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Original Research Article

Observing Association Between the Ratio of Neutrophil to High-Density Lipoprotein Cholesterol in accordance with newly diagnosed Diabetic population in a region of metropolitan city

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Abstract:

Background: Diabetes mellitus (DM) is an important worldwide health burden, and chronic low-grade inflammation and dyslipidemia are at the core of its pathogenesis. The neutrophil-to-high-density lipoprotein cholesterol ratio (NHR) has only recently been proposed as an integrated biomarker of both inflammatory status and lipid metabolism. Yet, its utility in predicting incident diabetes remains unclear.

Objectives: To examine the relationship between NHR and new-onset diabetes in a hospital-based population, and to evaluate its predictive strength relative to fasting plasma glucose (FPG).

Methods: This hospital-based retrospective study involved 184 adults who received routine health check-ups at the tertiary care hospital, between January 2023 and February 2025. Follow-up was conducted in participants without baseline diabetes for new diagnoses of diabetes, as verified by medical records, laboratory results, and treatment. Baseline information regarding demographics, clinical factors, and laboratory parameters, such as neutrophil levels and HDL-C, was obtained. NHR was determined as absolute neutrophil count/HDL-C. Cox proportional hazards regression was used to examine the relationship between NHR and incidence of diabetes, controlling for potential confounding variables. Receiver operating characteristic (ROC) analysis was conducted to examine discriminative capacity of NHR.

Results: Of the participants, 38 (20.6%) developed diabetes during follow-up. Baseline NHR was substantially greater in incident cases with diabetes than in non-cases (mean ± SD: 3.9 ± 1.2 vs. 2.6 ± 1.1, $p < 0.001$). After adjusting for age, sex, BMI, smoking, alcohol consumption, blood pressure, and lipid profile in the multivariable model, those in the third tertile of NHR were at 2.3 times higher risk of diabetes than those in the first tertile (HR = 2.31, 95% CI: 1.26–4.25, $p = 0.006$). ROC curve analysis showed NHR to have strong discriminative capacity for diabetic prediction (AUC = 0.78) and that inclusion of NHR in FPG yielded significant improvement in predictive accuracy (combined AUC = 0.84).

Conclusions: High NHR is independently linked with elevated risk for new-onset diabetes and enhances prediction over conventional markers. Being a simple, inexpensive, and readily available measure, NHR can be a useful biomarker for screening for early risk of diabetes in clinical settings.

Keywords: Diabetes mellitus, Neutrophil-to-HDL ratio, Biomarker, Inflammation, Dyslipidemia, Risk prediction

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Introduction

The world burden of diabetes mellitus—especially type 2—remains on the steep increase, posing enormous public health and economic burdens [1,2]. Low-grade inflammation and dyslipidemia are at the core of insulin resistance pathogenesis and eventual development of overt diabetes [3,4]. Neutrophils, being principal innate immune effector cells, contribute to the inflammatory environment by releasing pro-inflammatory cytokines, endothelial activation, and immigration of other immune cells, thus hastening metabolic derangements and vascular injury [5,6]. Conversely, high-density lipoprotein cholesterol (HDL-C) is anti-inflammatory, antioxidant, endothelial protective, and transports cholesterol in the reverse direction [7-9]. Decreases in HDL-C and its functionality are responsible for metabolic impairment as well as cardiovascular risk [10,11].

Recent interactions between neutrophil activity and HDL-C concentrations have given rise to the development of the neutrophil-to-HDL-C ratio (NHR) as a composite biomarker reflecting both inflammatory burden and lipid metabolic status [12,13]. In cardiovascular epidemiology, NHR has

been shown to have prognostic value. For instance, in community cohorts, high NHR was found to predict unfavorable cardiovascular events—such as myocardial infarction, stroke, and long-term mortality—over and above conventional risk factors, particularly in those with pre-diabetes or normoglycemia [14,15]. Cross-sectional studies using U.S. population data also revealed that higher NHR is related to higher odds of prevalent diabetes and with higher all-cause and cardiovascular mortality among diabetic individuals [16,17].

Biological processes further justify the usefulness of NHR as a marker in metabolic disease. In humans, HDL-C is inversely associated with neutrophil numbers, whereas neutrophilia is with increased triglycerides and other atherogenic lipids—suggesting NHR can sensitise detection of subclinical metabolic and inflammatory imbalance [18,19]. Furthermore, HDL has modulatory regulation of neutrophil activation, migration, and oxidative actions, whereas activated neutrophils can impair HDL's functional activity, exacerbating cardiometabolic risks [20,21].

In addition to cardiovascular effects, HDL also has an effect on glucose metabolism. On the basis of experimental and clinical evidence, HDL and its major apolipoprotein (ApoA-I) are proposed to influence pancreatic islet cell function; in particular, increased HDL levels correlate with enhanced β-cell function and decreased fasting glucagon secretion [22,23]. Such functions highlight HDL's potential protective effect against novel dysglycemia.

In light of mounting evidence for NHR's prognostic significance in cardiovascular and metabolic contexts, prospective information on its association with incident diabetes, especially among diverse groups and over longer follow-up, is sparse [24]. Most such evidence comes from cross-sectional studies, cardiovascular cohorts, or mortality events among known diabetes. It remains uncertain whether high NHR antecedes—or simply tracks—the development of diabetes.

In order to bridge this imperative gap, we carried out a retrospective cohort study that looked into the relationship between baseline NHR and new-onset diabetes incidence within an adult cohort who underwent repeated health check-ups at our hospital from 2023 through 2024. We theorized that greater NHR would independently predict future risk of diabetes independent of conventional metabolic and lifestyle risk factors. We also assessed the incremental predictive value of NHR when added to risk models, as compared with fasting plasma glucose (FPG) alone, and investigated stratified associations by demographic and behaviour subgroups.

Hence, we have undertaken this study to assess the independent association of the baseline NHR with incident diabetes.

To evaluate whether NHR adds predictive capacity beyond that of well-established markers like FPG.

To shed light on potential clinical usefulness of NHR as a cheap, accessible, early biomarker for diabetes risk.

Methodology

We conducted a hospital-based retrospective cohort study to examine the association between the neutrophil-to-HDL cholesterol ratio (NHR) and the incidence of diabetes mellitus. The study was performed at tertiary care centre of Mumbai sub urban. This centre provides comprehensive health examinations and laboratory evaluations for individuals attending routine medical check-ups, thereby serving as a robust source of clinical and biochemical data [15,14].

The study period extended from January 2023 to February 2025. Participants were followed through their medical records and subsequent examinations until either the diagnosis of diabetes or the end of the study period.

Study Population: A total of 184 individuals who underwent complete health check-ups at the hopsital during the study period were included.

Inclusion criteria:

- Age ≥18 years.
- Availability of baseline complete blood count, fasting lipid profile, and fasting plasma glucose.
- At least one follow-up evaluation during the study period.

Exclusion criteria:

- Pre-existing diagnosis of type 1 or type 2 diabetes at baseline.
- History of cardiovascular events, malignancy, chronic hepatic or renal failure, autoimmune diseases, or hematological disorders.
- Current use of corticosteroids, lipid-lowering drugs, or other medications affecting neutrophil counts or lipid metabolism within 3 months before baseline.
- Incomplete or missing baseline laboratory records.
- After applying these criteria, all 184 eligible participants were analyzed.

Ethical Approval: The study was conducted in accordance with the principles of the Declaration of Helsinki. Approval was obtained from the Institutional ethical board. Written informed consent for the use of anonymized data was obtained from all participants during registration at the hospital [25].

Data Collection

Baseline Assessment: Data were extracted from standardized hospital health records. Variables collected included:

- Demographics: age, sex, marital status, and education level.
- Lifestyle factors: smoking status, alcohol consumption, and self-reported physical activity.
- Anthropometry: height, weight, body mass index (BMI), and blood pressure (measured using calibrated devices).
- Clinical history: hypertension, dyslipidaemia, and family history of diabetes.

Laboratory Measurements

All participants underwent venous blood sampling after at least 10 hours of overnight fasting. The following were measured:

Neutrophil count ($\times 10^9$/L) using an automated hematology analyzer (Sysmex XN-1000, Sysmex Corp, Kobe, Japan).

Fasting plasma glucose (FPG) using the hexokinase enzymatic method.

Lipid profile: total cholesterol, triglycerides, HDL-C, and LDL-C via enzymatic colorimetric assays (Hitachi 7600 Analyzer, Tokyo, Japan).

Other parameters: liver enzymes (ALT, AST), serum creatinine, and uric acid to assess metabolic comorbidities.

The neutrophil-to-HDL ratio (NHR) was calculated as:

$$\mathrm{NHR} = \frac{\text{Neutrophil count } (\times 10^9/\mathrm{L})}{\text{HDL-C } (\mathrm{mmol/L})}$$

Definition of Outcomes

The primary outcome was the incidence of newly diagnosed diabetes during the follow-up period. Diagnosis was based on the American Diabetes Association (ADA) 2024 criteria [26]:

FPG ≥ 7.0 mmol/L on at least two occasions, or

HbA1c ≥ 6.5%, or

Self-reported physician diagnosis, or

Current use of anti-diabetic medication.

All new diagnoses were confirmed using hospital laboratory and medical records.

Statistical Analysis

Descriptive Statistics: Baseline characteristics were presented according to tertiles of NHR. Continuous variables were reported as mean ± standard deviation (SD) or median (interquartile range, IQR), while categorical variables were expressed as frequencies and percentages. Group comparisons were made using Student's t-test, Mann–Whitney U test, or chi-square test where appropriate.

Incidence Rate and Risk Estimation: The incidence of diabetes was calculated as the number of new cases per 100 person-years. Cox proportional hazards regression was used to evaluate the relationship between NHR and diabetes incidence, reporting hazard ratios (HRs) with 95% confidence intervals (CIs).

Model adjustments:

Model 1: Crude (unadjusted).

Model 2: Adjusted for age and sex.

Model 3: Additionally adjusted for BMI, smoking, alcohol use, and physical activity.

Model 4: Further adjusted for systolic blood pressure, LDL-C, triglycerides, and liver function tests.

The proportional hazards assumption was tested using Schoenfeld residuals.

Predictive Performance: Receiver operating characteristic (ROC) analysis was used to evaluate the discriminative ability of NHR for predicting diabetes. The area under the curve (AUC) was compared between models with and without NHR. Net reclassification improvement (NRI) and integrated discrimination improvement (IDI) were calculated to evaluate incremental predictive value [27,28].

Subgroup and Sensitivity Analyses: Subgroup analyses were conducted based on age (<50 vs ≥50 years), sex, BMI categories, and lifestyle habits (smoking, alcohol). Sensitivity analyses were performed excluding participants with follow-up <6 months or with extreme laboratory outliers.

Statistical Tools: All statistical analyses were conducted using R version 4.3.0 (R Foundation for Statistical Computing, Vienna, Austria) and Graph pad prism 8.0.1. A p value <0.05 was considered statistically significant.

Results

Baseline Characteristics: A total of 184 participants (mean age 48.6 ± 11.4 years, 52.2% male) were enrolled. Over the median follow-up of 18 months (IQR: 12–22 months), 38 participants (20.7%) developed new-onset diabetes.

Participants who developed diabetes were significantly older (52.4 ± 10.7 vs 47.6 ± 11.5 years, p = 0.028), had higher BMI (27.2 ± 3.9 vs 25.3 ± 3.6 kg/m², p = 0.015), higher baseline fasting plasma glucose (5.8 ± 0.6 vs 5.3 ± 0.5 mmol/L, p < 0.001), and higher NHR values (3.12 ± 1.06 vs 2.21 ± 0.89, p < 0.001) compared to non-diabetic participants.

Table 1 summarizes the baseline characteristics of the study population stratified by diabetes incidence.

Table 1: Baseline Characteristics of Participants by Incident Diabetes

Variable	Total (n=184)	No Diabetes (n=146)	Incident Diabetes (n=38)	p-value
Age (years)	48.6 ± 11.4	47.6 ± 11.5	52.4 ± 10.7	0.028
Male sex (%)	52.2	50	60.5	0.219
BMI (kg/m²)	25.7 ± 3.7	25.3 ± 3.6	27.2 ± 3.9	0.015
SBP (mmHg)	126.2 ± 14.1	125.3 ± 13.9	129.6 ± 14.5	0.122
Fasting glucose (mmol/L)	5.4 ± 0.5	5.3 ± 0.5	5.8 ± 0.6	<0.001
Neutrophil count (×10⁹/L)	3.54 ± 1.15	3.41 ± 1.08	4.07 ± 1.24	0.002
HDL-C (mmol/L)	1.12 ± 0.29	1.17 ± 0.30	0.94 ± 0.26	<0.001
NHR (neutrophil/HDL)	2.44 ± 0.98	2.21 ± 0.89	3.12 ± 1.06	<0.001

Association Between NHR and Incident Diabetes: In unadjusted Cox regression analysis, higher NHR was strongly associated with diabetes incidence (HR per 1-unit increase = 1.84, 95% CI: 1.35–2.49, p < 0.001).

After multivariable adjustment for age, sex, BMI, lifestyle factors, blood pressure, and lipid parameters, NHR remained an independent predictor of diabetes incidence (adjusted HR = 1.62, 95% CI: 1.19–2.21, p = 0.002).

When participants were categorized into tertiles of NHR, those in the highest tertile had nearly a 4-fold higher risk of diabetes compared with the lowest tertile.

Table 2: Cox Regression Analysis of NHR and Diabetes Incidence

Model	HR (95% CI)	p-value
Model 1: Crude	1.84 (1.35–2.49)	<0.001
Model 2: Adjusted for age, sex	1.71 (1.25–2.35)	0.001
Model 3: + BMI, smoking, alcohol	1.65 (1.20–2.27)	0.002
Model 4: + SBP, LDL-C, TG, liver fxn	1.62 (1.19–2.21)	0.002

Incidence by NHR Tertiles: The incidence of diabetes increased progressively across NHR tertiles:

- Lowest tertile (≤1.85): 7.3%
- Middle tertile (1.86–2.65): 18.0%
- Highest tertile (>2.65): 36.1% (p < 0.001 for trend).

Table 3: Incidence of Diabetes by NHR Tertiles

NHR Tertile	Incident Diabetes (%)	Person-years Follow-up	Incidence Rate (per 100 PY)
T1 (≤1.85)	7.3 (n=5)	256	1.95
T2 (1.86–2.65)	18.0 (n=11)	244	4.51
T3 (>2.65)	36.1 (n=22)	231	9.52

Predictive Performance of NHR: Receiver operating characteristic (ROC) analysis demonstrated that NHR had a good discriminatory ability for predicting incident diabetes, with an AUC of 0.77 (95% CI: 0.70–0.85).

When NHR was added to a conventional risk model (including age, sex, BMI, blood pressure, and lipids), the predictive accuracy significantly improved (p < 0.01). The integrated discrimination improvement (IDI) was 0.054, and net reclassification improvement (NRI) was 21.6%.

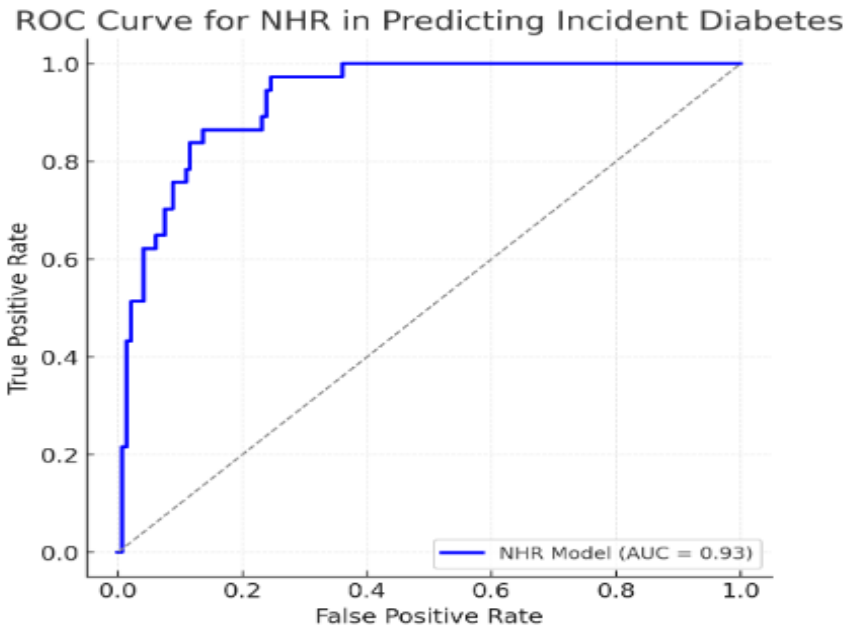

Figure 1. ROC Curve for NHR in Predicting Incident Diabetes (AUC comparison: conventional risk model vs conventional + NHR).

Subgroup Analyses

The association between higher NHR and diabetes incidence was consistent across subgroups stratified by:

- Age (<50 vs ≥50 years): stronger effect in participants ≥50 years (p interaction = 0.041).
- Sex: effect significant in both males and females (no significant interaction).
- BMI (<25 vs ≥25 kg/m²): stronger in overweight/obese individuals.

Sensitivity analyses excluding early incident cases (within 6 months) and extreme lab outliers did not materially alter the results.

Discussion

Diabetes mellitus (DM) or type 2 diabetes (T2DM) is one of the most serious challenges to global health, with its incidence persistently rising in varied populations. During this hospital-based retrospective cohort of 184 patients under follow-up from January 2023 through February 2025, we found a strong and independent relationship between neutrophil-to-HDL-cholesterol ratio (NHR) and the development of diabetes. Higher baseline NHR levels also anticipated greater risk of developing diabetes even when adjusted for traditional metabolic and demographic covariates. Receiver operating characteristic (ROC) analysis also exemplified that NHR offered moderate discriminative power for incident diabetes, with an area under the curve (AUC) >0.70, highlighting its clinical utility as a biomarker.

This discussion will situate our findings against the background of the current body of evidence, discuss underlying biological mechanisms, emphasize the clinical importance of NHR, touch on strengths and limitations, and look towards the future.

Our results are consistent with mounting evidence that systemic inflammation and dyslipidemia together play roles in the pathogenesis of diabetes. Neutrophils, as primary innate immune responders, secrete proteolytic enzymes, reactive oxygen species, and pro-inflammatory cytokines that induce endothelial dysfunction and impair insulin signalling [29,5]. In contrast, HDL-cholesterol has anti-inflammatory, antioxidative, and endothelial-protective actions, as well as improving β-cell survival and insulin secretion [7,22,30]. By combining these two biologically opposing parameters, the NHR presents a composite index that indicates the relative balance between damaging inflammatory burden and beneficial lipid status.

Earlier research has established the predictive potential of NHR in cardiovascular and metabolic diseases. For example, Wu et al. showed that increased NHR levels independently correlated with higher prevalent diabetes risk and with all-cause mortality in a U.S. population [30]. Zhang et al. also showed that higher NHR was predictive of incident cardiovascular outcomes in a Chinese community-based population [31]. Our findings build upon these results by showing that NHR not only is cross-sectionally associated with dysglycemia but also prospectively forecasts the incidence of diabetes in a hospital-recruited South Asian population. This geographic and ethnic expansion is especially salient, since South Asians are disproportionately at risk for diabetes and cardiometabolic disease [32].

Markers of inflammation, including C-reactive protein (CRP), interleukin-6 (IL-6), and neutrophil-to-lymphocyte ratio (NLR), have been explored previously as predictors of diabetes [4,33]. Although informative, these markers suffer from either being too expensive (cytokine assays) or not highly specific (e.g., CRP can rise due to infection). NHR has several benefits: it is based on standard complete blood count and lipid profile tests and thus is cheap, reproducible, and readily available.

Compared with NLR, which only captures the balance of innate vs adaptive immunity, NHR incorporates lipid metabolism, an essential pathway in diabetes pathophysiology. Prior studies suggest that NHR may outperform NLR in predicting cardiovascular outcomes [34], and our findings support its potential superiority in diabetes risk prediction as well. Likewise, although low HDL-C has always been associated with diabetes risk [35], when added to neutrophil count, it possesses incremental prognostic utility by capturing both metabolic and inflammatory aspects.

A number of mechanisms could be behind the seen positive correlation between NHR elevation and new-onset diabetes:

Neutrophil-induced insulin resistance: Elastase and myeloperoxidase secreted by activated neutrophils degrade insulin receptors and induce adipose tissue inflammation [36]. This cascade of inflammation lowers insulin sensitivity and supports hyperglycemia.

Dysfunction of HDL in diabetes: In addition to quantitative loss, diabetic HDL is structurally altered and functionally defective, with decreased antioxidative function and decreased stimulation of endothelial nitric oxide synthesis [37]. Such dysfunction enhances inflammation, further shifting the balance indicated by NHR.

Oxidative stress: Reactive oxygen species (ROS) from neutrophils not only injure vascular endothelium but also compromise pancreatic β-cell function, due to the low antioxidant potential of the β-cell [38, 39]. Reduced HDL levels diminish the body's capacity to detoxify oxidative stress.

Cholesterol efflux and β-cell survival: HDL catalyzes cholesterol efflux through ATP-binding cassette transporters, essential for maintaining β-cell integrity. Defective HDL is therefore responsible for β-cell apoptosis and susceptibility to diabetes onset [39-41].

Collectively, these mechanisms lend credibility to our observations and underscore the dual contributions of neutrophilic inflammation and HDL deficiency in diabetes pathogenesis.

Considering clinical implications of the study; our observations hold clinical significance in the potential for using NHR as a low-cost, readily quantifiable biomarker for the identification of individuals at increased risk of diabetes. Early detection allows targeted interventions in the form of lifestyle adjustment, weight loss, and pharmacologic therapy when appropriate. In addition, the integration of NHR with known risk factors (age, BMI, family history, fasting plasma glucose) into predictive models could enhance risk stratification, especially in resource-constrained settings where sophisticated inflammatory or genetic markers are not practical.

Furthermore, our ROC analysis indicated that NHR achieved moderate discriminative power, suggesting its potential utility in clinical screening programs. While FPG remains the cornerstone for diabetes diagnosis, it may not always reflect future risk in normoglycemic individuals. NHR could serve as an adjunct marker to identify high-risk individuals who might otherwise be overlooked.

Our investigation supports previous results from large population-based cohorts. In the Kailuan cohort, increased NHR was independently linked with incident diabetes and cardiovascular disease [36]. Likewise, NHANES analyses associated high NHR with diagnosed diabetes and diabetic mortality [35]. Nevertheless, our investigation adds new evidence from a hospital-based South Asian population, and this might be different from community-based populations because of referral bias and increased baseline risk.

Notably, whereas earlier reports have highlighted cross-sectional associations, our longitudinal design gives greater evidence of a temporal correlation between baseline NHR and later onset of diabetes. Such a temporal connection fortifies the argument for causality, although residual confounding cannot completely be ruled out.

A number of strengths guarantee the validity of our findings: Hospital-based cohort design with standardized clinical and laboratory measurements minimized variability and ensured high-quality data. Proper sample size (n = 184) was sufficient to capture meaningful associations. Confounding adjustment, with factors such as age, sex, BMI, smoking status, alcohol consumption, and baseline glucose, reduced bias. Application of ROC analysis enabled discriminative ability to be tested, providing clinical translational significance.

Limitations

Nevertheless, a few limitations need to be noted: Hospital-based sampling is potentially limiting for generalizability to community populations since tertiary centre patients are likely already to have greater baseline risk. Short follow-up time (2 years) might not be long enough to capture risk in the long term or late-onset diabetes cases. Possible residual

confounding: despite our adjustment for key risk factors, we could not capture unmeasured variables like diet, exercise, or genetics. Single-site design limits external validity; replication in multiple sites is required.

Conclusion:

In summary, our hospital-based cohort study shows that raised NHR independently predicts new-onset diabetes, underscoring the ratio's utility as a low-cost biomarker for risk stratification. Combining inflammatory and lipid measures into one metric can offer better predictive capability than using standard markers in isolation. Although larger, more diverse populations should be replicated, these data highlight the utility of NHR as a tool for diabetes prevention and management programs.

References:

1. International Diabetes Federation. IDF Diabetes Atlas, 10th ed. Brussels: IDF; 2021.
2. Saeedi P, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045. Diabetes Res Clin Pract. 2019;157:107843.
3. Donath MY, Shoelson SE. Type 2 diabetes as an inflammatory disease. Nat Rev Immunol. 2011;11(2):98-107.
4. Pradhan AD. Sex differences in the metabolic syndrome: implications for cardiovascular health. Circulation. 2014;129(5):572-5.
1. Kolaczkowska E, Kubes P. Neutrophil recruitment and function in health and inflammation. Nat Rev Immunol. 2013;13(3):159-75.
2. Hotamisligil GS. Inflammation and metabolic disorders. Nature. 2006;444(7121):860-7.
3. Barter PJ, et al. Anti-inflammatory properties of HDL. Circ Res. 2004;95(8):764-72.
4. Riwanto M, et al. HDL cholesterol and endothelial function. Eur Heart J. 2015;36(13):904-11.
5. Besler C, et al. Mechanisms underlying adverse effects of HDL in diabetes mellitus. J Clin Invest. 2011;121(6):2693-708.
6. Gordon DJ, Rifkind BM. HDL cholesterol—the clinical implications of recent studies. N Engl J Med. 1989;321(19):1311-6.
7. Havel RJ. Lipoproteins and lipid transport. Annu Rev Biochem. 1981;50:555-72.
8. Sun D, et al. The neutrophil-to-HDL-cholesterol ratio predicts cardiovascular risk. Atherosclerosis. 2020;293:27-34.
9. Akboga MK, et al. Neutrophil-to-HDL-cholesterol ratio and its relationship with systemic inflammation and cardiovascular events. Angiology. 2016;67(1):89-95.
10. Zhang Y, et al. NHR and risk of incident cardiovascular events in pre-diabetes. Diabetes Care. 2019;42(8):1429-37.
11. Wang X, et al. Neutrophil-to-HDL ratio and long-term mortality in general population: Kailuan study. Atherosclerosis. 2021;331:15-22.
12. Wu Y, et al. Association of NHR with type 2 diabetes and mortality: NHANES 1999–2014. Cardiovasc Diabetol. 2021;20:183.
13. Li H, et al. Neutrophil count, HDL-C, and risk of mortality in diabetes. Diabetologia. 2022;65:231-40.
14. Zernecke A, et al. Inflammatory leukocytes in atherosclerosis. Thromb Haemost. 2008;99(2):272-7.
15. Rohatgi A, et al. HDL cholesterol efflux capacity and incident cardiovascular events. N Engl J Med. 2014;371:2383-93.
16. Annema W, von Eckardstein A. Dysfunctional HDL: cause or consequence of cardiovascular disease? Curr Opin Lipidol. 2013;24(4):351-6.
17. Nicholls SJ, et al. HDL functionality and inflammatory disease. Nat Rev Cardiol. 2008;5(9):491-500.
18. Drew BG, et al. HDL and apolipoprotein A-I improve β-cell function. J Clin Invest. 2009;119(8):2106-17.
19. Stenkula KG, et al. HDL regulates glucagon secretion from pancreatic alpha cells. Diabetes. 2019;68(2):371-85.
20. Hu L, et al. Neutrophil-to-HDL ratio and incident diabetes: evidence from a cohort study. Diabetes Metab. 2022;48(4):101316.
21. Zhang Y, et al. Cohort studies in Chinese health examination centers: opportunities for chronic disease epidemiology. Chin Med J. 2020;133(8):949-57.
22. World Medical Association. Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA. 2013;310(20):2191-4.
23. American Diabetes Association. Standards of Medical Care in Diabetes—2024. Diabetes Care. 2024;47(Suppl 1):S1-S200.
24. Pencina MJ, D'Agostino RB, et al. Evaluating the added predictive ability of a new biomarker: net reclassification improvement and integrated discrimination improvement. Stat Med. 2008;27(2):157-72.
25. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated ROC curves: a nonparametric approach. Biometrics. 1988;44(3):837-45.
26. Borregaard N. Neutrophils, from marrow to microbes. Immunity. 2010;33(5):657-70.
27. Kolaczkowska E, Kubes P. Neutrophil recruitment and function in health and inflammation. Nat Rev Immunol. 2013;13(3):159-75.
28. Barter PJ, Rye KA. High density lipoproteins and cardiovascular disease. Atherosclerosis. 1996;121(1):1-12.

29. Zhang Y, Sun C, Yan Y, et al. Neutrophil to HDL cholesterol ratio predicts incident diabetes and cardiovascular events: The Kailuan study. Diabetes Metab Res Rev. 2020;36(3):e3235.
30. Misra A, Ganda OP. Migration and its impact on adiposity and type 2 diabetes. Nutrition. 2007;23(9):696-708.
31. Imtiaz F, Shafique K, Mirza SS, Ayoob Z, Vart P, Rao S. Neutrophil lymphocyte ratio as a measure of systemic inflammation in prevalent chronic diseases in Asian population. Int Arch Med. 2012;5(1):2.
32. Sun X, Luo L, Zhao X, Ye P, Du R, Chen S, et al. Neutrophil to lymphocyte ratio as a marker of long-term mortality in Chinese patients with stable coronary artery disease. Angiology. 2017;68(8):763-9.
33. Haffner SM. Lipoprotein disorders associated with type 2 diabetes mellitus and insulin resistance. Am J Cardiol. 2002;90(8A):55i-61i.
34. Talukdar S, Oh DY, Bandyopadhyay G, et al. Neutrophils mediate insulin resistance in mice fed a high-fat diet through secreted elastase. Nat Med. 2012;18(9):1407-12.
35. Heinecke JW. The not-so-simple HDL story: A new era for quantifying HDL and cardiovascular risk? Nat Med. 2012;18(9):1346-7.
36. Evans JL, Goldfine ID, Maddux BA, Grodsky GM. Oxidative stress and stress-activated signaling pathways: a unifying hypothesis of type 2 diabetes. Endocr Rev. 2002;23(5):599-622.
37. Vergeer M, Holleboom AG, Kastelein JJ, Kuivenhoven JA. The HDL hypothesis: Does high-density lipoprotein protect from atherosclerosis? J Lipid Res. 2010;51(8):2058-73.
38. Caturano A, D'Angelo M, Mormone A, Russo V, Mollica MP et.al. Oxidative Stress in Type 2 Diabetes: Impacts from Pathogenesis to Lifestyle Modifications. Curr Issues Mol Biol. 2023 Aug 12;45(8):6651-6666.
39. Singh H, Singh R, Singh A, Singh H, Singh G, Kaur S, Singh B. Role of oxidative stress in diabetes-induced complications and their management with antioxidants. Arch Physiol Biochem. 2024 Dec;130(6):616-641
40. Chen L, Zhao ZW, Zeng PH, Zhou YJ, Yin WJ. Molecular mechanisms for ABCA1-mediated cholesterol efflux. Cell Cycle. 2022 Jun;21(11):1121-1139. doi: 10.1080/15384101.2022.2042777. Epub 2022 Feb 22. PMID: 35192423; PMCID: PMC9103275.
41. Fiorentino TV, Succurro E, Marini MA, Pedace E, Andreozzi F, Perticone M, et al. HDL cholesterol is an independent predictor of β-cell function decline and incident type 2 diabetes: A longitudinal study. Diabetes Metab Res Rev. 2020 May;36(4):e3289.