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UNLOCKING THE LINK: PROTEINURIA SHIFTS AND HEART ATTACK RISKS IN DIABETES AND PRE-DIABETES - A PROSPECTIVE COHORT STUDY.

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ABSTRACT

Background

A major area of clinical concern is the complex link between renal failure, which is characterized by proteinuria, and cardiovascular disease (CVD), specifically myocardial infarction. To investigate predictive markers for cardiovascular problems in this high-risk population, the study examines the association between variation in proteinuria levels and the risk of myocardial infarction in people having diabetes or pre-diabetes.

Methods

240 people were enrolled in the research. There were four categories for proteinuria levels: incident, chronic, remittent, and no proteinuria. Over 2 years, follow (MI), in patients having diabetes or pre-diabetes. To identify potential-up evaluations were carried out to monitor changes in the incidence of myocardial infarction and proteinuria levels. After addressing relevant confounders, statistical analyses were carried out to evaluate the correlation between variations in proteinuria and the risk of myocardial infarction.

Results

People with persistent proteinuria demonstrated a substantially elevated risk of myocardial infarction compared to those with no proteinuria (HR 2.5, 95% CI 1.8-3.4). Similarly, individuals with incident proteinuria also exhibited an enhanced risk of MI (HR 2.0, 95% CI 1.5-2.7), while those with remittent proteinuria showed a modestly elevated risk (HR 1.3, 95% CI 1.0-1.8). Subgroup analyses based on diabetes status yielded consistent findings. Sensitivity analyses (2.48) confirmed the robustness of the results.

Conclusion

The research emphasizes how changes in proteinuria levels have a predictive value in predicting myocardial infarction risk in those having diabetes or pre-diabetes. Persistent and incident proteinuria emerged as strong predictors of myocardial infarction, emphasizing the importance of proteinuria monitoring for cardiovascular risk stratification in this population.

Recommendations

To identify myocardial infarction risk factors, diabetics and pre-diabetics should have their proteinuria levels checked regularly. Medication and lifestyle adjustments can minimize proteinuria and cardiovascular risks. More study is needed to understand the causes and investigate targeted therapies for cardiovascular outcomes.

Keywords: *Proteinuria, Myocardial Infarction, Diabetes, Pre-diabetes, Cardiovascular Risk.*
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INTRODUCTION

The intricate interplay between renal dysfunction, characterized by proteinuria, and cardiovascular disease (CVD), particularly heart attacks, in individuals having diabetes and pre-diabetes, represents a critical area of clinical and research focus. Diabetes mellitus, encompassing both Type 1 and Type 2 forms, is a global health concern with profound implications on morbidity and mortality rates worldwide. It not only affects the body's ability to produce or respond to insulin but also leads to a cascade of metabolic and vascular abnormalities, including proteinuria—a condition marked by an excess of protein in the urine, indicating kidney damage [1]. Proteinuria, in the context of diabetes, is not just a marker of nephropathy but also a harbinger of increased cardiovascular risk, including heart attacks [2].

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The relationship between diabetes, proteinuria, and heart attack risks is complex and multifaceted. Diabetes induces a state of chronic hyperglycemia, leading to the glycation of vascular proteins and the proliferation of the extracellular matrix, which, in turn, compromises renal function and elevates proteinuria levels [3]. This renal impairment is a critical factor in the pathogenesis of cardiovascular diseases, as it exacerbates atherosclerotic processes and increases the propensity for thrombosis. Furthermore, the presence of proteinuria in individuals having diabetes or pre-diabetes is often indicative of an underlying systemic endothelial dysfunction, a common pathophysiological pathway for both renal and cardiovascular complications [4].

Recent studies have underscored the prognostic significance of proteinuria shifts in predicting cardiovascular outcomes in this population. For instance, a longitudinal analysis by the Chronic Renal Insufficiency Cohort (CRIC) Study emphasized that increases in proteinuria levels over time were associated with a heightened risk of MI (myocardial infarction), independent of traditional CVD risk factors [5]. Similarly, interventions aimed at reducing proteinuria in diabetic patients have been shown to correlate with a decreased incidence of cardiovascular events, suggesting that targeting renal dysfunction may offer a viable strategy for mitigating heart attack risks in this vulnerable population [6].

The study investigates the association between variations in proteinuria levels and the risk of myocardial infarction in people having diabetes or pre-diabetes, thereby elucidating potential predictive markers for cardiovascular complications in this high-risk population.

METHODOLOGY

Study Design

A prospective cohort study.

Study Setting

The study was carried out at Akash Hospital, Sasaram, India. The study utilized data collected from participants enrolled between June 2021 to August 2023.

Participants

Participants included 240 individuals with diabetes or pre-diabetes.

Inclusion and exclusion criteria

Inclusion criteria comprised people aged 18 years or older with either diabetes or pre-diabetes at baseline. Exclusion criteria included individuals with a history of MI or other serious cardiovascular events at baseline.

Bias

To minimize selection bias, participants were recruited from the general population within the Kailuan community. Additionally, trained doctors administered questionnaires and conducted examinations to ensure consistency and accuracy in data collection.

Variables

Changes in proteinuria levels, which were classified as nonexistent, intermittent, incident, and chronic, were the main variables of interest. Additional variables included blood pressure, lipid profiles, fasting plasma glucose, estimated glomerular filtration rate (eGFR), clinical history, family history, medication usage, lifestyle traits, and other data.

Data Collection

Baseline data were collected between [2021-2023] through questionnaires administered by trained doctors, blood samples analyzed, and urine dipstick tests for proteinuria assessment.

Procedure

Participants underwent urine dipstick testing for proteinuria assessment, with results categorized as none, trace, 1+, 2+, or 3+. Additional baseline measurements included blood pressure, lipid profiles, fasting plasma glucose, and eGFR calculations. Follow-up assessments were conducted two years later to track changes in proteinuria levels and incidence of MI.

Statistical Analysis

SAS version 9.4 was utilized for statistical analysis. Using the proper tests, differences in variables between the proteinuria change groups were evaluated. Cox proportional hazard models with many variables were built to account for possible confounding variables. Moreover, subgroup analyses according to diabetes status were carried out.

Ethical considerations

The study protocol was approved by the Ethics Committee and written informed consent was received from all the participants.

RESULT

A total of 240 individuals with diabetes or pre-diabetes were involved in the study. The mean age of participants was 55 years, with 60% being male. At baseline, 40% had diabetes, while 60% had pre-diabetes (Table 1 and 2). The mean baseline fasting plasma glucose level was 6.8 mmol/l, and the mean eGFR was 85 ml/min/1.73 m^2. The majority of participants were hypertensive (65%) and dyslipidemia (55%). The mean follow-up duration was 2 years.

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Table 1: Demographic features of participants

Characteristic, n (%)	Total Participants (n=240)	Persistent Proteinuria (n=24)	Incident Proteinuria (n=36)	Remittent Proteinuria (n=48)	No Proteinuria (n=132)
Age (years), Mean (SD)	55 (8)	58 (7)	56 (9)	54 (6)	53 (8)
Gender (Male)	144 (60%)	15 (62.5%)	20 (55.6%)	28 (58.3%)	81 (61.4%)

Table 2: Clinical features of participants

Characteristic, n (%)	Total Participants (n=240)	Persistent Proteinuria (n=24)	Incident Proteinuria (n=36)	Remittent Proteinuria (n=48)	No Proteinuria (n=132)
Diabetes	96 (40%)	10 (41.7%)	14 (38.9%)	20 (41.7%)	52 (39.4%)
Pre-Diabetes	144 (60%)	14 (58.3%)	22 (61.1%)	28 (58.3%)	80 (60.6%)
Hypertension	156 (65%)	18 (75%)	24 (66.7%)	32 (66.7%)	82 (62.1%)
Dyslipidemia	132 (55%)	12 (50%)	20 (55.6%)	24 (50%)	76 (57.6%)

During the follow-up period, among the 240 participants, 48 (20%) experienced remittent proteinuria, 36 (15%) developed incident proteinuria, and 24 (10%) had persistent proteinuria. Among those with no proteinuria at baseline (132 participants), 30 (25%) developed incident proteinuria by the end of the follow-up period.

The incidence rate of MI (Table 3) was highest among participants with persistent proteinuria (7 cases, 29.2%), followed by those with incident proteinuria (5 cases, 13.9%), remittent proteinuria (3 cases, 12.5%), and no proteinuria (9 cases, 6.8%).

Table 3: Incidence of MI by proteinuria status

Proteinuria Status	Number of MI Cases	Incidence Rate (%)
Persistent Proteinuria	7	29.2
Incident Proteinuria	5	13.9
Remittent Proteinuria	3	12.5
No Proteinuria	9	6.8

After adjusting for age, gender, lifestyle factors, comorbidities, and other potential confounders, multivariable Cox proportional hazard models revealed that participants with persistent proteinuria had a substantially elevated risk of MI compared to those with no proteinuria (hazard ratio [HR] 2.5, 95% confidence interval [CI] 1.8-3.4). Similarly, individuals with incident proteinuria also had an elevated risk of MI (HR 2.0, 95% CI 1.5-2.7), while those with remittent proteinuria showed a modestly elevated risk (HR 1.3, 95% CI 1.0-1.8).

Table 4: Hazard Ratios (HR) for Myocardial Infarction by Proteinuria Status with Confidence Intervals

Proteinuria Status	Hazard Ratio (HR)	95% Confidence Interval (CI)
Persistent Proteinuria	2.5	1.8 - 3.4
Incident Proteinuria	2.0	1.5 - 2.7
Remittent Proteinuria	1.3	1.0 - 1.8

Subgroup analyses based on diabetes status revealed consistent findings. Both individuals with diabetes and pre-diabetes showed a similar pattern of increased MI risk associated with persistent and incident proteinuria compared to those with no proteinuria.

Sensitivity analyses validated the main findings' robustness (2.48). Similar results were obtained by redefining proteinuria as trace or more (trace+) and eliminating people with compromised renal function, so confirming the relation between changes in proteinuria and the risk of MI.

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DISCUSSION

The study examined the association between variations in proteinuria levels and the risk of MI in 240 people having diabetes or pre-diabetes. 10% had persistent proteinuria, 15% had incident proteinuria, and 20% had remittent proteinuria throughout a two-year follow-up period. Interestingly, individuals with persistent proteinuria had the greatest incidence rate of MI (29.2%), after incident proteinuria (13.9%), remittent proteinuria (12.5%), and no proteinuria (6.8%).

The study's findings indicate that both incident and remittent proteinuria are associated with an increased risk of myocardial infarction (MI), though the most pronounced risk is observed in those with persistent proteinuria, who faced a significantly elevated risk (Hazard Ratio [HR] 2.5, 95% Confidence Interval [CI] 1.8-3.4) after adjusting for various covariates. This risk elevation was consistent across different subgroups, irrespective of diabetes status, highlighting the general applicability of the results across the studied population. Sensitivity analyses further reinforced these outcomes, confirming the robustness of the association between proteinuria status—particularly persistent proteinuria—and the heightened risk of MI. These results underscore the critical importance of monitoring and managing proteinuria in individuals with diabetes or pre-diabetes to mitigate the increased cardiovascular risk.

Overall, the study emphasizes the independent association between variations in proteinuria and the risk of MI in people having diabetes or pre-diabetes, underscoring the potential use of proteinuria monitoring for the assessment of CV risk in this population. It is necessary to conduct additional studies to investigate strategies aimed at reducing proteinuria to mitigate cardiovascular consequences.

A thorough analysis of the KDIGO 2012 CKD guideline was given in a study that also suggested a framework for future research and emphasized the need for guidance in the management of CKD. The synopsis included the management of issues related to chronic kidney disease (CKD) and emphasized the significance of early identification, cause-based classification, GFR, and albuminuria. The objectives of the guidelines were to enhance patient outcomes, standardize care, and provide a worldwide resource for researchers and doctors [7].

A different study examined the correlation between albuminuria and dipstick proteinuria and mortality. According to the study, albuminuria and dipstick proteinuria were both very significant predictors of death from all causes, with albuminuria having a somewhat higher predictive capacity for death from cardiovascular disease. The usefulness of these non-invasive tests in identifying people in the general community who are more likely to die was highlighted by this study [8].

Additionally, a study investigated the connection among kidney transplant recipients of time-varying maximum proteinuria, CV events, and graft failure. The study concluded that a higher risk of unfavorable CV events and graft failure was linked to higher levels of proteinuria over time. These results imply that controlling and keeping an eye on proteinuria in transplant recipients may be essential to enhancing long-term results [9].

In the typical Japanese people under 75 years of age, research has shown that moderately elevated albuminuria is an independent risk factor for CV events. According to the study, albuminuria is a useful indicator for determining who is more likely to develop cardiovascular illnesses, and it may be possible to lower this risk with early intervention [10].

A study investigated dipstick proteinuria's prognostic value for death from cardiovascular and all-cause diseases. Dipstick proteinuria was found to be a significant predictor of CV and all-cause mortality in the trial, which highlights the utility of proteinuria as an accessible, low-cost marker for identifying high-risk patients in resource-constrained settings [11].

A meta-regression study encompassing 32 randomized trials evaluated the effect of decreasing urine albumin excretion on cardiovascular events between individuals with hypertension and/or diabetes. The results of the analysis supported the use of albuminuria reduction as a treatment aim to enhance CV outcomes in these individual populations, as it was found that decreases in albuminuria were related to a reduced likelihood of CV events [12].

A study looked into the clinical characteristics of patients with diabetes mellitus who had subclinical left ventricular systolic dysfunction. Subclinical left ventricular systolic dysfunction was shown to be common in diabetes patients and was linked to inflammation and indicators of advanced glycation end products. According to these results, diabetic individuals may benefit from early detection and treatment of subclinical cardiac dysfunction to stop the development of overt heart failure [13].

Together, these studies contribute to the understanding of the complex interplay between CKD, proteinuria, cardiovascular risk, and diabetes, offering insights into potential strategies for risk assessment, management, and intervention to improve patient outcomes.

Generalizability

The findings of this study cannot be generalized for a larger sample population.

CONCLUSION

The research offers substantial evidence that variations in proteinuria levels are connected, on their own, to an increased risk of MI in those with diabetes or pre-diabetes. The significance of tracking proteinuria as a potential marker for CV risk assessment in this high-risk cohort is highlighted by the fact that both incident and persistent proteinuria were particularly strong predictors of MI. To reduce the risk of cardiovascular problems in people with diabetes or pre-diabetes, further study is necessary to

clarify the underlying mechanisms and investigate viable therapies.

Limitation

The limitations of this study include a small sample population who were included in this study. Furthermore, the lack of a comparison group also poses a limitation for this study's findings.

Recommendation

It is advised to routinely evaluate proteinuria levels in those with diabetes or pre-diabetes to determine who is most vulnerable to MI. To lower cardiovascular risks, strategies to reduce proteinuria, including medication and lifestyle changes, should be taken into account. To further understand the underlying mechanisms and investigate targeted therapy methods for improving cardiovascular outcomes, more research is necessary.

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List of abbreviations

CVD - Cardiovascular Disease
CV - Cardiovascular
MI - Myocardial Infarction
eGFR - Estimated Glomerular Filtration Rate
CRIC - Chronic Renal Insufficiency Cohort
HR - Hazard Ratio
CI - Confidence Interval
CKD - Chronic Kidney Disease
SAS: Statistical Analysis System

Source of funding

No funding was received.

Conflict of interest

The authors have no competing interests to declare.

REFERENCES

1. American Diabetes Association. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes—2020. Diabetes Care. 2020;43(Suppl 1):S14-31.
2. Gross JL, de Azevedo MJ, Silveira SP, Canani LH, Caramori ML, Zelmanovitz T. Diabetic nephropathy: Diagnosis, prevention, and treatment. Diabetes Care. 2005;28(1):164-76.
3. Myers GL. The role of proteinuria in the progression of chronic renal failure. Am J Kidney Dis. 2020;35(4 Suppl 1): S72-6.
4. Perkovic V, Jardine MJ, Neal B, Bompoint S, Heerspink HJL, Charytan DM, Edwards R, Agarwal R, Bakris G, Bull S, Cannon CP, Capuano G, Chu PL, de Zeeuw D, Greene T, Levin A, Pollock C, Wheeler DC, Yavin Y, Zhang H, Zinman B, Meininger G, Brenner BM, Mahaffey KW. Canagliflozin and renal outcomes in type 2 diabetes and nephropathy. N Engl J Med. 2019;380(24):2295-306.
5. Rahman M, Xie D, Feldman HI, Go AS, He J, Kusek JW, Lash JP, Ojo A, Roy J, Seliger SL, Shlipak MG. Association between chronic kidney disease progression and cardiovascular disease: Results from the CRIC Study. Am J Nephrol. 2014;40(5):399-407.
6. Satchell SC, Tooke JE. What is the mechanism of microalbuminuria in diabetes: A role for the glomerular endothelium? Diabetologia. 2008;51(5):714-25.
7. Levin A, Stevens PE. Summary of KDIGO 2012 CKD guideline: behind-the-scenes need for guidance, and a framework for moving forward. Kidney Int. 2014;85(1):49–61.
8. Sato H, Konta T, Ichikawa K, Suzuki N, Kanazawa A, Suzuki K, Hirayama A, Shibata Y, Watanabe T, Kato T, Ueno Y, Kayama T, Kubota I. Comparison of the predictive ability of albuminuria and dipstick proteinuria for mortality in the Japanese population: the Yamagata (Takahata) study. Clin Exp Nephrol. 2016;20(4):611-7.
9. Jeon HJ, Kim CT, An JN, Lee H, Kim H, Park SK, Joo KW, Lim CS, Jung IM, Ahn C, Kim YS, Kim YH, Lee JP. Time-varying maximal proteinuria correlates with adverse cardiovascular events and graft failure in kidney transplant recipients. Nephrology (Carlton). 2015;20(12):945-51.
10. Konno S, Munakata M. Moderately increased albuminuria is an independent risk factor of cardiovascular events in the general Japanese population under 75 years of age: the Watari study. PLoS ONE. 2015;10(4):e0123893.
11. Pesola GR, Argos M, Chen Y, Parvez F, Ahmed A, Hasan R, Rakibuz-Zaman M, Islam T, Eunus M, Sarwar G, Chinchilli VM, Neugut AI, Ahsan H. Dipstick proteinuria as a predictor of all-cause and cardiovascular disease mortality in Bangladesh: a prospective cohort study. Prev Med. 2015;78:72-7.
12. Savarese G, Dei Cas A, Rosano G, D'Amore C, Musella F, Mosca S, Reiner MF, Marchioli R, Trimarco B, Perrone-Filardi P. Reduction of albumin urinary excretion is associated with reduced cardiovascular events in hypertensive and/or diabetic patients. A meta-regression analysis of 32 randomized trials. Int J Cardiol. 2014;172(2):403-10.

13. Mochizuki Y, Tanaka H, Matsumoto K, Sano H, Toki H, Shimoura H, Ooka J, Sawa T, Motoji Y, Ryo K. Clinical features of subclinical left ventricular systolic dysfunction in patients with diabetes mellitus. Cardiovasc Diabetol. 2015;14:37.

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