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The Relationship between Insulin Resistance and Neutrophil to Lymphocyte Ratio

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ABSTRACT: There is increasing interest in the role of chronic inflammation on the pathogenesis of various diseases, and one of its markers, high Neutrophil-to-Lymphocyte Ratio, is associated with multiple mortality and morbidity risk, suggesting Insulin Resistance might be one potential associate factor. However, epidemiological studies on the association between NLR and IR are scarce, and they only included diabetes mellitus patients, excluding the general population. This study aims to determine if there is a direct correlation between NLR and IR in the US general population. The Homeostatic Model Assessment for Insulin Resistance value was calculated to evaluate the IR of the 3,307 samples provided by the NHANES. As insulin usage could result in inaccurate HOMA-IR estimation, we excluded them and ran a subgroup analysis. The relationship was shown when insulin users were included, having a beta coefficient value of 0.010 (95% confidence interval [CI] of 0.003-0.017). However, without insulin users, the beta value decreased to 0.004 (95% CI of -0.006-0.015). The statistical significance wasn't reached when age, sex, and BMI were adjusted for in the multivariate analyses. Therefore, IR might not explain the variation of NLR value in healthy people, and further studies are needed to reveal the associated factor of high NLR.

KEYWORDS: Neutrophil-to-Lymphocyte Ratio, Insulin Resistance, HOMA-IR, Diabetes Mellitus.

Introduction

There has been an increase in the study of Neutrophil-to-Lymphocyte Ratio (NLR) and its correlation to various health issues among the human population. NLR is a new biomarker of chronic inflammation, calculated by dividing the Neutrophil count by the lymphocyte count in the blood.[1] Neutrophil is a type of White Blood Cell (WBC) that supports the healing process of damaged tissues and the process of resolving infections. Their role is to recognize phagocytose microbes, kill pathogens through mechanisms that produce reactive oxygen species, release antimicrobial peptides, and expulse their nuclear content to form traps.[2] Lymphocytes are also a type of WBC for the immune system, including the B-Cells and the T-Cells. NLR, therefore, reflects the balance of acute and chronic inflammation (neutrophil count) and adaptive immunity (lymphocyte count).[1] It is a popular marker for medical examinations because NLR calculations are more straightforward and cheaper than other biomarkers.[3] Previous studies have found that an increase in NLR is associated with an increase in mortality[4], diabetes mellitus[5], ischemic stroke[4], cerebral hemorrhage[6], major cardiac events[7], sepsis, and infectious diseases.[4-8]

Insulin resistance (IR) is regarded as crucial pathophysiology of diabetes mellitus, when the target tissue of the insulin does not respond to the stimulation, prohibiting blood glucose levels from decreasing.[9] In normal circumstances, as the glucose level increases in the bloodstream, the pancreas releases insulin to stimulate a series of receptors in muscle cells, enabling glucose to enter the cells. Through this process, glucose is converted to a form of energy reserved for long-term storage. IR, which prevents this process from happening, is also associated with inflammation, obesity, CVD, nonalcoholic fatty liver disease, metabolic syndrome, and polycystic ovary syndrome.[9-11]

Several studies suggested a linkage between NLR and metabolic syndrome.[3,12] However, while NLR is highly correlated with metabolic syndrome, it is a cluster of risk factors and does not directly mean insulin resistance. In one previous study with diabetes patients, IR and NLR were associated. The two comparison groups they had were DM patients without IR and DM patients with IR. Patients without IR showed lower NLR values than patients with IR, and the logistic regression analysis also revealed significance in the correlation between IR and NLR.[3] As a result, the study concluded that NLR could play a role as an important biomarker when predicting IR in diabetic patients.[3] A limitation of this study was that they did not consider insulin usage, which might affect the calculation of the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR), the indicator of insulin resistance.[13]

To current knowledge, no study has investigated the relationship between NLR and IR in the general population and with the consideration of insulin use. A new study of the general population and examining the specific DM and insulin usage would be essential to discover the correlation between IR and NLR.

Hypothesis and Aim:

This study will examine the association between NLR and IR in the general population, considering DM and insulin treatment status. It was hypothesized that increasing IR would affect the increase of NLR.

Methods

Data source:

For the study participants, the general data was collected in The National Health and Nutrition Examination Survey

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(NHANES), a cross-sectional study conducted by the National Center for Health Statistics (NCHS) to obtain a sample representing the United States population, was used. It has constantly been releasing updated data since 1959 to the public; however, it stopped in March 2020 due to the COVID-19 breakout. The NHANES website contains information on physical examination, questionnaire data, webinars, and surveys that portray the US population's health and nutrition status at 2-year intervals.[14] The data used in this study was obtained through a pre-pandemic community-based survey between 2017 and March 2020.

Study population:

Of the 15,560 people in the data who completed the physical examination between 2017-March 2020, samples over the age of 19 and those who have completed data on insulin usage, BMI, and CBC were included. To establish a more accurate analysis, the following were excluded: participants with a fasting glucose level that exceeds 140 mg/dL, as the normal range of fasting blood glucose level, is below 140mg/dL; participants with more than 10,000 WBC in the collected blood sample, because healthy individuals show values between 4,500-10,000 WBC and >10,000 suggest acute inflammatory status; participants with NLR over 9, as it becomes an outlier considering that normal NLR value in adults is between 0.78 and 3.53, and >9 might mean critically ill status.[15-17] NLR values were calculated by dividing the absolute count of neutrophil by the absolute count of lymphocytes. These factors were eliminated due to the possibility of the data being altered as they showed abnormal figures and could be possible outliers. After all the eliminations, 3,375 samples remained.

During the analysis, 68 insulin users were removed as they could be a confounding variable in the overall analysis. This decision was made due to the HOMA-IR used in this study to measure how much insulin the pancreas creates to regulate blood glucose levels. The HOMA-IR values were calculated by multiplying fasting insulin and fasting glucose levels and dividing by 22.5.

Data collection:

Final data collection was done on the individual's gender, race, height, weight, fasting glucose level, BMI, WBC level, and NLR. (Figure 1) Body measurements were collected in the Mobile Examination Center (MEC). General information, such as age, gender, disease status, etc., was collected through surveys, and experts performed body measurement data with the individual's consent. Overnight fasting blood samples were obtained for fasting glucose, insulin, and other laboratory values.

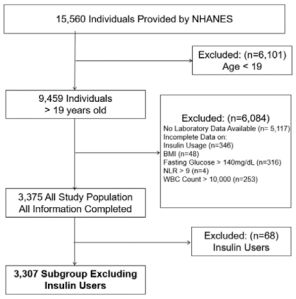

Figure 1: Shows the process of exclusion.

Statistical analyses:

Descriptive statistics (mean, standard deviation (SD) for continuous variables and number and percentage for categorical variables) were used to describe the study population. The distribution of NLR and HOMA-IR level was visualized by a histogram. They showed right skewness for both.

Statistical analyses were performed to see how NLR levels related to HOMA-IR and insulin status. The correlation between NRL and HOMA-IR was displayed in a scatter plot and a line of best fit (regression line). Due the right skewness of the NLR and HOMA-IR, the relationship was also displayed after logarithmic transformation, calculating the values of Log HOMA-IR and Log NLR. We also showed it in three groups: non-DM (Diabetes Mellitus), DM not on insulin, and DM on insulin.

DM and insulin status were considered in our analyses with an a priori hypothesis. The means SD of HOMA-IR and NLR by DM and insulin status were shown by a bar graph. It showed that HOMA-IR and NLR were significantly higher when the subjects were on insulin treatment. Therefore, insulin users were excluded from the additional data analysis. Bivariate and Multivariate linear regression analyses were performed to examine the statistical significance of the relationship between NLR and HOMA-IR. As done in previous studies, multivariate linear regression analyses were performed controlling for age, sex, and BMI, as they could be confounding variables that influence NLR values.[12] BMI was controlled because a high BMI is linked to an increase in insulin resistance and NRL, which may also alter the relationship overall.[17,18] We took HOMA-IR as an independent variable and NLR as a dependent variable, as we hypothesized that insulin resistance would induce chronic inflammation. While several studies suggested a bidirectional relationship, the most recent knock-out mice model suggested such a direction.[3,19]

All statistical analyses were made using STATA 14.0 (College Station, TX), and considering that p-values<0.05 are statistically significant.

Results and Discussion

Study population :

Table 1 shows the participants' characteristics with the sample including insulin users and the sample excluding insulin users. Among the 3,307 participants, 1,731 (52.3%) were female, and the mean age was 49.4 (SD 17.8). 298 (8.83%) were diabetes mellitus patients, and 68 (2.01%) used insulin.

Table 1: Analysis of all participants (N=3,375) and participants without insulin users (N=3,307).

	All participants (N=3,375)			Excluding insulin user (N= 3,307)	
	N or mean	% Or SD		N or mean	% Or SD
Age	49.35	17.83		49.02	17.79
Sex, Female	1762.00	52.21		1731.00	52.34
Diabetes Mellitus	298.00	8.83		230.00	6.95
On insulin	68.00	2.01		-	-
Hypertension	1187.00	35.17		34	0.48

Asthma	518.00	15.35		503.00	15.21
Arthritis	945.00	28.00		910.00	27.52
Heart failure	99.00	2.93		84.00	2.54
Coronary heart disease	119.00	3.53		111.00	3.36
Stroke	150.00	4.44		140.00	4.23
Chronic obstructive pulmonary disease	267.00	7.91		257.00	7.77
BMI (kg/m2)	29.41	7.32		29.35	7.31
Fasting insulin (μU/mL)	13.25	17.63		12.41	11.20
HOMA-IR	3.30	4.73		3.06	3.05
ALT (IU/L)	21.81	20.56		21.9.	20.73
AST (units/L)	21.90	15.63		21.93	15.72
ALP (units/L)	76.41	24.60		76.17	24.37
Albumin (g/dL)	4.03	0.33		4.03	0.33
Blood urea nitrogen (mg/dL)	14.54	5.57		29.35	7.31
Sodium Bicarbonate (mg/dL)	25.59	2.38		25.59	2.36
Creatinine (mg/dL)	0.89	0.50		0.88	0.44
Gamma-glutamyl transferase (units/L)	30.75	56.13		14.39	5.31
Total cholesterol (mg/dL)	184.37	40.31		184.89	40.25
Triglyceride (mg/dL)	117.65	87.53		117.40	87.86
Uric acid (mg/dL)	5.44	1.44		5.42	1.42

Figure 2A shows the distribution of baseline NLR values according to the general population information from NHANES. The graph suggests that the general population (3.307 samples in this study) has a mean of 2 ± 0.02 and a median of 1.82. Also, the range between the 25th and 75th percentile was 1.08 for neutrophil and lymphocyte count. **Figure 2B** shows the distribution of baseline HOMA-IR values in the general population. The graph suggests a mean of 3.3 ± 4.73 and a median of 2.23. Also, the range between the 25th and 75th percentile was 2.48 for HOMA-IR.

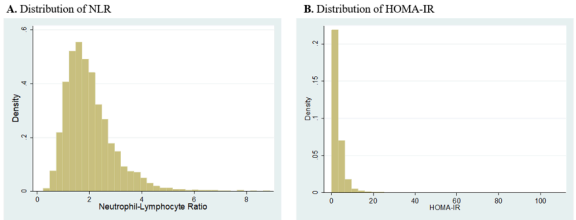

Figure 2: The distribution of neutrophil-to-lymphocyte ratios (A) and HOMA-IR (B) among individuals. The x-axis is truncated at an NLR of 9.

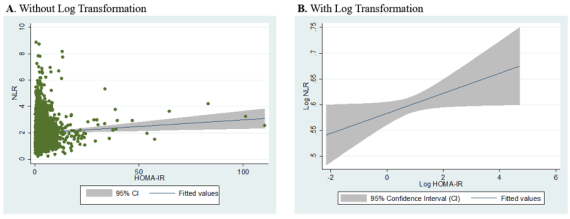

Figure 3: The regression line and 95% Confidence Interval of the relationship between Log HOMA-IR and Log NLR before (3A) and after log transformation (3B).

Figure 3 presents a weak positive correlation between HOMA-IR and NLR. This graph went through a logarithmic transformation due to the skewness, representing the relationship between Log HOMA-IR and Log NLR. The regression line showed a weak, positive correlation. As the Log HOMA-IR slightly increased, the Log NLR value would also increase.

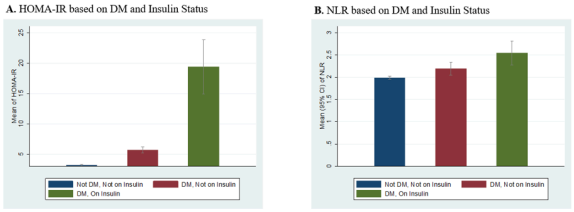

Figure 4: Bar graph comparing the mean (95% Confidence Interval) HOMA-IR (A) and NLR level (B) of individuals: not Diabetes Mellitus (DM) and not on insulin, DM and not on insulin, and DM and on insulin.

Figure 4A shows the different mean HOMA-IR value for each criterion. With the inclusion of insulin users, the data on HOMA-IR will show an abnormally large number when compared to individuals who are not on insulin treatment (for detail, see **Figure 4A**) and offer an unsteady insulin concentration in blood depending on when they receive the treatment.[13] Individuals without DM and insulin had a mean HOMA-IR value of 3.24 ± 0.07, individuals with DM but no insulin treatment had a mean of 5.76 ± 0.27, and individuals with both DM and insulin treatment had a mean of 19.42 ± 2.27. Here, the effect of the insulin treatment on HOMA-IR was evident, suggesting the need to exclude this group in additional analysis.

Figure 4B describes the different NLR value depending on the individual's current DM and insulin status. The results showed each criterion's mean 95% confidence interval (CI). Individuals without DM and insulin had a mean NLR value of 2.06 ± 0.02, individuals with DM but no insulin treatment had a mean of 2.32 ± 0.59, and individuals with both DM and insulin treatment had a mean of 2.65 ± 0.10.

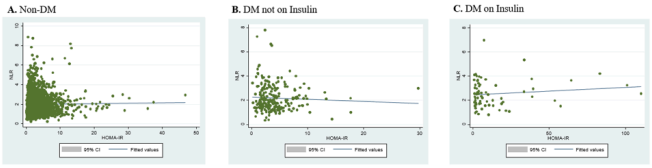

Figure 5: Scatterplot for each criterion, comparing HOMA-IR distribution.

Figure 5 suggests the difference in HOMA-IR - NLR association by DM and insulin status. The non-DM groups showed nearly no significant correlation. Also, DM not in the Insulin group showed a weak, negative correlation. However, the DM in the Insulin group showed a drastically increased HOMA-IR value; therefore, the group individuals were eliminated for further analysis.

Bivariate and Multivariate Linear regression analyses:

Table 2 shows the difference in the linear regression and significance of all study subjects (n=3,375) and the subjects after excluding insulin users (n=3,307). Bivariate linear regression analysis showed a significant positive relationship between

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HOMA-IR and NLR (beta-coefficient 0.010, 95% CI 0.003-0.017, P-value 0.004). After adjusting age, sex, and BMI, it lost statistical significance due to the altered values (beta-coefficient 0.004, 95% CI -0.006-0.014).

With the exclusion of insulin users, the beta value changed from 0.01 to 0.004, and the 95% CI interval drastically changed from 0.003-0.017 to -0.006-0.015, indicating no significance. This suggests that there is no true association between HOMA-IR and NLR.

Table 2: Univariate and Multivariate Linear Regression Model of HOMA-IR on NLR

All study subjects (N=3,375)						
	β	SE	t	P>t	95% CI	
Bivariate						
HOMA-IR	0.010	0.003	2.880	0.004	0.003	0.017
Constant	1.982	0.020	98.200	0.000	1.942	2.022
Multivariate						
Age	0.010	0.001	10.670	0.000	0.008	0.012
Sex	0.033	0.033	1.010	0.315	-0.031	0.097
BMI	0.004	0.002	1.820	0.069	0.000	0.009
HOMA-IR	0.006	0.004	1.720	0.086	-0.001	0.013
Constant	1.371	0.084	16.290	0.000	1.206	1.536
Excluding Insulin Users (N=3,307)						
Bivariate						
HOMA-IR	0.004	0.005	0.770	0.439	-0.006	0.015
Constant	1.992	0.024	84.510	0.000	1.945	2.038
Multivariate						
Age	0.010	0.001	10.360	0.000	0.008	0.011
Sex	0.028	0.033	0.850	0.396	-0.037	0.093
BMI	0.006	0.003	2.460	0.396	0.001	0.011
HOMA-IR	-0.003	0.006	-0.550	0.584	-0.015	0.009
Constant	1.352	0.085	15.860	0.000	1.185	1.519

BMI: Body mass index; HOMA-IR: Homeostasis model assessment of insulin resistance; β: coefficient; SE: standard error; 95% CI: 95% Confidence Interval

Summary:

In this study using the US general population data, the observation showed a weak, positive association in the relationship between NLR and IR in the overall population but a null association when insulin users were excluded.

Previous Studies/ Mechanism:

We hypothesized that a high HOMA-IR value, indicative of insulin resistant state, could predict high NLR because previous preclinical studies suggested a relationship between the two. Some studies found that chronic inflammations can induce systemic insulin resistance: for example, Uysal *et al*. revealed that proinflammatory cytokine TNF-alpha could generate IR by showing protection from obesity-induced insulin resistance in mice lacking TNF-alpha function; in addition, Talukdar *et al*. showed neutrophil mediate insulin resistance by using mice without neutrophil elastase, an enzyme that responses to tissue injury, in high-fat diet-fed mice via secreted elastase.[20, 21]

Others examined the relationship opposite: Simobayashi used Knockout mice, genetically modified to lack mTORC2 gene (causing mice to have IR), to observe the relationship between IR and inflammation.[19] mTORC2 is a protein complex that regulates glycolysis and the pentose phosphate pathway.[22] These mice were also on a high-fat diet (HFD) and were observed for ten weeks. Simobayashi found that insulin resistance caused macrophage numbers to increase while B and T cell numbers remained consistent.[19] In addition, the increase in macrophages in the KO mice, was disproportionate to other variables, indicating that IR promotes inflammation.[19]

In line with those studies, an epidemiological study done by Lou *et al*. showed a positive relationship between NLR and IR. They collected data from diabetic patients regardless of their insulin usage status and had an additional 130 healthy subjects for comparison.[3] They found that the NLR values were significantly higher in patients with diabetes than in healthy control subjects, interpreted their results as NLR being a marker for IR, and discovered that T2DM patients were in a state of low-degree chronic inflammation that induces inflammatory factors, elevating neutrophil counts.[3] Luo concluded that NLR has a direct relationship with IR and suggested that NLR can be a biomarker to predict IR in diabetic patients.

However, this study showed results that differ from the above studies because there was no significant correlation between NLR and IR after controlling for potential confounders and considering insulin use. A difference in Uysal's and Simobayashi's studies was that they used KO mice while this study focused on human subjects. Since the human subjects did not undergo a gene deletion process, it could have shown a less definite relationship than the correlation shown in mice samples. Also, a difference between Lou's study is that they were focused on patients with diabetes while this study observed the general population. They also included insulin users (insulin-deficient individuals) who dramatically increased the HOMA-IR value. Due to these differences, this study, which focused on the general human population, found no significance or a very weak significance in the correlation between NLR and IR.

Conclusion

As shown in Figure 6, it was revealed that there is no significant association between IR and NLR. Contrary to our hypothesis, insulin resistance did not explain chronic inflammation, represented by NLR. While the increase in each NLR and insulin resistance can cause an increase in mortality, disease, and several types of cancer, they seem to be risk factors independent of each other. Therefore, further studies on other factors that increase chronic inflammation and NLR values in the general population would be needed to develop a strategy to prevent chronic inflammation related to several morbidity and mortality.

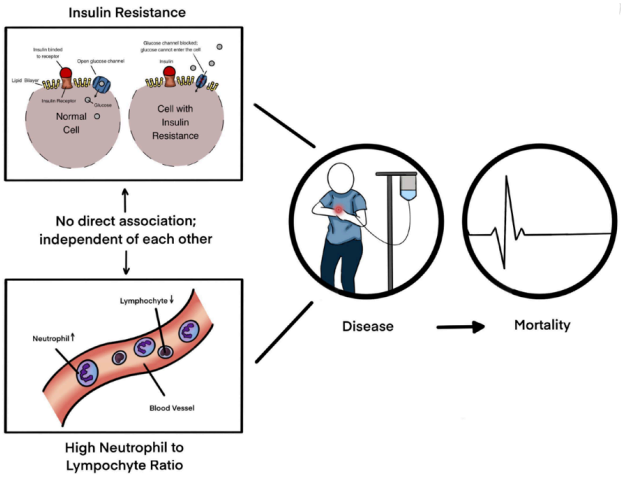

Figure 6: Summary of this study.

Acknowledgements

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References

1. Song, M., B. I. Graubard, C. S. Rabkin, and E. A. Engels. 2021. "Neutrophil-to-lymphocyte ratio and mortality in the United States general population." *Sci Rep* 11 (1):464. DOI: 10.1038/s41598-020-79431-7.
2. Mayadas, Tanya N., Xavier Cullere, and Clifford A. Lowell. 2014. "The Multifaceted Functions of Neutrophils." *Annual Review of Pathology: Mechanisms of Disease* 9 (1):181-218. doi: 10.1146/annurev-pathol-020712-164023.
3. Lou, M., P. Luo, R. Tang, Y. Peng, S. Yu, W. Huang, and L. He. 2015. "Relationship between neutrophil-lymphocyte ratio and insulin resistance in newly diagnosed type 2 diabetes mellitus patients." *BMC Endocr Disord* 15:9. DOI: 10.1186/s12902-015-0002-9.
4. Liu, Yong-Lin, Jie-Kai Lu, Han-Peng Yin, Pei-Shan Xia, Dong-Hai Qiu, Man-Qiu Liang, Jian-Feng Qu, and Yang-Kun Chen. 2020. "High Neutrophil-to-Lymphocyte Ratio Predicts Hemorrhagic Transformation in Acute Ischemic Stroke Patients Treated with Intravenous Thrombolysis." *International Journal of Hypertension* 2020:5980261. Doi: 10.1155/2020/5980261.
5. Guo, X., S. Zhang, Q. Zhang, L. Liu, H. Wu, H. Du, H. Shi, C. Wang, Y. Xia, X. Liu, C. Li, S. Sun, X. Wang, M. Zhou, G. Huang, Q. Jia, H. Zhao, K. Song, and K. Niu. 2015. "Neutrophil: lymphocyte ratio is positively related to type 2 diabetes in a large-scale adult population: a Tianjin Chronic Low-Grade Systemic Inflammation and Health cohort study." *Eur J Endocrinol* 173 (2):217-25. doi: 10.1530/eje-15-0176.
6. Lattanzi, Simona, Francesco Brigo, Eugen Trinka, Claudia Cagnetti, Mario Di Napoli, and Mauro Silvestrini. 2019. "Neutrophil-to-Lymphocyte Ratio in Acute Cerebral Hemorrhage: A System Review." *Translational Stroke Research* 10 (2):137-145. DOI: 10.1007/s12975-018-0649-4.
7. Park, Jin-Sun, Kyoung-Woo Seo, Byoung-Joo Choi, So-Yeon Choi, Myeong-Ho Yoon, Gyo-Seung Hwang, Seung-Jea Tahk, and Joon-Han Shin. 2018. "Importance of prognostic value of neutrophil to lymphocyte ratio in patients with ST-elevation myocardial infarction." *Medicine 97* (48):e13471. DOI: 10.1097/md.0000000000013471.
8. de Jager, Cornelis P. C., Paul T. L. van Wijk, Rejiv B. Mathoera, Jacqueline de Jongh-Leuvenink, Tom van der Poll, and Peter C. Wever. 2010. "Lymphocytopenia and neutrophil-lymphocyte count ratio predict bacteremia better than conventional infection markers in an emergency care unit." *Critical Care* 14 (5): R192. Doi: 10.1186/cc9309.
9. Freeman, A. M., and N. Pennings. 2021. "Insulin Resistance." In *StatPearls.* Treasure Island (FL): StatPearls Publishing
10. McDade, Thomas W. 2012. "Early environments and the ecology of inflammation." *Proceedings of the National Academy of Sciences* 109 (Supplement 2):17281-17288. doi: 10.1073/pnas.1202244109.
11. Shoelson, S. E., J. Lee, and A. B. Goldfine. 2006. "Inflammation and insulin resistance." *J Clin Invest* 116 (7):1793-801. doi: 10.1172/jci29069.
12. Surendar, J., K. Indulekha, V. Mohan, and R. Pradeepa. 2016. "Association of neutrophil-lymphocyte ratio with metabolic syndrome and its components in Asian Indians (CURES-143)." *J Diabetes Complications* 30 (8):1525-1529. doi: 10.1016/j.jdiacomp.2016.08.006.
13. Wallace, T. M., J. C. Levy, and D. R. Matthews. 2004. "Use and abuse of HOMA modeling." *Diabetes Care* 27 (6):1487-95. doi: 10.2337/diacare.27.6.1487.
14. Center for Disease Control and Prevention. "National Health and Nutrition Examination Survey." accessed Nov 25. https://www.cdc.gov/nchs/nhanes/index.htm.
15. Rao SS, Disraeli P, McGregor T. 2004. "Impaired glucose tolerance and impaired fasting glucose." Am Fam Physician. 69 (8):1961-8.
16. SHOBHA S. RAO, M.D., PHILLIP DISRAELI, M.D., and TAMARA MCGREGOR, M.D., University of Texas Southwestern Medical Center at Dallas, Dallas, Texas.
17. Aminzadeh, Z., and E. Parsa. 2011. "Relationship between Age and Peripheral White Blood Cell Count in Patients with Sepsis." *Int J Prev Med* 2 (4):238-42.
18. Rajwani, A., R. M. Cubbon, and S. B. Wheatcroft. 2012. "Cell-specific insulin resistance: implications for atherosclerosis." *Diabetes Metab Res Rev* 28 (8):627-34. doi: 10.1002/dmrr.2336.
19. Martinez, Keilah E., Larry A. Tucker, Bruce W. Bailey, and James D. LeCheminant. 2017. "Expanded Normal Weight Obesity and Insulin Resistance in US Adults of the National Health and Nutrition Examination Survey." *Journal of Diabetes Research* 2017:9502643. Doi: 10.1155/2017/9502643.
20. Shimobayashi, M., V. Albert, B. Woelnerhanssen, I. C. Frei, D. Weissenberger, A. C. Meyer-Gerspach, N. Clement, S. Moes, M. Colombi, J. A. Meier, M. M. Swierczynska, P. Jenö, C. Beglinger, R. Peterli, and M. N. Hall. 2018. "Insulin resistance causes inflammation in adipose tissue." *J Clin Invest* 128 (4):1538-1550. doi: 10.1172/jci96139.
21. Uysal, K. T., S. M. Wiesbrock, M. W. Marino, and G. S. Hotamisligil. 1997. "Protection from obesity-induced insulin resistance in mice lacking TNF-alpha function." *Nature* 389 (6651):610-4. DOI: 10.1038/39335.
22. Talukdar, S., D. Y. Oh, G. Bandyopadhyay, D. Li, J. Xu, J. McNelis, M. Lu, P. Li, Q. Yan, Y. Zhu, J. Ofrecio, M. Lin, M. B. Brenner, and J. M. Olefsky. 2012. "Neutrophils mediate insulin resistance in mice fed a high-fat diet through secreted elastase." *Nat Med* 18 (9):1407-12. DOI: 10.1038/nm.2885.
23. Fu, W., and M. N. Hall. 2020. "Regulation of mTORC2 Signaling." *Genes (Basel)* 11 (9). DOI: 10.3390/genes11091045.

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