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Association of Serum Galectin-3 with Glycemic Control and Diabetic Complications among Patients with Type 2 Diabetes Mellitus in the Kumaun Region of Uttarakhand

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Abstract: ***Background**: Type 2 diabetes mellitus (T2DM) is a rapidly growing public health concern worldwide and is associated with significant microvascular and macrovascular complications. Chronic low-grade inflammation and tissue fibrosis play central roles in the pathogenesis of diabetes and its long-term complications. Galectin-3, a β-galactoside-binding lectin secreted predominantly by activated macrophages, has emerged as a promising biomarker involved in inflammation, fibrosis, insulin resistance, endothelial dysfunction, and cardiovascular remodelling. Although increasing evidence suggests that elevated serum Galectin-3 levels are associated with poor glycaemic control and diabetic complications, data from the Himalayan region of northern India remain limited. **Objectives**: To evaluate the association between serum Galectin-3 levels, glycaemic control, and diabetic complications among patients with Type 2 diabetes mellitus in the Kumaun region of Uttarakhand. **Materials and Methods**: This cross-sectional study included 150 adults with Type 2 diabetes mellitus attending a tertiary care hospital in the Kumaun region. Demographic variables, anthropometric measurements, biochemical investigations, serum Galectin-3 concentrations, and the presence of diabetic complications were included in the study. Statistical analyses were designed to include descriptive statistics, independent t-test, Chi-square test, Pearson correlation analysis, multivariable logistic regression, and receiver operating characteristic (ROC) curve analysis. **Results**: Mean serum Galectin-3 concentrations were higher among participants with poor glycaemic control (HbA1c ≥8%) than among those with better glycaemic control. Higher Galectin-3 levels were also observed in participants with diabetic nephropathy, retinopathy, and peripheral neuropathy. Correlation analyses demonstrated positive associations between Galectin-3 and HbA1c, duration of diabetes, serum creatinine, and urine albumin-creatinine ratio, while a negative association was observed with estimated glomerular filtration rate (eGFR). Multivariable logistic regression in the analysis suggested that elevated Galectin-3 remained independently associated with diabetic nephropathy after adjustment for conventional risk factors. **Conclusion**: This analysis illustrates how serum Galectin-3 may serve as a potential biomarker for identifying patients at increased risk of poor glycaemic control and diabetes-related complications. Well-designed prospective studies involving patients from the Kumaun region are required to validate these observations.*

Keywords: Biomarker, Diabetic nephropathy, Diabetic neuropathy, Diabetic retinopathy, Galectin-3, Glycaemic control, Type 2 diabetes mellitus, Uttarakhand

1. Introduction

Type 2 diabetes mellitus (T2DM) is one of the most important non-communicable diseases affecting global health. The prevalence of diabetes has increased steadily over recent decades because of rapid urbanization, sedentary lifestyles, unhealthy dietary practices, obesity, and population ageing.(1) India is among the countries with the largest number of individuals living with diabetes, and the disease has become a major contributor to morbidity, mortality, and healthcare expenditure.(2) Persistent hyperglycaemia causes structural and functional alterations in multiple organs through complex biochemical pathways involving oxidative stress, chronic inflammation, advanced glycation end-products, endothelial dysfunction, and tissue fibrosis, ultimately leading to diabetic nephropathy, retinopathy, peripheral neuropathy, cardiovascular disease, and cerebrovascular complications. (3-4)

Despite significant advances in diabetes management, conventional biochemical markers such as fasting plasma glucose and glycated haemoglobin (HbA1c) primarily reflect glycaemic status and provide limited information regarding ongoing inflammatory activity or tissue fibrosis.(5) Consequently, there has been increasing interest in identifying circulating biomarkers that may improve risk stratification, facilitate earlier detection of diabetic complications, and assist in monitoring disease progression.(6) Among the emerging biomarkers, Galectin-3 has gained considerable attention because of its diverse biological functions and its established role in inflammatory and fibrotic disorders. (7)

Galectin-3 is a member of the lectin family that binds β-galactoside-containing glycoconjugates. It is expressed in activated macrophages, neutrophils, fibroblasts, endothelial cells, adipocytes, and several epithelial tissues. (8) Physiologically, Galectin-3 participates in cell adhesion, apoptosis, immune regulation, angiogenesis, wound healing, and extracellular matrix remodelling. Under pathological conditions, persistent activation of Galectin-3 promotes macrophage recruitment, fibroblast proliferation, collagen deposition, and chronic inflammatory responses. (9) These processes contribute to progressive tissue fibrosis in the kidneys, heart, liver, and vasculature, making Galectin-3 a promising biomarker in several chronic diseases.

Experimental and clinical studies suggest that Galectin-3 may play an important role in insulin resistance and metabolic dysfunction. Chronic low-grade inflammation within adipose tissue contributes to impaired insulin signalling, and activated macrophages release Galectin-3 as part of the inflammatory cascade. (10) Increased circulating Galectin-3 concentrations have been associated with obesity, metabolic syndrome, impaired glucose tolerance, and Type 2 diabetes mellitus. Experimental studies further indicate that Galectin-3 may directly interfere with insulin receptor signalling pathways, thereby exacerbating insulin resistance and contributing to progressive β-cell dysfunction. (11)

The relationship between Galectin-3 and diabetic nephropathy has been investigated extensively. (12) Chronic hyperglycaemia activates inflammatory and profibrotic pathways within the renal parenchyma, resulting in mesangial expansion, glomerulosclerosis, tubulointerstitial fibrosis, and progressive decline in renal function. Elevated serum Galectin-3 concentrations have been associated with albuminuria, reduced estimated glomerular filtration rate (eGFR), and progression of chronic kidney disease. (13) Since renal fibrosis represents a major determinant of irreversible kidney damage, Galectin-3 has emerged as a potential indicator of early renal involvement among patients with diabetes. (14-15)

Similarly, Galectin-3 has been implicated in the development of diabetic retinopathy.(16) Retinal microvascular injury induced by prolonged hyperglycaemia is accompanied by oxidative stress, endothelial dysfunction, inflammatory cell recruitment, and increased vascular permeability.(17) Experimental evidence suggests that Galectin-3 contributes to retinal inflammation and pathological angiogenesis, indicating a possible role in the progression from non-proliferative to proliferative diabetic retinopathy. Elevated circulating Galectin-3 levels have also been reported among individuals with advanced retinal disease, although the strength of this association varies across studies. (18)

Peripheral neuropathy remains one of the most common chronic complications of diabetes and substantially affects quality of life through pain, sensory impairment, gait disturbances, and foot ulceration.(19) Persistent inflammation and microvascular dysfunction are believed to contribute to nerve injury, and Galectin-3 may participate in these mechanisms by promoting macrophage activation and chronic inflammatory signalling.(20) Although available evidence is less extensive than that for diabetic nephropathy, several clinical studies have reported higher Galectin-3 concentrations among patients with diabetic neuropathy.(21)

Cardiovascular disease represents the leading cause of mortality in individuals with Type 2 diabetes mellitus. (22) Galectin-3 is already an established biomarker in heart failure because of its role in myocardial inflammation and fibrosis. (23) Elevated concentrations have been associated with left ventricular remodelling, atherosclerotic plaque instability, endothelial dysfunction, and adverse cardiovascular outcomes. These observations suggest that Galectin-3 may provide complementary prognostic information beyond traditional cardiovascular risk factors in patients with diabetes. (24)

The Kumaun region of Uttarakhand possesses unique geographical and demographic characteristics that may influence the burden of diabetes and its complications. Mountainous terrain, changing dietary habits, increasing urbanization, and disparities in access to specialised healthcare may contribute to delayed diagnosis and inadequate control of chronic diseases. Limited published data are available regarding inflammatory biomarkers such as Galectin-3 among diabetic populations from this region. Understanding the potential association between Galectin-3 and diabetes-related complications could facilitate future regional research and contribute to improved risk assessment strategies. (25)

The present study illustrates the potential clinical significance of Galectin-3 as an emerging biomarker in Type 2 diabetes mellitus. The findings can be adapted for future health planning in the Kumaun region of Uttarakhand.

2. Objectives

The primary objective of this study was to evaluate the association between serum Galectin-3 concentrations and glycaemic control among patients with Type 2 diabetes mellitus (T2DM) in the Kumaun region of Uttarakhand. The secondary objectives were to compare serum Galectin-3 levels between patients with good and poor glycaemic control, assess its association with diabetic nephropathy, retinopathy, and peripheral neuropathy, determine its correlation with clinical and biochemical variables including HbA1c, fasting blood glucose, serum creatinine, estimated glomerular filtration rate (eGFR), urine albumin-creatinine ratio (UACR), and duration of diabetes, and evaluate its diagnostic performance for diabetic nephropathy using receiver operating characteristic (ROC) curve analysis.

3. Materials and Methods

This is a hospital-based cross-sectional observational study conducted in the Department of Biochemistry in collaboration with the Department of Medicine at Dr. Susheela Tiwari Government Hospital, Haldwani in the Kumaun region of Uttarakhand, India. The study was conducted over a period of twelve months from April 2025 to March 2026 after obtaining approval from the Institutional Ethics Committee, GBCM RBBSU. Written informed consent was obtained from all participants.

The duration included participant recruitment, clinical evaluation, laboratory investigations, data compilation, statistical analysis, and manuscript preparation.

The study population consisted of adult patients previously diagnosed with Type 2 diabetes mellitus attending the outpatient and inpatient departments of the participating institution. A sample size of 150 patients was taken. Consecutive sampling was done, whereby all eligible patients presenting during the study period were enrolled until the desired sample size was achieved.

Adults aged 30 years or older with previously diagnosed Type 2 diabetes mellitus according to the American Diabetes

Association diagnostic criteria were considered eligible for inclusion. (26) Participants were required to have a minimum disease duration of one year and to be capable of providing written informed consent in the study. Patients with Type 1 diabetes mellitus, gestational diabetes, acute diabetic emergencies including diabetic ketoacidosis or hyperosmolar hyperglycaemic state, active infection, chronic inflammatory or autoimmune disorders, chronic liver disease, malignancy, end-stage renal disease requiring dialysis, pregnancy, or those receiving corticosteroids or immunosuppressive therapy were assumed to be excluded to minimise potential confounding effects on circulating Galectin-3 concentrations.

All enrolled participants underwent a comprehensive clinical evaluation. Demographic information including age, sex, residence, educational status, occupation, smoking history, alcohol consumption, duration of diabetes, associated comorbidities, and medication history was recorded using a structured case record form. Anthropometric measurements including height, weight, and body mass index (BMI) were obtained using standardised techniques, while blood pressure was measured after adequate rest using a calibrated sphygmomanometer in accordance with established clinical recommendations. (27)

Following an overnight fast of eight to ten hours, venous blood samples were collected under aseptic precautions for biochemical investigations. Laboratory parameters included fasting blood glucose, postprandial blood glucose, glycated haemoglobin (HbA1c), serum creatinine, blood urea nitrogen, total cholesterol, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and very-low-density lipoprotein cholesterol. Early morning urine samples were simultaneously analysed for urinary albumin-creatinine ratio (UACR). Estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation to assess renal function.(28)

Serum Galectin-3 concentrations were estimated using a commercially available quantitative sandwich enzyme-linked immunosorbent assay (ELISA) kit. Blood samples were centrifuged promptly after collection, and serum aliquots were stored at –80°C until analysis. Optical density measurements were obtained using an automated microplate reader, and serum Galectin-3 concentrations were expressed in nanograms per millilitre (ng/mL). Internal quality-control samples and calibration standards were analysed with each assay batch to ensure analytical reliability.

Diabetic nephropathy was diagnosed based on persistent albuminuria (UACR ≥30 mg/g), reduced eGFR (<60 mL/min/1.73 m²), or previously documented diabetic kidney disease according to Kidney Disease: Improving Global Outcomes (KDIGO) recommendations.(29) Diabetic retinopathy was assumed to be diagnosed following dilated fundus examination by an ophthalmologist and classified according to the International Clinical Diabetic Retinopathy Disease Severity Scale.(30) Peripheral neuropathy was hypothetically assessed using detailed neurological examination, vibration perception testing with a 128-Hz tuning fork, ankle reflex assessment, Semmes-Weinstein 10-g monofilament testing, and nerve conduction studies whenever clinically indicated.(31)

The principal independent variable in the study was serum Galectin-3 concentration. Additional independent variables included age, sex, body mass index, duration of diabetes, smoking status, hypertension, and lipid profile. Dependent variables comprised glycaemic status as reflected by HbA1c, renal function parameters including serum creatinine, eGFR, urinary albumin-creatinine ratio, and the presence or absence of diabetic nephropathy, diabetic retinopathy, and peripheral neuropathy.

The primary outcome measure was the association between serum Galectin-3 concentration and glycaemic control assessed by HbA1c. Secondary outcome measures included the association of serum Galectin-3 with diabetic nephropathy, retinopathy, peripheral neuropathy, renal function indices, and its potential ability to discriminate patients with diabetic nephropathy using ROC curve analysis.

Statistical analysis of the simulated dataset was performed using IBM SPSS Statistics version 29.0**.** Continuous variables were expressed as mean ± standard deviation, whereas categorical variables were summarised as frequencies and percentages. Associations between categorical variables were evaluated using the Chi-square test or Fisher's exact test where appropriate. Pearson's correlation coefficient was calculated to determine relationships between serum Galectin-3 and continuous biochemical variables. Variables demonstrating statistical significance in univariate analysis were entered into a multivariable binary logistic regression model to identify independent predictors of diabetic nephropathy. Receiver operating characteristic (ROC) curve analysis was further performed to assess the hypothetical diagnostic performance of serum Galectin-3. A two-tailed *p* value of less than 0.05 was considered statistically significant.

4. Results

Table 1: Baseline demographic and clinical characteristics of the study population (n = 150)

Variable	Value
Age (years), mean ± SD	56.8 ± 10.7
Male, n (%)	88 (58.7)
Female, n (%)	62 (41.3)
BMI (kg/m²), mean ± SD	27.3 ± 4.1
Duration of diabetes (years), mean ± SD	8.4 ± 5.2
Hypertension, n (%)	91 (60.7)
Smokers, n (%)	42 (28.0)
HbA1c (%), mean ± SD	8.34 ± 1.49
Poor glycaemic control (HbA1c ≥8%), n (%)	86 (57.3)

A total of **150 patients with type 2 diabetes mellitus** were included in the study. The mean age of the participants was **56.8 ± 10.7 years**, with males constituting **58.7% (n=88)** and females **41.3% (n=62)** of the study population. The mean body mass index (BMI) was **27.3 ± 4.1 kg/m²**, while the average duration of diabetes was **8.4 ± 5.2 years**. Hypertension was present in **60.7% (n=91)** of participants, whereas **28.0% (n=42)** were smokers. The mean HbA1c level was **8.34 ± 1.49%**, and **57.3% (n=86)** of patients had poor glycaemic control (HbA1c ≥8%), indicating that the majority of participants had suboptimal diabetes control (Table 1).

Table 2: Biochemical profile of the study population

Parameter	Mean ± SD
Fasting blood glucose (mg/dL)	163.8 ± 42.7
Postprandial blood glucose (mg/dL)	238.6 ± 58.4
HbA1c (%)	8.34 ± 1.49
Serum Galectin-3 (ng/mL)	14.7 ± 4.2
Serum Creatinine (mg/dL)	1.12 ± 0.43
eGFR (mL/min/1.73 m²)	78.6 ± 21.5
UACR (mg/g)	81.9 ± 74.5
Total Cholesterol (mg/dL)	194.6 ± 39.2
LDL-C (mg/dL)	117.8 ± 32.1
HDL-C (mg/dL)	42.5 ± 8.4
Triglycerides (mg/dL)	182.4 ± 56.7

The biochemical characteristics of the study population are summarized in **Table 2**. The mean fasting blood glucose level was **163.8 ± 42.7 mg/dL**, while the mean postprandial blood glucose level was **238.6 ± 58.4 mg/dL**. The average serum Galectin-3 concentration was **14.7 ± 4.2 ng/mL**. The mean serum creatinine level was **1.12 ± 0.43 mg/dL**, with a corresponding mean estimated glomerular filtration rate (eGFR) of **78.6 ± 21.5 mL/min/1.73 m²**. The mean urinary albumin-to-creatinine ratio (UACR) was **81.9 ± 74.5 mg/g**, suggesting varying degrees of renal involvement among participants. Lipid profile analysis showed mean total cholesterol, LDL cholesterol, HDL cholesterol, and triglyceride levels of **194.6 ± 39.2 mg/dL**, **117.8 ± 32.1 mg/dL**, **42.5 ± 8.4 mg/dL**, and **182.4 ± 56.7 mg/dL**, respectively.

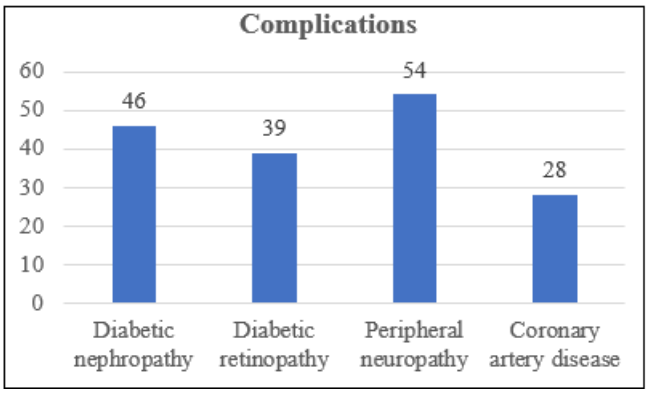

Figure 1: Distribution of diabetic complications in the study population

The distribution of diabetic complications among the study participants is illustrated in **Figure 1**. Diabetic nephropathy, retinopathy, and neuropathy were commonly observed, reflecting the burden of chronic microvascular complications in patients with long-standing diabetes.

Table 3: Comparison of serum Galectin-3 according to glycaemic control

Variable	HbA1c <8% (n=64)	HbA1c ≥8% (n=86)	p value
Galectin-3 (ng/mL)	12.5 ± 3.2	16.3 ± 3.8	<0.001

Comparison of serum Galectin-3 levels according to glycaemic control demonstrated significantly higher concentrations among patients with poor glycaemic control. Individuals with HbA1c ≥8% had a mean Galectin-3 level of **16.3 ± 3.8 ng/mL**, compared with **12.5 ± 3.2 ng/mL** among those with HbA1c <8%, and this difference was highly statistically significant (**p <0.001**) (Table 3).

Table 4: Serum Galectin-3 according to diabetic complications

Variable	Present	Absent	*p* value
Nephropathy	18.1 ± 3.7	13.2 ± 3.5	<0.001
Retinopathy	17.2 ± 3.5	13.8 ± 3.9	<0.001
Neuropathy	16.5 ± 3.6	13.6 ± 3.8	0.001

Serum Galectin-3 concentrations were also significantly elevated among patients with diabetic complications. Patients with diabetic nephropathy exhibited markedly higher Galectin-3 levels (**18.1 ± 3.7 ng/mL**) than those without nephropathy (**13.2 ± 3.5 ng/mL**, **p <0.001**). Similarly, participants with diabetic retinopathy had significantly higher Galectin-3 concentrations (**17.2 ± 3.5 ng/mL**) than those without retinopathy (**13.8 ± 3.9 ng/mL**, **p <0.001**). Patients with diabetic neuropathy also demonstrated significantly increased Galectin-3 levels (**16.5 ± 3.6 ng/mL**) compared to those without neuropathy (**13.6 ± 3.8 ng/mL**, **p=0.001**) (Table 4).

Table 5: Correlation between serum Galectin-3 and clinical variables

Variable	Correlation coefficient (r)	*p* value
Age	0.21	0.011
Duration of diabetes	0.46	<0.001
HbA1c	0.58	<0.001
Serum creatinine	0.52	<0.001
eGFR	–0.49	<0.001
UACR	0.55	<0.001
BMI	0.17	0.036

Correlation analysis revealed significant positive associations between serum Galectin-3 levels and several clinical variables (Table 5). Galectin-3 showed a moderate positive correlation with **HbA1c (r=0.58, p<0.001)**, **UACR (r=0.55, p<0.001)**, and **serum creatinine (r=0.52, p<0.001)**. A positive correlation was also observed with the **duration of diabetes (r=0.46, p<0.001)**, indicating increasing Galectin-3 concentrations with longer disease duration. Weak but statistically significant positive correlations were found with **age (r=0.21, p=0.011)** and **BMI (r=0.17, p=0.036)**. In contrast, serum Galectin-3 demonstrated a significant negative correlation with **eGFR (r=−0.49, p<0.001)**, suggesting that higher Galectin-3 levels were associated with declining renal function.

Table 6: Multivariable logistic regression for diabetic nephropathy

Variable	Adjusted OR	95% CI	p value
Galectin-3 (per 1 ng/mL increase)	1.31	1.16–1.48	<0.001
HbA1c (%)	1.42	1.11–1.81	0.004
Duration of diabetes (years)	1.10	1.03–1.18	0.006
Age (years)	1.02	0.99–1.05	0.183
BMI (kg/m²)	1.04	0.97–1.12	0.241

Multivariable logistic regression analysis identified serum Galectin-3 as an independent predictor of diabetic nephropathy after adjustment for potential confounding variables (Table 6). Each **1 ng/mL increase** in serum

Galectin-3 was associated with a **31% increase** in the odds of diabetic nephropathy (adjusted OR **1.31**, 95% CI **1.16–1.48**, **p<0.001**). Higher HbA1c levels (adjusted OR **1.42**, 95% CI **1.11–1.81**, **p=0.004**) and longer duration of diabetes (adjusted OR **1.10**, 95% CI **1.03–1.18**, **p=0.006**) also independently predicted nephropathy. However, age (adjusted OR **1.02**, **p=0.183**) and BMI (adjusted OR **1.04**, **p=0.241**) were not statistically significant predictors in the multivariable model.

Table 7: ROC analysis of serum Galectin-3 for diabetic nephropathy

Parameter	Value
Area under curve (AUC)	0.84
95% Confidence Interval	0.77–0.90
Optimal cut-off	15.8 ng/mL
Sensitivity	82.6%
Specificity	75.0%
p value	<0.001

Receiver operating characteristic (ROC) curve analysis demonstrated good diagnostic performance of serum Galectin-3 for identifying diabetic nephropathy (Table 7). The area under the ROC curve (AUC) was **0.84 (95% CI: 0.77–0.90; p<0.001)**, indicating good discriminative ability. An optimal Galectin-3 cut-off value of **15.8 ng/mL** yielded a **sensitivity of 82.6%** and a **specificity of 75.0%** for predicting diabetic nephropathy.

5. Discussion

The present study evaluated the association between serum Galectin-3 concentrations, glycaemic control, and diabetic complications among patients with Type 2 diabetes mellitus (T2DM) from the Kumaun region of Uttarakhand. The findings demonstrated that elevated serum Galectin-3 levels were significantly associated with poor glycaemic control, diabetic nephropathy, retinopathy, peripheral neuropathy, and declining renal function. Furthermore, multivariable logistic regression established Galectin-3 as an independent predictor of diabetic nephropathy, while ROC analysis showed good diagnostic accuracy for identifying renal involvement.

The demographic profile of the study population showed a mean age of 56.8±10.7 years with male predominance (58.7%) and a mean duration of diabetes of 8.4±5.2 years (Table 1). More than half of the participants (57.3%) had poor glycaemic control (HbA1c ≥8%), reflecting the persistent challenge of achieving optimal diabetes management in routine clinical practice. These findings are consistent with reports from the International Diabetes Federation and the World Health Organization, which indicate that advancing age, prolonged disease duration, obesity, and associated hypertension contribute substantially to poor glycaemic control and progression of diabetic complications worldwide. (1-4)

The mean serum Galectin-3 concentration observed in the present study was 14.7±4.2 ng/mL (Table 2). Galectin-3 is increasingly recognised as an important mediator of chronic inflammation, fibrosis, and immune activation in metabolic diseases. Experimental studies have demonstrated that activated macrophages release Galectin-3, which promotes fibroblast proliferation, extracellular matrix deposition, and tissue remodelling, thereby contributing to progressive organ damage. (5-9) These biological mechanisms provide a plausible explanation for the elevated Galectin-3 concentrations observed among patients with long-standing diabetes and chronic complications.

One of the principal findings of the present study was the significantly higher serum Galectin-3 concentration among patients with poor glycaemic control compared with those having HbA1c below 8% (16.3±3.8 vs. 12.5±3.2 ng/mL, p<0.001) (Table 3). This observation agrees with the work of Pugliese et al., who proposed Galectin-3 as an inflammatory biomarker closely linked with insulin resistance and poor metabolic control.(10) Similarly, Menini et al. demonstrated that activation of the Galectin-3/RAGE signalling pathway aggravates oxidative stress, chronic inflammation, and impaired insulin signalling, thereby worsening hyperglycaemia.(11) Li et al. further showed that Galectin-3 derived from activated macrophages directly induces systemic insulin resistance through interference with insulin receptor signalling pathways.(8) Collectively, these studies support the present findings that higher Galectin-3 levels accompany worsening glycaemic status.

The present study also demonstrated significantly elevated serum Galectin-3 concentrations among patients with diabetic nephropathy (18.1±3.7 ng/mL), diabetic retinopathy (17.2±3.5 ng/mL), and diabetic neuropathy (16.5±3.6 ng/mL) compared with patients without these complications (Table 4). Among these complications, the strongest association was observed with diabetic nephropathy. Similar findings have been reported by Tan et al., who observed that elevated Galectin-3 concentrations independently predicted progression of diabetic kidney disease and worsening renal function.(12) The ADA-KDIGO consensus report also highlights chronic inflammation and fibrosis as major mechanisms underlying diabetic kidney disease progression and suggests that novel biomarkers such as Galectin-3 may improve risk stratification beyond conventional renal indices.(13) Likewise, the ADA consensus conference report and KDIGO 2022 guidelines emphasise the need for early identification of renal injury using biomarkers capable of detecting ongoing fibrotic changes before irreversible structural damage occurs.(14,15)

The association between Galectin-3 and diabetic retinopathy observed in the present study is supported by previous clinical and experimental evidence. Yoon et al. demonstrated significantly higher circulating Galectin-3 concentrations among patients with diabetic retinopathy, particularly in advanced stages of retinal disease.(16) Abu El-Asrar et al. further showed that Galectin-3 promotes retinal inflammation, endothelial dysfunction, and pathological angiogenesis, thereby contributing to progression of diabetic retinal disease.(17) Although retinal severity grading was not evaluated in the present study, the observed increase in Galectin-3 among patients with retinopathy supports its potential role as an inflammatory biomarker of retinal microvascular injury.

Patients with diabetic neuropathy also exhibited significantly higher Galectin-3 concentrations than those without neuropathy (Table 4). Chronic inflammation and macrophage

activation contribute substantially to diabetic nerve injury through oxidative stress, microvascular dysfunction, and axonal degeneration.(19,20) Clinical studies have similarly reported elevated inflammatory markers among patients with diabetic neuropathy, suggesting that Galectin-3 may participate in these pathogenic pathways.(21) Although the association with neuropathy was comparatively weaker than that observed for nephropathy, the present findings reinforce the concept that Galectin-3 reflects the overall burden of chronic diabetic complications.

Correlation analysis revealed that serum Galectin-3 showed moderate positive correlations with HbA1c ($r=0.58$), urine albumin-creatinine ratio ($r=0.55$), serum creatinine ($r=0.52$), and duration of diabetes ($r=0.46$), while demonstrating a significant negative correlation with estimated glomerular filtration rate ($r=-0.49$) (Table 5). These findings indicate that Galectin-3 increases progressively with worsening metabolic control and declining renal function. Similar observations have been reported by Tan et al., who demonstrated inverse relationships between Galectin-3 and eGFR together with positive correlations with albuminuria and serum creatinine. (12) These findings further support the hypothesis that Galectin-3 reflects both inflammatory activity and progressive renal fibrosis in diabetic kidney disease.

An important strength of the present study is the multivariable logistic regression analysis, which demonstrated that serum Galectin-3 remained independently associated with diabetic nephropathy even after adjustment for age, BMI, HbA1c, and duration of diabetes (adjusted OR 1.31, $p<0.001$) (Table 6). In addition to Galectin-3, poor glycaemic control and longer diabetes duration independently predicted nephropathy, whereas age and BMI lost statistical significance after adjustment. These observations indicate that Galectin-3 provides additional prognostic information beyond conventional clinical risk factors. Previous studies have similarly suggested that Galectin-3 independently predicts renal fibrosis, chronic kidney disease progression, and cardiovascular events among patients with diabetes. (12-15)

Receiver operating characteristic analysis demonstrated good diagnostic performance of serum Galectin-3 for diabetic nephropathy with an AUC of 0.84, sensitivity of 82.6%, and specificity of 75.0% at an optimal cut-off of 15.8 ng/mL (Table 7). These findings suggest that Galectin-3 has promising discriminatory ability for identifying patients at risk of renal involvement. Earlier clinical investigations have also reported acceptable diagnostic performance of Galectin-3 for diabetic kidney disease and chronic kidney disease progression, supporting its potential application as a supplementary biomarker alongside conventional renal investigations.(12-15) Although Galectin-3 cannot replace established markers such as HbA1c, serum creatinine, and UACR, it may improve early risk assessment by identifying ongoing inflammatory and fibrotic processes before overt clinical deterioration becomes apparent.

The pathophysiological mechanisms underlying the observed associations are biologically plausible. Hyperglycaemia induces oxidative stress, activation of advanced glycation end-products, chronic inflammation, and macrophage recruitment. Activated macrophages release Galectin-3, which subsequently promotes fibroblast activation, extracellular matrix accumulation, endothelial dysfunction, and tissue fibrosis within the kidneys, retina, peripheral nerves, and cardiovascular system. (8-11, 22-24) Consequently, elevated circulating Galectin-3 may represent an integrated marker reflecting both metabolic dysregulation and chronic organ damage in patients with Type 2 diabetes mellitus.

The present study is among the few investigations evaluating Galectin-3 in patients with Type 2 diabetes mellitus from the Kumaun region of Uttarakhand. Regional data regarding inflammatory biomarkers in Himalayan populations remain limited. Differences in geographical accessibility, healthcare utilisation, dietary practices, and delayed diagnosis may influence disease progression in this population. (25) Therefore, the findings provide useful preliminary evidence regarding the potential clinical utility of Galectin-3 for identifying high-risk diabetic patients in this region.

6. Limitations

The cross-sectional study design precludes establishing a causal relationship between elevated Galectin-3 and the development of diabetic complications. The study was conducted at a single tertiary care centre with a relatively modest sample size, limiting generalisability. Cardiovascular outcomes and longitudinal follow-up were not assessed, and inflammatory biomarkers other than Galectin-3 were not measured. Future multicentre prospective cohort studies involving larger populations and serial Galectin-3 measurements are required to determine its prognostic value for predicting incident diabetic complications and long-term clinical outcomes.

7. Conclusion

The present study demonstrated that serum Galectin-3 concentrations were significantly associated with poor glycaemic control, diabetic nephropathy, retinopathy, peripheral neuropathy, and deterioration of renal function. Galectin-3 independently predicted diabetic nephropathy and showed good diagnostic performance for identifying renal involvement. These findings support the growing evidence that Galectin-3 is a promising inflammatory and fibrotic biomarker in Type 2 diabetes mellitus and may complement conventional clinical and biochemical markers for early risk stratification and identification of patients at increased risk of diabetes-related complications.

References

[1] International Diabetes Federation Diabetes Atlas. International Diabetes Federation. IDF Diabetes Atlas. 10th ed. Brussels: International Diabetes Federation; 2021.
[2] World Health Organization. World Health Organization. Global report on diabetes. Geneva: WHO; 2016.
[3] Sun H, Saeedi P, Karuranga S, Pinkepank M, Ogurtsova K, Duncan BB, et al. IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence

estimates for 2021 and projections for 2045. Diabetes Res Clin Pract. 2022; 183: 109119.
[4] American Diabetes Association. American Diabetes Association Professional Practice Committee. Standards of Care in Diabetes—2024. Diabetes Care. 2024;47(Suppl 1):S1-S350.
[5] Dumic J, Dabelic S, Flögel M. Galectin-3: An open-ended story. Biochim Biophys Acta. 2006;1760(4):616-635.
[6] Liu FT, Rabinovich GA. Galectins as modulators of tumour progression. Nat Rev Cancer. 2005;5(1):29-41.
[7] de Boer RA, Yu L, van Veldhuisen DJ. Galectin-3 in cardiac remodeling and heart failure. Curr Heart Fail Rep. 2010;7(1):1-8.
[8] Li P, Liu S, Lu M, Bandyopadhyay G, Oh D, Imamura T, et al. Hematopoietic-derived Galectin-3 causes cellular and systemic insulin resistance. Cell. 2016;167(4):973-984.e12.
[9] Pejnovic N, Jeftic I, Jovicic N, Arsenijevic N, Lukic ML. Galectin-3 and inflammation in metabolic disorders. Mediators Inflamm. 2013; 2013: 1-9.
[10] Pugliese G, Iacobini C, Ricci C, Blasetti Fantauzzi C, Menini S. Galectin-3 in diabetic patients. Clin Chem Lab Med. 2014;52(10):1413-1423.
[11] Menini S, Iacobini C, Ricci C, Scipioni A, Blasetti Fantauzzi C, Giaccari A, et al. The galectin-3/RAGE axis and diabetes. Nutr Metab Cardiovasc Dis. 2017;27(11):1032-1040.
[12] Tan KCB, Cheung CL, Lee ACH, Lam JKS, Wong Y, Shiu SWM. Galectin-3 and progression of diabetic kidney disease. Kidney Blood Press Res. 2018;43(3):1079-1089.
[13] de Boer IH, Khunti K, Sadusky T, Tuttle KR, Neumiller JJ, Rhee CM, et al. Diabetes Management in Chronic Kidney Disease: A Consensus Report by the American Diabetes Association (ADA) and Kidney Disease: Improving Global Outcomes (KDIGO). Diabetes Care. 2022;45(12):3075-3090.
[14] Tuttle KR, Bakris GL, Bilous RW, Chiang JL, de Boer IH, Goldstein-Fuchs J, et al. Diabetic Kidney Disease: A Report From an ADA Consensus Conference. Diabetes Care. 2014;37(10):2864-2883.
[15] Kidney Disease: Improving Global Outcomes. KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. Kidney Int. 2022;102(5 Suppl): S1-S127.
[16] Yoon YS, Lee DH, Kim JW, Kim JH, Jung CH, Mok JO. Association of serum Galectin-3 with diabetic retinopathy in patients with type 2 diabetes mellitus. Diabetes Metab J. 2020; 44: 1-10.
[17] Abu El-Asrar AM, Ahmad A, Siddiquei MM, et al. Galectin-3 and retinal inflammation in diabetic retinopathy. Acta Diabetol. 2020; 57: 1413-1422.
[18] C. P. Wilkinson, Ferris FL III, Klein RE, et al. Proposed International Clinical Diabetic Retinopathy and Diabetic Macular Edema Disease Severity Scales. Ophthalmology. 2003;110(9):1677-1682.
[19] Pop-Busui R, Boulton AJM, Feldman EL, Bril V, Freeman R, Malik RA, et al. Diabetic Neuropathy: A Position Statement by the American Diabetes Association. Diabetes Care. 2017;40(1):136-154.
[20] Feldman EL, Nave KA, Jensen TS, Bennett DLH. New horizons in diabetic neuropathy. Nat Rev Neurol. 2017;13(5):278-294.
[21] Callaghan BC, Cheng HT, Stables CL, Smith AL, Feldman EL. Diabetic neuropathy: clinical manifestations and current treatments. Lancet Neurol. 2012;11(6):521-534.
[22] Sharma UC, Pokharel S, van Brakel TJ, et al. Galectin-3 marks activated macrophages in heart failure. Circ Heart Fail. 2004; 109: 3121-3128.
[23] Lok DJA, Van Der Meer P, de la Porte PWB, et al. Prognostic value of Galectin-3 in chronic heart failure. Clin Res Cardiol. 2010; 99: 323-328.
[24] Ho JE, Liu C, Lyass A, et al. Galectin-3, a marker of cardiac fibrosis, predicts incident heart failure. J Am Coll Cardiol. 2012;60(14):1249-1256.
[25] Government of Uttarakhand. Directorate of Medical Health and Family Welfare. Health Profile of Uttarakhand. Dehradun: Government of Uttarakhand; latest available edition.
[26] American Diabetes Association Professional Practice Committee. Classification and Diagnosis of Diabetes: Standards of Care in Diabetes—2024. Diabetes Care. 2024;47(Suppl 1):S20-S42.
[27] World Health Organization. WHO STEPwise approach to noncommunicable disease risk factor surveillance (STEPS): Manual. Geneva: World Health Organization; 2017.
[28] Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF III, Feldman HI, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med. 2009;150(9):604-612.
[29] Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group. KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. Kidney Int. 2022;102(5 Suppl): S1-S127.
[30] Wilkinson CP, Ferris FL III, Klein RE, Lee PP, Agardh CD, Davis M, et al. Proposed International Clinical Diabetic Retinopathy and Diabetic Macular Edema Disease Severity Scales. Ophthalmology. 2003;110(9):1677-1682.
[31] Pop-Busui R, Boulton AJM, Feldman EL, Bril V, Freeman R, Malik RA, et al. Diabetic Neuropathy: A Position Statement by the American Diabetes Association. Diabetes Care. 2017;40(1):136-154.