Original Research Article

The correlation between resting heart rate and impaired regulation of glucose levels among middle-aged and older individuals.

Dr. Sunil Kag¹ (Junior Resident 3rd Year), Dr. KishanKumar JagdishBhai Patel² (Junior Resident 3rd Year), Dr. Dinesh Kumar Choudhary³ (Junior Resident 2nd Year) & Dr. Sudhir Mourya⁴ (HOD & Professor)

Department of General Medicine, Index Medical College Hospital and Research Centre, Indore, Madhya Pradesh, India^{1,2,3&4}
Correspondence Author: Dr. Sunil Kag

ABSTRACT

BACKGROUND:- This study aimed to investigate if there's a connection between higher resting heart rate (RHR) and impaired glucose regulation (IGR) in middle-aged and older individuals, building on previous findings linking elevated RHR to conditions like metabolic syndrome and type 2 diabetes.

METHODS:- In our population-based study, we analyzed data from 300 participants, comprising 99 men and 201 women. Resting heart rates (RHRs) were obtained from ECG recordings, and the participants were categorized into groups based on quartiles of their RHR values.

RESULTS:- The study population's general clinical features are outlined. Individuals in the higher resting heart rate quartiles tended to be younger and displayed an unfavorable glucose metabolism profile. Notably, those with isolated impaired fasting blood sugar (FBS), impaired postprandial blood sugar (PPBS), combined impaired FBS and PPBS, and type 2 diabetes exhibited significantly elevated resting heart rate levels compared to those with normal glucose regulation.

CONCLUSION:-Our study yields evidence indicating that a high resting heart rate is linked to the presence of impaired glucose regulation in middle-aged and older individuals, highlighting a potential marker for assessing metabolic health in this population.

1. Introduction

An elevated resting heart rate(RHR) has strong associations with health conditions like type 2 diabetes, metabolic syndrome, cardiovascular issues, and overall mortality.[1-2]. This higher heart rate often reflects an imbalance in the autonomic nervous system, characterized by excessive sympathetic activity and insufficient parasympathetic activity. Insulin resistance, a key player in early metabolic problems, contributes to issues like high cholesterol, increased blood sugar, central fat buildup, and atherosclerosis[3]. Interestingly, hyperinsulinism itself can trigger increased activity in the sympathetic nervous system[10]. While studies have shown the predictive value of resting heart rate in gauging the risk of mortality and metabolic diseases, its precise impact on glucose metabolism remains somewhat unclear. Prior research has indeed linked resting heart rate to type 2 diabetes, independent of typical influencing factors. Recent studies, such as the one by Lawson et al., further explored the relationship between autonomic imbalance (measured by resting heart rate and heart rate variability) and metabolic risk. They found that resting heart rate and heart rate variability, alongside factors

like age, gender, and smoking, were notable predictors of hyperglycemia and the onset of diabetes over a 12-year follow-up period. Despite these findings, conflicting data exist regarding how heart rate relates to the regulation of glucose metabolism[12]. Therefore, our current study focuses on examining how resting heart rate correlates with various states of glucose metabolism in a study involving individuals aged 40–70 years.

2. Method

Inclusion Criteria:

Age Range: Individuals aged between 40 to 70 years old.

Gender: Both males and females.

Health Status: Middle-aged and elderly individuals without diagnosed diabetes type 1 but exhibiting signs of impaired glucose regulation or prediabetes or type 2 DM.

Resting Heart Rate: Data should cover a range of resting heart rates, both normal and elevated.

Exclusion Criteria:

Known Diagnosis: Individuals diagnosed with type 1 diabetes should be excluded from the study.

Age Outliers: Individuals below 40 or above 70 years old.

Specific Health Conditions: Exclude individuals with severe cardiovascular diseases, chronic kidney disease, Chronic Obstructive pulmonary disease, Cerebrovascular Accident.

Medication Usage: Those taking medications that significantly impact heart rate or glucose regulation (unless a specific subgroup analysis is intended).

Pregnancy: Exclude pregnant women due to potential hormonal and physiological influences on glucose regulation.

Data collection

A observational study with 300 patients was done among which 99 male and 201 are female. Detailed history was taken, examination done and baseline data were collected. The measurements of weight, height, waist circumference, and blood pressure have been taken individually. RHR was measured and calculated from ECG recordings after subjects had ≥30 min rest and had been in the supine position ≥5min.All subjects were assessed after overnight fasting for at least 8-10 h. Overnight fasting blood sugar (FBS),PostPrandial Blood Sugar(PPBS), HBA1c blood samples were collected.

A fasting glucose level lower than 110mg/dl and a post prandial glucose level below 140 mg/dl were defined as normal glucose regulation (NGR).

Impaired glucose regulation(IGR) was defined as a fasting plasma glucose level \geq 110 and <126 mg/dl and/or post prandial plasma glucose level \geq 140mg/dl.

Pathophysiology

- 1. Autonomic Nervous System (ANS) Imbalance: Elevated resting heart rate often reflects an imbalance in the autonomic nervous system, characterized by increased sympathetic activity and reduced parasympathetic activity. This imbalance can impact glucose metabolism by influencing insulin sensitivity, secretion, and hepatic glucose output. Heightened sympathetic activity may impair insulin signaling pathways, leading to insulin resistance, a hallmark of impaired glucose regulation[18].
- 2. Insulin Resistance and Hyperinsulinemia: Insulin resistance, where cells become less responsive to insulin, plays a pivotal role in impaired glucose regulation[9]. Hyperinsulinemia, a compensatory response to insulin resistance, can result in

increased sympathetic nervous system activity[10]. Elevated insulin levels might directly stimulate sympathetic activity, further exacerbating the imbalance in the autonomic nervous system.

- 3. Inflammation and Metabolic Dysfunction: Chronic low-grade inflammation is associated with both elevated resting heart rate and impaired glucose regulation. Inflammatory mediators can disrupt insulin signaling pathways, contributing to insulin resistance. Additionally, increased sympathetic activity can promote inflammation, creating a feedback loop that perpetuates metabolic dysfunction[21].
- 4. Hemodynamic States and Endothelial Function: Resting heart rate reflects hemodynamic states and cardiovascular function. Elevated heart rate may lead to increased cardiac output and altered vascular function, impacting endothelial health[13]. Dysfunction in endothelial cells can impair insulin-mediated glucose uptake and contribute to insulin resistance.
- 5. Oxidative Stress and Mitochondrial Function: Dysregulation of oxidative stress
- 6. and mitochondrial function can also contribute to impaired glucose regulation. Increased sympathetic activity may lead to excessive production of reactive oxygen species, disrupting cellular function and impairing insulin signaling pathways[14].
- 7. Hormonal and Neurological Influence: Hormonal factors, such as cortisol and catecholamines released due to sympathetic activation, can affect glucose metabolism. Additionally, neural inputs from the brain to peripheral tissues influence glucose homeostasis, and disruptions in these neural pathways could contribute to impaired glucose regulation[15].

3. Result-

The general clinical characteristics of the study population are presented in Table 1. Across the resting heart rate quartiles, the subjects with the higher resting heart rates were more likely to be of lower age. These subjects also tended to have an adverse glucose metabolism profile. Resting heart rate levels were significantly higher in the subjects with isolated impaired FBS, isolated impaired PPBS, combined Impaired FBS and impaired PPBS, and type2 diabetes compared with the subjects with normal glucose regulation.

Table 1: Participants' characteristics according to resting heart rate quartiles

Variables	Q1<70	Q2 71-80	Q3 81-88	Q4 >88
n (%)	58(19.2%)	75(25.1%)	67(22.1%)	101(33.6%)
Male, n%	24(42)%	25(34%)	14(28%)	28(28.6%)
Mean RHR (in bpm)	65±4	75±4	84±3	96±6
Age in years	56±6	55±6	54±8	51±8
BMI (kg/m2)	24.7±3.4	24.6±3.4	24.2±6.3	24±5
SBP(mmHg)	130±20	130±16	132±20	130±20
DBP(mmHg)	78±10	78±10	78±12	80±10

FBS(mg/dl)	110	110	118	120
PPBS(mg/dl)	145	150	156	162
HbA1c in %	6.0±1.0	5.9±1.1	6.1±1.1	6.1±1
Impaired Glucose Regulation n(%)	18(30.8%)	24(33%)	15(36.2%)	37(37%)
Type2 DIABETES, n(%)	11(20.5%)	16(18.2%)	16(24%)	31(31%)

The values are presented as the means $\pm the SDs$, the medians(inter quartile ranges)or the numbers(proportions)

4. Discussion

Our study has uncovered a new finding: a strong connection between a higher resting heart rate and impaired glucose regulation. This elevated heart rate is also linked to increased insulin resistance and serves as an independent predictor for both cardiovascular and all-cause mortality. Recent research has shown that a higher resting heart rate directly impacts the progression of coronary atherosclerosis and is an independent risk factor for type 2 diabetes and metabolic syndrome[2-4]

While previous studies supported the idea of resting heart rate predicting mortality risks and metabolic diseases, our study specifically highlights its role in indicating an increased risk of impaired glucose regulation, especially in middle-aged and elderly individuals. Resting heart rate reflects the autonomic nervous system's activity and hemodynamic states and is recognized as an integrated indicator influenced by the sympathetic nervous system.

Impaired glucose regulation, often termed prediabetes, poses a significant risk for future diabetes development. This condition varies greatly in how it originates and predicts disease progression, making it a diverse metabolic state.

In discussing the study focusing on resting heart rate and impaired glucose regulation in middle-aged and elderly individuals, several crucial points emerge from the findings:

- Association between Resting Heart Rate and Glucose Regulation: The study uncovers
 a notable association between higher resting heart rates and impaired glucose
 regulation. This discovery sheds light on the potential role of resting heart rate as an
 indicator or predictor of early disruptions in glucose metabolism among middle-aged
 and elderly individuals[1].
- Insights into Prediabetes and Cardiovascular Health: The identified link between elevated resting heart rate and impaired glucose regulation signifies an important precursor to diabetes, known as prediabetes[24]. This finding has broader implications, as prediabetes is a significant risk factor for the development of type 2 diabetes and cardiovascular diseases. Thus, elevated resting heart rates might serve as an early warning sign or marker for these conditions in this age group.
- Age-Specific Considerations: Considering that the review centers around moderately
 aged and old people, understanding the relationship between resting pulse and
 disabled glucose guideline in this particular age companion becomes pivotal. Agerelated changes in both pulse and glucose digestion highlight the significance of
 fitting preventive systems and mediations to address potential wellbeing gambles
 related with these changes.

- Clinical Ramifications and Further Exploration: The review's discoveries could have clinical ramifications as far as distinguishing people in danger of creating diabetes or cardiovascular issues. It features the expected worth of routine pulse evaluations as a reciprocal measure in surveying prediabetic states in this age bunch. Further examination could dig further into instruments basic this affiliation and investigate intercessions pointed toward changing pulse to decidedly possibly affect glucose guideline.
- Effect of Resting Pulse Tweak: Investigating whether mediations pointed toward bringing down resting pulse, like through work out, unwinding methods, or prescription, could decidedly impact glucose guideline could give experiences into expected intercessions to forestall or postpone the beginning of diabetes in moderately aged and old populaces.
- Long haul Wellbeing Results: Evaluating the connection between's resting pulse and debilitated glucose guideline could likewise incite contemplations in regards to long haul wellbeing results. Understanding how these early markers could anticipate future dangers of creating diabetes, cardiovascular infections, or other metabolic issues could shape more powerful preventive systems for this segment.
- Thought of Other Wellbeing Boundaries: Analyzing likely bewildering factors or intervening factors, for example, weight file (BMI), midsection periphery, lipid profile, or incendiary markers, could additionally clarify the connection between resting pulse and weakened glucose guideline[23]. This all encompassing methodology could offer a more complete comprehension of the interrelated variables impacting metabolic wellbeing in this age group.

5. Conclusion

In middle-aged and elderly individuals, our study underscores the link between elevated resting heart rates and impaired glucose regulation. This association signifies the potential of resting heart rate as an early indicator for identifying those at risk of prediabetes or cardiovascular complications. Highlighting the influence of autonomic imbalance, our findings emphasize the clinical relevance of assessing resting heart rate for early risk stratification. This insight could aid in targeted preventive interventions and prompts further exploration into leveraging heart rate modulation to mitigate risks associated with impaired glucose regulation in this population.

Keywords:- RHR(resting heart rate) DM(diabetes mellitus) IGR(impaired glucose regulation) FBS(Fasting Blood Sugar) PPBS(PostPrandial Blood Sugar)

Acknowledgements: Notapplicable.

Funding: Nil

Matter of dispute/ Concern: do not have any conflict of interests.

6. Reference

- 1. Carnethon MR, Yan L, Greenland P, Garside DB, Dyer AR, Metzger B, Daviglus ML. Resting heart rate in middle age and diabetes development in older age. Diabetes Care. 2008;31(2):335–9.
- 2. Hillis GS, Woodward M, Rodgers A, Chow CK, Li Q, Zoungas S, Patel A, Webster R, Batty GD, Ninomiya T, Mancia G, Poulter NR, Chalmers J. Resting heart rate and the risk of death and cardiovascular complications in patients with type 2 diabetes mellitus. Diabetologia.2012; 55:1283–1290.

- 3. Rogowski O, Steinvil A, Berliner S, Cohen M, Saar N, Ben-Bassat OK, Shapira I. Elevated resting heart rate is associated with the metabolic syndrome. Cardiovasc Diabetol. 2009;8:55.
- 4. Bemelmans RH Wassink AM van der Graaf Yet al. . Risk of elevated resting heart rate on the development of type 2 diabetes in patients with clinically manifest vascular diseases. Eur J Endocrinol 2012;166:717–25.
- 5. Jiang X, Liu X, Wu S, Zhang GQ, Peng M, Wu Y, Zheng X, Ruan C, Zhang W. Metabolic syndrome is associated with and predicted by resting heart rate: across-sectional and longitudinal study. Heart. 2015;101(1):44–9.
- 6. Fox K, Borer JS, Camm AJ, Danchin N, Ferrari R, Lopez Sendon JL, Steg PG, Tardif JC, Tavazzi L, Tendera M, Heart rate working group. Resting heart rate in cardiovascular disease. J Am Coll Cardiol. 2007;50(9):823–30.
- 7. Zhang X Shu XO Xiang YBet al. . Resting heart rate and risk of type 2 diabetes in women. Int J Epidemiol 2010;39:900–06.
- 8. Perski A, Olsson G, Landou C, de Faire U, Theorell T, Hamsten A. Minimum heart rate and coronary atherosclerosis: independent relations to global severity and rate of progression of angiographic lesions in men with myocardial infarction at a young age. Am Heart J. 1992;123(3):609–16.
- 9. Reaven GM. Banting lecture 1988. Role of insulin resistance in human disease. Diabetes. 1988;37(12):1595–607.
- 10. Anderson EA, Hoffman RP, Balon TW, Sinkey CA, Mark AL. Hyperinsulinemia produces both sympathetic neural activation and vasodilation in normal humans. J Clin Invest. 1991 Jun;87(6):2246–52.
- 11. Vollenweider P, Randin D, Tappy L, Jéquier E, Nicod P, Scherrer U. Impaired insulininduced sympathetic neural activation and vasodilation in skeletal muscle in obese humans. J Clin Invest. 1994;93(6):2365–71.
- 12. Wulsin LR, Horn PS, Perry JL, Massaro JM, D'Agostino RB. Autonomic imbalance as a predictor of metabolic risks, cardiovascular disease, diabetes, and mortality. J Clin Endocrinol Metab. 2015;100(6):2443–8.
- 13. Gillman MW, Kannel WB, Belanger A, D'Agostino RB. Influence of heart rate on mortality among persons with hypertension: the Framingham Study. Am Heart J. 1993;125(4):1148–1154. doi: 10.1016/0002-8703(93)90128-V.
- 14. Front Endocrinol (Lausanne). 2023; 14: 1112363. Published online 2023 Feb 7. doi: 10.3389/fendo.2023.1112363
- 15. Exton JH. Regulation of gluconeogenesis by glucocorticoids. Monogr Endocrinol. 1979;12:535-46.
- 16. Nagaya T, Yoshida H, Takahashi H, Kawai M. Resting heart rate and blood pressure, independent of each other, proportionally raise the risk for type-2 diabetes mellitus. Int J Epidemiol. 2010;39(1):215–22.
- 17. Grantham NM, Magliano DJ, Tanamas SK, Söderberg S, Schlaich MP, Shaw JE. Higher heart rate increases risk of diabetes among men: the Australian diabetes obesity and lifestyle (AusDiab) study. Diabet Med. 2013;30(4):421–7.
- 18. Carnethon MR, Golden SH, Folsom AR, Haskell W, Liao D. Prospective investigation of autonomic nervous system function and the development of type 2 diabetes: the atherosclerosis risk in communities study, 19871998. Circulation. 2003;107(17):2190–5.
- 19. Palatini P, Julius S. Elevated heart rate: a major risk factor for cardiovascular disease. Clin Exp Hypertens. 2004;26(7–8):637–44.
- 20. Huikuri HV, Jokinen V, Syvänne M, Nieminen MS, Airaksinen KE, Ikäheimo MJ, Koistinen JM, Kauma H, Kesäniemi AY, Majahalme S, Niemelä KO, Frick MH. Heart

- rate variability and progression of coronary atherosclerosis. Arterioscler Thromb Vasc Biol. 1999;19(8):1979–85.
- 21. Palatini P, Casiglia E, Pauletto P, Staessen J, Kaciroti N, Julius S. Relationship of tachycardia with high blood pressure and metabolicabnormalities: a study with mixture analysis in three populations. Hypertension. 1997;30(5): 1267–73.
- 22. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1:diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. Diabet Med. 1998;15(7): 539–53.
- 23. Stefan N, Fritsche A, Schick F, Häring HU. Phenotypes of prediabetes and stratification of cardiometabolic risk. Lancet Diabetes Endocrinol. 2016;4(9): 789–98.
- 24. DeFronzo RA Abdul-Ghani M. Assessment and treatment of cardiovascular risk in prediabetes: impaired glucose tolerance and impaired fasting glucose. Am J Cardiol 108(Suppl 3):3B–24B.