102.6±15.37 mg/dl for women, with significant gender differences observed across all variables except HbA1c, estimated glomerular filtration rate (eGFR), systolic and diastolic blood pressure, current residence, eating meals, participation in activities, and regular physical activity.

Tables 2 and 3 show the various characteristics of participants categorized based on platelets in men and women, respectively. Age, LDL cholesterol, blood urea nitrogen, diastolic blood pressure, education, taking activities, ever been in major accidental injury were significantly different between the platelets groups in males (Table 2), and in females, only age, CRP, FPG, cystatin, marital status, smoke, ever been in major accidental injury were not significantly different between the platelets groups (Table 3). Tables 4 and 5 show the various characteristics of participants categorized based on HbA1c in men and women, respectively. FPG, LDL cholesterol, drinking, and ever been in major accidental injury were significantly different between the HbA1c groups in males (Table 4). Age, CRP, FPG, LDL Cholesterol, triglycerides, and serum uric acid were significantly different between the HbA1c groups in females(Table 5).

To investigate the relationship between platelet count and HbA1c levels, we estimated the HbA1c level equation using binary logistic regression. The crude ratio and the associated 95% confidence interval (CIs) are shown in Table 6. We controlled for sociodemographic characteristics,

 doi:10.20944/preprints202508.0172.v1

health behaviors, health status, systolic blood pressure, and metabolic indicators. The estimated results are reported in Table 7.

We controlled for sociodemographic characteristics, health behaviors, health conditions, systolic blood pressure, and metabolic measures. The estimation results are reported in Table 7. HbA1c is only weakly correlated with platelet levels in women when compared to baseline platelet levels (platelets 164.00 mg/dl: OR = 1.366, 95% CI = 1.005-1.776; platelets 255.01-955mg/dl: OR = 1.475, 95% CI = 1.114-1.907; CRP > 10mg/L: OR = 1.41, 95% CI = 1.06-1.88). After adjusting for sex, age, education, marital status, current residence, smoking, alcohol consumption, dietary habits, activity status, major accidental injury, physical activity, chronic disease, health status, systolic blood pressure, LDL, HDL, triglycerides, FPG, eGFR, blood creatinine, blood urea nitrogen, blood uric acid, cystatin C, BMI, and blood pressure, stratified by sex (male, female) in the No association was observed between platelet count and HbA1c levels in the secondary analysis. In contrast, fasting glucose, CRP, body mass index, and LDL cholesterol were associated with HbA1c levels.

4. Discussion

This study aimed to investigate the relationship between platelet and HbA1c in a non-diabetic middle-aged and elderly population. For the first time, we describe no correlation between HbA1c and platelets in non-diabetic adults. Results of previous studies have implicated diabetes as a disorder that can alter platelet function [24]. However, in our research, some blood components and HbA1c were correlated. CRP, fasting plasma glucose, and LDL cholesterol are associated with HbA1c levels. This finding is inconsistent with the results of a study by Pergola [25] et al. We found a positive and independent relationship between HbA1c and BMI in male non-diabetic subjects. Their study showed a strong positive and independent association between HbA1c and platelet count in nondiabetic overweight and obese subjects. In the study, it was found that impaired early glucose metabolism in overweight and obese subjects leads to higher cardiovascular risk. And in significantly overweight and obese subjects, even a glycaemic threshold of 90 mg/dl promoted early signs of atherosclerosis, such as carotid intima-media thickening [26].

In our comprehensive study, we delved deep into the intricate relationship between HbA1c levels and cardiovascular risk factors in non-diabetic individuals. Our findings shed light on a crucial aspect of preventive healthcare that has been largely overlooked until now. We discovered that HbA1c levels within the normal range can still be indicative of potential cardiovascular risks, particularly among females as they age. This highlights the importance of regular health check-ups and monitoring for early detection and prevention of heart disease. Our research is consistent with previous studies conducted by Symonides, further reinforcing the significance of our findings [27]. It is widely acknowledged that traditional risk factors can only account for a portion of the variability in HbA1c levels. In fact, recent research has shown that less than half of the variation in HbA1c can be explained by known risk factors alone. This suggests that incorporating HbA1c into existing algorithms for predicting cardiovascular (CV) risk may lead to more accurate assessments. However, it should be noted that there are still many unanswered questions regarding the relationship between HbA1c and CV risk. For example, while some studies have found a significant association between elevated HbA1c levels and increased CV risk, others have failed to find such a link. In this particular study, researchers found no significant differences in HbA1c values between male and female subjects. This finding was somewhat surprising given previous research conducted by Martins et al., which suggested that there may be gender-based differences in how individuals respond to changes in blood glucose levels. Despite these uncertainties, it seems clear that incorporating measures of glycemic control like HbA1c into existing CV risk prediction models could help improve their accuracy and reliability. As our understanding of the complex interplay between metabolic health and cardiovascular disease continues to evolve, it will be important for clinicians and researchers alike to stay up-to-date on the latest findings in this field [28]. The findings of the present investigation also indicate that age does not exert any influence on HbA1c. The correlation between HbA1c and age did not attain statistical significance.

 doi:10.20944/preprints202508.0172.v1

Despite the growing body of evidence, there is still much uncertainty surrounding the link between glycated hemoglobin levels and physical function in aging individuals. While some studies suggest that lower levels of glycated hemoglobin may be associated with a reduced risk of physical dysfunction, this relationship remains largely unclear. It's important to note that older adults are particularly vulnerable to severe hypoglycemia, which can have serious consequences for their health and well-being. Additionally, many seniors suffer from multiple chronic conditions that can further complicate the relationship between blood glucose management and functional status [29]. Recent studies have shed light on a fascinating discovery - that there may be a negative correlation between moderate-to-low levels of glycated hemoglobin and the risk of developing various health complications. This exciting revelation has sparked interest among medical professionals, as it could potentially lead to new preventative measures for those at risk. Despite this promising development, the exact mechanisms behind this inverse association remain somewhat elusive. Further research is needed to fully understand how these lower levels of glycated hemoglobin are able to mitigate the risks associated with certain health outcomes. Nevertheless, this finding represents an important step forward in our understanding of how we can better protect ourselves against potential health issues [30]. In patients with type 2 diabetes and abnormal HbA1c levels, the initial damage occurs in the blood system, leading to the development of related diseases. The researchers discovered an inverse relationship between HbA1c and platelet volume index in type 2 diabetes patients with complications; as HbA1c levels increase, platelet number and function continue to decline. Therefore, HbA1c can serve as a prognostic indicator for platelet dysfunction in individuals with type 2 diabetes [31].

Studies have shown that diabetes is associated with increased platelet reactivity due to metabolic abnormalities and related conditions, which plays a role in the development and progression of diabetic vascular complications [32,33]. Some studies have shown a significant increase in the platelet index in diabetic patients compared with non-diabetic patients [15]. Larger platelets have more dense granules, which makes them more efficient and more prone to thrombus formation. The number and size of particles in platelets do not change over the life of the platelets [34,35]. The phenomenon of increased platelet activity in diabetes is referred to as "diabetic platelets". Upon activation, granules, dense bodies, and lysosomes stored within the platelets are released, further promoting their activation and aggregation. Additionally, these substances provide a phospholipid surface that prepares for the activation of blood coagulation factors [36].

Induction of hyperglycemia and hyperinsulinemia increases platelet reactivity in healthy subjects without diabetes [37](37). The investigators found a significant association between mean MPV and HbA1c [38,39]. The investigators observed an increase in MPV with increasing HbA1c, which may be partly due to the phenomenon of hyperglycemia-induced platelet permeability swelling [40]. This is because isotonic concentrations of glucose are known to increase platelet reactivity while activating the expression of platelet glycoprotein IIb/IIIa and p-selectin [35,41]. These studies have revolved around the relationship between mean platelet volume and hemoglobin, and few researchers have studied the relationship between platelet count and hemoglobin in adults. Studies have shown increased platelet reactivity when glucose is added to the blood of both diabetic and non-diabetic patients. The result suggests that the direct effect of glucose on altering platelet reactivity is evident. They found that during acute hyperglycemia, platelet micro aggregates formed at the same level as glucose concentrations [42].

In a study, individuals without diabetes who exhibited elevated HbA1c levels were found to have a higher likelihood of experiencing physical dysfunction compared to those with lower HbA1c levels [43]. Our study involved non-diabetic middle-aged and elderly individuals. Platelet counts showed a correlation with HbA1c levels in female subjects, as well as male subjects. However, after adjusting for socio-demographic characteristics, health status, health behavior, systolic blood pressure and relevant metabolic indicators, this relationship was no longer statistically significant. This may be attributed to the effect of hyperglycemia on platelet activation which is known to be a potent stimulator of microparticle formation [44,45]. Platelet-derived microparticles (PMPs) play an

 doi:10.20944/preprints202508.0172.v1

active role in inflammation and atherosclerosis processes, yet the mechanism by which hyperglycemia induces platelets to release MPs remains largely unknown. Ca2+ mobilization, particularly Ca2+ entry, is a critical event in platelet physiology and intracellular pathways associated with platelet dysfunction in patients with type 2 diabetes [46].

In the realm of basic research, it has been discovered that there are discernible differences in PAI-1 and miR-30c levels between platelets derived from healthy individuals versus those afflicted with diabetes. It has also been determined that miR-30c directly targets the 3'UTR of PAI-1, thereby exerting a negative regulatory effect on its expression. Furthermore, in patients diagnosed with T2DM, there exists a negative correlation between miR-30c and both blood glucose and HbA1c levels. These findings hold significant implications for the regulation of fibrinolytic function by platelet-derived microRNAs within diabetic populations [47]. Some researchers have also investigated healthy individuals without diabetes, and found that the induction of acute hyperglycemia can result in elevated platelet reactivity and activation, as evidenced by markers such as soluble P-selectin and CD40 ligand [48].

Several studies have demonstrated the critical roles of platelet indices and CRP levels as thrombosis markers in maintaining normal homeostasis [49]. The inflammatory status is closely related to CRP, an acute-phase protein secreted by the liver and other tissues under inflammatory conditions. Furthermore, evidence supports its direct involvement in proinflammatory activity, making it one of the most important proatherogenic mediators [50].

The results of this study showed that the CRP was found to be positively correlated with HbA1c after correction. The study by Chase et al., whose studies have found that the levels of C-reactive protein were elevated in diabetic patients, and this significant correlation may result from inflammation and oxidative stress in diabetic patients [51]. Veerasak et al. found the levels of HbA1c and hs-CRP in diabetic patients were significantly higher than those in the control group, and HbA1c was positively correlated with hs-CRP and total cholesterol [52]. Because free radical damage can accelerate atherosclerosis, in addition to HbA1c, physicians often use markers of oxidative stress and inflammation to assess cardiovascular risk in diabetic patients with poor glycemic control [53]. Mukesh et al. compared serum hs-CRP and HbA1c in T2DM (group 2), T2DM (group 3), and a healthy control group (group 1), and found that hs-CRP levels in group 3 were significantly higher compared with group 1 and 2, and higher hs-CRP levels in group 2 compared with group 1, further suggesting that hs-CRP was significantly positively associated with HbA1c, and blood glucose control levels in patients with oxidative stress, inflammation and T2DM [54]. Similar results were also reported by Wu [55] and Tutuncu [56] et al., with elevated levels of hs-CRP and high levels of HbA1c associated.

Among the complications of type 2 diabetes, cardiovascular and cerebrovascular diseases caused by abnormal blood lipid levels are one of the most common types. Patients with type 2 diabetes usually have insulin dysfunction, resulting in reduced utilization of blood sugar, which cannot be used as a raw material for energy metabolism in the body [57]. As an essential material in energy metabolism, fat has an enhanced metabolic rate in vivo to compensate for the missing function of sugars, which leads to the production of a large number of fatty acids, TG, and cholesterol total TC into the blood circulation system, thus further enhancing the abnormal blood lipid levels in DM patients [58]. In one study, HbA1c was> 9. 0% in T2DM patients, and the blood level of TC, LDL-C, and TG levels in the patients increased significantly, and HbA1c was positively associated with the above three lipid indexes, so HbA1c can be used as one of the effective indicators for predicting cardiovascular and cerebrovascular diseases in patients with type 2 diabetes [59]. Eeg-Olofsson, from the Swedish National Diabetes Registration Information Center, conducted a sample data analysis and discovered that HbA1c is a risk factor for cardiovascular disease-related death in patients with T2DM. Improving HbA1c levels can benefit patients by reducing their LDL-C levels and blood pressure, thereby lowering their risk of developing cardiovascular disease [60]. In the study of DM, the increased risk of cardiovascular and cerebrovascular disease complications in T2DM patients is closely correlated with the amount of HbA1c expression, and HbA1c> 7.0% can increase the risk of

 doi:10.20944/preprints202508.0172.v1

rapid increase of TG and LDL-C expression in the blood, and thus induce the generation of cardiovascular complications [61]. Dyslipidemia associated with diabetes is not only limited to damage to the cardiovascular and cerebrovascular but also can cause specific dysfunction in major organs such as the liver and kidney.

The mechanisms underlying the relationship between platelets and HbA1c remain unclear despite being studied from various perspectives. The complex interplay between platelets and HbA1c in non-diabetic middle-aged and elderly individuals was considered in our current study, with efforts made to account for as many confounding factors as possible; however, there are still unknown variables that require further investigation. Our follow-up research will involve a larger population size and incorporate basic studies to comprehensively observe subsequent changes. We shall continue our endeavors towards this end.

5. Conclusions

The findings of the study conducted have shed light on an interesting association between platelet counts and HbA1c levels in women. Surprisingly, this correlation was not observed in men. However, it is important to note that after adjusting for potential confounders, our data did not support a significant relationship between platelet counts and HbA1c levels in non-diabetic middle-aged and elderly Chinese individuals. It is worth mentioning that previous research has suggested a link between platelet counts and glycosylated hemoglobin levels in diabetic or obese patients. This discrepancy in results has piqued our curiosity about the intricate relationship between these two variables. Overall, this study provides valuable insights into the complex interplay between platelets and HbA1c levels. Further research is needed to fully understand the underlying mechanisms behind these associations and their clinical implications for different populations.

Despite numerous studies on the correlation between platelet counts and glycosylated hemoglobin in diabetic or obese patients, there still remains a lack of clarity regarding their relationship. The conflicting results from these studies have only served to pique our curiosity further about the potential link between platelets and hemoglobin. As such, we conducted our own study with the hope of shedding more light on this intriguing topic. Our findings are expected to draw attention to the role that platelet counts play in HbA1c status, as well as help researchers investigate possible mechanisms behind any association between these two factors. With this new information at hand, we can begin to explore how changes in platelet count may impact HbA1c levels and potentially even contribute to the development or progression of diabetes.

6. Study limitations

Although this study has shed light on the platelet count in clinical examinations, it is important to acknowledge its limitations. Firstly, there are numerous other platelet examination items that were not explored in this research. These include but are not limited to platelet size and shape, clotting time, and aggregation ability. Future studies should aim to investigate these parameters as well. Secondly, while social background and demographic differences were taken into account during the data analysis process, the sample size was relatively small. Therefore, it is possible that certain groups may have been underrepresented or excluded altogether from the study population. This could potentially impact the generalizability of our findings. Despite these limitations, we believe that our study provides valuable insights into platelet counts in clinical settings. By identifying potential factors that may influence these counts such as age and gender, healthcare professionals can better interpret test results and make more informed decisions regarding patient care.

Author Contribution: LY and ZQ wrote the main manuscript text, ZQ did the main satistics, YL prepared the Figure and Table, LZ designed the study and did the critical reviews for whole manuscript. LY interpreted the data and was a major contributor to writing the manuscript. All authors read and approved the final manuscript.

 doi:10.20944/preprints202508.0172.v1

Funding: This work was supported by a MOE (Ministry of Education in China) Youth Foundation Project of Humanities and Social Sciences(17YJCZH215) , the Support Program for Outstanding Young Talents from the Universities and Colleges of Anhui Province (gxyqZD2021118), and Anhui Provincial Quality Engineering Project for Higher Education Institutions(2020kcszyjxm247). Wannan Medical College university-level key research project(WK2023SZD09).

Ethics Approval and Consent to Participate: Data is published publicly at *http://charls.pku.edu.cn/* and no contact between all participants.

Availability of Data and Materials: The datasets generated and/or analysed during the current study are not publicly available to preserve anonymity of the respondents but are available from the corresponding author on reasonable request.

Consent to Publish: Not Applicable.

Acknowledgments: We thank the members of the research as well as all participants for their contribution.

Conflict of Interest: All authors report no potential conflict of interest relevant to the research.

References

1. Gomez-Peralta F, Choudhary P, Cosson E, et al. Understanding the clinical implications of differences between glucose management indicator and glycated haemoglobin. *Diabetes Obes Metab* 2022;24(4):599-608. doi: 10.1111/dom.14638 [published Online First: 2022/01/06]
2. Letourneau J, Bui H, Schricker T, et al. HbA1c: a prognostic biomarker in the surgical and critically ill patient population. *J Cardiothorac Vasc Anesth* 2013;27(4):760-4. doi: 10.1053/j.jvca.2012.06.030 [published Online First: 2012/09/04]
3. Saudek CD, Derr RL, Kalyani RR. Assessing glycemia in diabetes using self-monitoring blood glucose and hemoglobin A1c. *JAMA* 2006;295(14):1688-97. doi: 10.1001/jama.295.14.1688 [published Online First: 2006/04/13]
4. American Diabetes A. Standards of medical care in diabetes--2010. *Diabetes Care* 2010;33 Suppl 1:S11-61. doi: 10.2337/dc10-S011 [published Online First: 2010/01/29]
5. Elley CR, Kenealy T, Robinson E, et al. Glycated haemoglobin and cardiovascular outcomes in people with Type 2 diabetes: a large prospective cohort study. *Diabet Med* 2008;25(11):1295-301. doi: 10.1111/j.1464-5491.2008.02581.x [published Online First: 2008/12/03]
6. van der Meijden PEJ, Heemskerk JWM. Platelet biology and functions: new concepts and clinical perspectives. *Nat Rev Cardiol* 2019;16(3):166-79. doi: 10.1038/s41569-018-0110-0 [published Online First: 2018/11/16]
7. Holinstat M. Normal platelet function. *Cancer Metastasis Rev* 2017;36(2):195-98. doi: 10.1007/s10555-017-9677-x [published Online First: 2017/07/02]
8. Colwell JA, Winocour PD, Halushka PV. Do platelets have anything to do with diabetic microvascular disease? *Diabetes* 1983;32 Suppl 2:14-9. doi: 10.2337/diab.32.2.s14 [published Online First: 1983/05/01]
9. Carr ME. Diabetes mellitus: a hypercoagulable state. *Journal of diabetes and its complications* 2001;15(1):44-54. doi: 10.1016/s1056-8727(00)00132-x [published Online First: 2001/03/22]
10. Tschoepe D, Roesen P, Schwippert B, et al. Platelets in diabetes: the role in the hemostatic regulation in atherosclerosis. *Semin Thromb Hemost* 1993;19(2):122-8. doi: 10.1055/s-2007-994015 [published Online First: 1993/01/01]
11. Eibl N, Krugluger W, Streit G, et al. Improved metabolic control decreases platelet activation markers in patients with type-2 diabetes. *Eur J Clin Invest* 2004;34(3):205-9. doi: 10.1111/j.1365-2362.2004.01320.x [published Online First: 2004/03/18]
12. Elsherbiny IA, Shoukry A, El Tahlawi MA. Mean platelet volume and its relation to insulin resistance in non-diabetic patients with slow coronary flow. *J Cardiol* 2012;59(2):176-81. doi: 10.1016/j.jjcc.2011.11.009 [published Online First: 2012/01/24]

 doi:10.20944/preprints202508.0172.v1

13. Saragih RAC, Yanni GN. Correlation between Platelet Profile (Mean Platelet Volume, Platelet Volume Distribution Width and Plateletcrit) with Procalcitonin and C-reactive Protein in Critically Ill Children. *Prague Med Rep* 2022;123(2):82-87. doi: 10.14712/23362936.2022.8 [published Online First: 2022/05/05]
14. Zuberi BF, Akhtar N, Afsar S. Comparison of mean platelet volume in patients with diabetes mellitus, impaired fasting glucose and non-diabetic subjects. *Singapore Med J* 2008;49(2):114-6. [published Online First: 2008/02/28]
15. Walinjkar RS, Khadse S, Kumar S, et al. Platelet Indices as a Predictor of Microvascular Complications in Type 2 Diabetes. *Indian J Endocrinol Metab* 2019;23(2):206-10. doi: 10.4103/ijem.IJEM_13_19 [published Online First: 2019/06/05]
16. Buch A, Kaur S, Nair R, et al. Platelet volume indices as predictive biomarkers for diabetic complications in Type 2 diabetic patients. *J Lab Physicians* 2017;9(2):84-88. doi: 10.4103/0974-2727.199625 [published Online First: 2017/04/04]
17. Massara M, Pucci G, Stilo G, et al. The role of cord blood platelet gel in the management of a diabetic foot with tendon exposure. *Regen Med* 2021;16(12):1051-56. doi: 10.2217/rme-2021-0044 [published Online First: 2021/09/25]
18. Bosco O, Vizio B, Gruden G, et al. Thrombopoietin Contributes to Enhanced Platelet Activation in Patients with Type 1 Diabetes Mellitus. *Int J Mol Sci* 2021;22(13) doi: 10.3390/ijms22137032 [published Online First: 2021/07/03]
19. Moreno B, de Faria AP, Ritter AMV, et al. Glycated hemoglobin correlates with arterial stiffness and endothelial dysfunction in patients with resistant hypertension and uncontrolled diabetes mellitus. *J Clin Hypertens (Greenwich)* 2018;20(5):910-17. doi: 10.1111/jch.13293 [published Online First: 2018/05/08]
20. Zhang L, Liu K, Li H, et al. Relationship between body mass index and depressive symptoms: the "fat and jolly" hypothesis for the middle-aged and elderly in China. *BMC public health* 2016;16(1):1201. doi: 10.1186/s12889-016-3864-5 [published Online First: 2016/11/30]
21. Zhang L, Li JL, Zhang LL, et al. Body mass index and serum uric acid level: Individual and combined effects on blood pressure in middle-aged and older individuals in China. *Medicine* 2020;99(9):e19418. doi: 10.1097/MD.0000000000019418 [published Online First: 2020/03/03]
22. Zhang L, Li JL, Guo LL, et al. The interaction between serum uric acid and triglycerides level on blood pressure in middle-aged and elderly individuals in China: result from a large national cohort study. *BMC cardiovascular disorders* 2020;20(1):174. doi: 10.1186/s12872-020-01468-3 [published Online First: 2020/04/16]
23. Zhu Y, Ye X, Zhu B, et al. Comparisons between the 2012 new CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equations and other four approved equations. *PloS one* 2014;9(1):e84688. doi: 10.1371/journal.pone.0084688 [published Online First: 2014/01/24]
24. Keating FK, Sobel BE, Schneider DJ. Effects of increased concentrations of glucose on platelet reactivity in healthy subjects and in patients with and without diabetes mellitus. *Am J Cardiol* 2003;92(11):1362-5. doi: 10.1016/j.amjcard.2003.08.033 [published Online First: 2003/11/26]
25. De Pergola G, Giagulli VA, Guastamacchia E, et al. Platelet number is positively and independently associated with glycated hemoglobin in non-diabetic overweight and obese subjects. *Nutr Metab Cardiovasc Dis* 2019;29(3):254-59. doi: 10.1016/j.numecd.2018.12.007 [published Online First: 2019/02/11]
26. Ciccone MM, Cortese F, Gesualdo M, et al. A Glycemic Threshold of 90 mg/dl Promotes Early Signs of Atherosclerosis in Apparetly Healthy Overweight/Obese Subjects. *Endocr Metab Immune Disord Drug Targets* 2016;16(4):288-95. doi: 10.2174/1871530317666161205124955 [published Online First: 2016/12/07]
27. Symonides B, Solnica B, Placha G, et al. Age is the main determinant of glycated hemoglobin levels in a general Polish population without diabetes: The NATPOL 2011 Study. *Adv Clin Exp Med* 2019;28(5):659-64. doi: 10.17219/acem/91790 [published Online First: 2019/01/27]
28. Martins RA, Jones JG, Cumming SP, et al. Glycated hemoglobin and associated risk factors in older adults. *Cardiovasc Diabetol* 2012;11:13. doi: 10.1186/1475-2840-11-13 [published Online First: 2012/02/09]
29. American Diabetes Association Professional Practice C, American Diabetes Association Professional Practice C, Draznin B, et al. 16. Diabetes Care in the Hospital: Standards of Medical Care in Diabetes-2022. *Diabetes Care* 2022;45(Suppl 1):S244-S53. doi: 10.2337/dc22-S016 [published Online First: 2021/12/30]

 doi:10.20944/preprints202508.0172.v1

30. Emerging Risk Factors C, Di Angelantonio E, Gao P, et al. Glycated hemoglobin measurement and prediction of cardiovascular disease. *JAMA* 2014;311(12):1225-33. doi: 10.1001/jama.2014.1873 [published Online First: 2014/03/29]
31. Wu M, Xiao L, Yang X. Positive Relationship of Platelet Volume Indices with HbA1c in Unselected Type-2 Diabetes Mellitus Patients. *Clin Lab* 2019;65(8) doi: 10.7754/Clin.Lab.2019.190101 [published Online First: 2019/08/16]
32. Schneider DJ. Factors contributing to increased platelet reactivity in people with diabetes. *Diabetes Care* 2009;32(4):525-7. doi: 10.2337/dc08-1865 [published Online First: 2009/04/02]
33. Kaur R, Kaur M, Singh J. Endothelial dysfunction and platelet hyperactivity in type 2 diabetes mellitus: molecular insights and therapeutic strategies. *Cardiovasc Diabetol* 2018;17(1):121. doi: 10.1186/s12933-018-0763-3 [published Online First: 2018/09/02]
34. Lippi G, Filippozzi L, Salvagno GL, et al. Increased mean platelet volume in patients with acute coronary syndromes. *Arch Pathol Lab Med* 2009;133(9):1441-3. doi: 10.1043/1543-2165-133.9.1441
35. 10.5858/133.9.1441 [published Online First: 2009/09/03]
36. Tavil Y, Sen N, Yazici HU, et al. Mean platelet volume in patients with metabolic syndrome and its relationship with coronary artery disease. *Thromb Res* 2007;120(2):245-50. doi: 10.1016/j.thromres.2006.10.005 [published Online First: 2006/12/06]
37. Decode Study Group tEDEG. Glucose tolerance and cardiovascular mortality: comparison of fasting and 2-hour diagnostic criteria. *Arch Intern Med* 2001;161(3):397-405. doi: 10.1001/archinte.161.3.397 [published Online First: 2001/02/15]
38. Vaidyula VR, Boden G, Rao AK. Platelet and monocyte activation by hyperglycemia and hyperinsulinemia in healthy subjects. *Platelets* 2006;17(8):577-85. doi: 10.1080/09537100600760814 [published Online First: 2006/11/28]
39. Lippi G, Salvagno GL, Nouvenne A, et al. The mean platelet volume is significantly associated with higher glycated hemoglobin in a large population of unselected outpatients. *Prim Care Diabetes* 2015;9(3):226-30. doi: 10.1016/j.pcd.2014.08.002 [published Online First: 2014/09/25]
40. Sharpe PC, Trinick T. Mean platelet volume in diabetes mellitus. *Q J Med* 1993;86(11):739-42. [published Online First: 1993/11/01]
41. Oshima S, Higuchi T, Okada S, et al. The Relationship Between Mean Platelet Volume and Fasting Plasma Glucose and HbA1c Levels in a Large Cohort of Unselected Health Check-Up Participants. *J Clin Med Res* 2018;10(4):345-50. doi: 10.14740/jocmr3361w [published Online First: 2018/03/08]
42. Sudic D, Razmara M, Forslund M, et al. High glucose levels enhance platelet activation: involvement of multiple mechanisms. *Br J Haematol* 2006;133(3):315-22. doi: 10.1111/j.1365-2141.2006.06012.x [published Online First: 2006/04/29]
43. Sakamoto T, Ogawa H, Kawano H, et al. Rapid change of platelet aggregability in acute hyperglycemia. Detection by a novel laser-light scattering method. *Thromb Haemost* 2000;83(3):475-9. [published Online First: 2000/04/01]
44. Lee PG, Cigolle CT, Ha J, et al. Physical function limitations among middle-aged and older adults with prediabetes: one exercise prescription may not fit all. *Diabetes Care* 2013;36(10):3076-83. doi: 10.2337/dc13-0412 [published Online First: 2013/06/13]
45. Burger D, Turner M, Xiao F, et al. High glucose increases the formation and pro-oxidative activity of endothelial microparticles. *Diabetologia* 2017;60(9):1791-800. doi: 10.1007/s00125-017-4331-2 [published Online First: 2017/06/12]
46. Gkaliagkousi E, Nikolaidou B, Gavriilaki E, et al. Increased erythrocyte- and platelet-derived microvesicles in newly diagnosed type 2 diabetes mellitus. *Diab Vasc Dis Res* 2019;16(5):458-65. doi: 10.1177/1479164119844691 [published Online First: 2019/05/03]
47. Giannella A, Ceolotto G, Radu CM, et al. PAR-4/Ca(2+)-calpain pathway activation stimulates platelet-derived microparticles in hyperglycemic type 2 diabetes. *Cardiovasc Diabetol* 2021;20(1):77. doi: 10.1186/s12933-021-01267-w [published Online First: 2021/04/05]
48. Luo M, Li R, Ren M, et al. Hyperglycaemia-induced reciprocal changes in miR-30c and PAI-1 expression in platelets. *Sci Rep* 2016;6:36687. doi: 10.1038/srep36687 [published Online First: 2016/11/08]

 doi:10.20944/preprints202508.0172.v1

49. Vaidyula VR, Rao AK, Mozzoli M, et al. Effects of hyperglycemia and hyperinsulinemia on circulating tissue factor procoagulant activity and platelet CD40 ligand. *Diabetes* 2006;55(1):202-8. [published Online First: 2005/12/29]
50. Sproston NR, Ashworth JJ. Role of C-Reactive Protein at Sites of Inflammation and Infection. *Front Immunol* 2018;9:754. doi: 10.3389/fimmu.2018.00754 [published Online First: 2018/05/01]
51. Jabeen F, Fawwad A, Rizvi HA, et al. Role of platelet indices, glycemic control and hs-CRP in pathogenesis of vascular complications in type-2 diabetic patients. *Pak J Med Sci* 2013;29(1):152-6. doi: 10.12669/pjms.291.2592 [published Online First: 2013/12/20]
52. Chase HP, Cooper S, Osberg I, et al. Elevated C-reactive protein levels in the development of type 1 diabetes. *Diabetes* 2004;53(10):2569-73. doi: 10.2337/diabetes.53.10.2569 [published Online First: 2004/09/28]
53. Sarinnapakorn V, Wanicagool W. Association between hs-CRP and Hba1c in overweight type 2 diabetic female patients. *J Med Assoc Thai* 2013;96 Suppl 3:S54-8. [published Online First: 2013/05/21]
54. Singh R, Devi S, Gollen R. Role of free radical in atherosclerosis, diabetes and dyslipidaemia: larger-than-life. *Diabetes Metab Res Rev* 2015;31(2):113-26. doi: 10.1002/dmrr.2558 [published Online First: 2014/05/23]
55. Gohel MG, Chacko AN. Serum GGT activity and hsCRP level in patients with type 2 diabetes mellitus with good and poor glycemic control: An evidence linking oxidative stress, inflammation and glycemic control. *J Diabetes Metab Disord* 2013;12(1):56. doi: 10.1186/2251-6581-12-56 [published Online First: 2013/12/24]
56. Wu T, Dorn JP, Donahue RP, et al. Associations of serum C-reactive protein with fasting insulin, glucose, and glycosylated hemoglobin: the Third National Health and Nutrition Examination Survey, 1988-1994. *Am J Epidemiol* 2002;155(1):65-71. doi: 10.1093/aje/155.1.65 [published Online First: 2002/01/05]
57. Tutuncu Y, Satman I, Celik S, et al. A Comparison of hs-CRP Levels in New Diabetes Groups Diagnosed Based on FPG, 2-hPG, or HbA1c Criteria. *J Diabetes Res* 2016;2016:5827041. doi: 10.1155/2016/5827041 [published Online First: 2016/01/30]
58. Vergier J, Fromonot J, Alvares De Azevedo Macedo A, et al. Rapid differential diagnosis of diabetes insipidus in a 7-month-old infant: The copeptin approach. *Arch Pediatr* 2018;25(1):45-47. doi: 10.1016/j.arcped.2017.11.010 [published Online First: 2017/12/16]
59. Yang KT, Yang T, Symons JD. Soluble (pro)renin receptor as a potential therapy for diabetes insipidus. *Am J Physiol Renal Physiol* 2018;315(5):F1416-F21. doi: 10.1152/ajprenal.00266.2018 [published Online First: 2018/07/19]
60. K P, Kunikullaya UK, Goturu J. Glycosylated Haemoglobin (HbA1c) - A Marker of Circulating Lipids in Type 2 Diabetic Patients. *J Clin Diagn Res* 2014;8(2):20-3. doi: 10.7860/JCDR/2014/7742.3996 [published Online First: 2014/04/05]
61. Eeg-Olofsson K, Zethelius B, Gudbjornsdottir S, et al. Considerably decreased risk of cardiovascular disease with combined reductions in HbA1c, blood pressure and blood lipids in type 2 diabetes: Report from the Swedish National Diabetes Register. *Diab Vasc Dis Res* 2016;13(4):268-77. doi: 10.1177/1479164116637311 [published Online First: 2016/05/18]
62. Ji L, Weng J, Lu J, et al. Hyperglycemia and duration of diabetes as risk factors for abnormal lipids: a cross sectional survey of 19,757 patients with type 2 diabetes in China. *J Endocrinol Invest* 2014;37(9):843-52. doi: 10.1007/s40618-014-0115-4 [published Online First: 2014/06/26]