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Metabolic Spillover of Dysglycemia: Multiorgan Biochemical Signatures Across Kidney, Liver, and Lipid Pathways

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Abstract

Background: Glycated hemoglobin (HbA1c) is a widely used indicator of chronic glycemic exposure and is central to diabetes diagnosis, monitoring, and prevention of microvascular and macrovascular complications. Because diabetes affects multiple organ systems, interpretation of HbA1c may be strengthened when renal, hepatic, and lipid biomarkers are assessed concurrently.

Objective: This study evaluated the age- and sex-stratified distribution of HbA1c-tested diabetic patients between 2019 and 2022 and explored the relationship between poor glycemic control and selected renal, hepatic, and lipid biomarkers in the 2022 dataset.

Methods: A retrospective cross-sectional laboratory analysis was performed using anonymized patient records from 2019-2022. Patients were stratified into three age categories (<30, 30-60, and >60 years) and by sex. For 2022, additional biomarkers, including micro-creatinine ratio, urea, creatinine/Glomerular Filtration Rate (GFR) ratio, uric acid, bilirubin, alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, gamma-glutamyl transferase, albumin, total protein, cholesterol, triglycerides, low-density lipoprotein, high-density lipoprotein, and very-low-density lipoprotein, were summarized according to age and sex. Descriptive analysis was used to identify year-wise demographic patterns and biomarker abnormalities associated with elevated HbA1c.

Results: The dataset showed a persistent burden of abnormal HbA1c across adult age groups. The 30-60-year age band contributed the largest number of HbA1c records in 2020 and 2021, whereas the >60-year group was prominent in 2022. In the 2022 biomarker subset, abnormal renal markers, dyslipidemia, and liver enzyme variations were observed among patients with elevated HbA1c. Younger males showed a high proportion of abnormal cholesterol and triglyceride results, while younger females showed comparatively higher abnormal urea, uric acid, and alanine aminotransferase proportions. These findings support the clinical value of paired HbA1c-biomarker monitoring.

Conclusion: The study emphasizes that HbA1c should not be interpreted in isolation in patients with diabetes. Combined assessment with renal, hepatic, and lipid biomarkers may improve early recognition of diabetic complications and guide personalized care. Larger patient-level analyses with standardized denominators are recommended to confirm the observed patterns.

Keywords: Diabetes Mellitus; HbA1c; Glycemic Control; Renal Biomarkers; Lipid Profile; Liver Function Tests

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Introduction

Diabetes mellitus is one of the most important noncommunicable diseases worldwide and continues to expand rapidly in low- and middle-income countries. The 11th edition of the International Diabetes Federation Diabetes Atlas estimated that 589 million adults aged 20-79 years were living with diabetes in 2024 and projected a rise to approximately 853 million by 2050 [1]. Pakistan is of particular concern because recent global estimates place it among countries with the highest age-standardized diabetes prevalence [1]. In this setting, accessible laboratory indicators that help identify poor glycemic control and related organ-system risk are essential for routine care and public health planning.

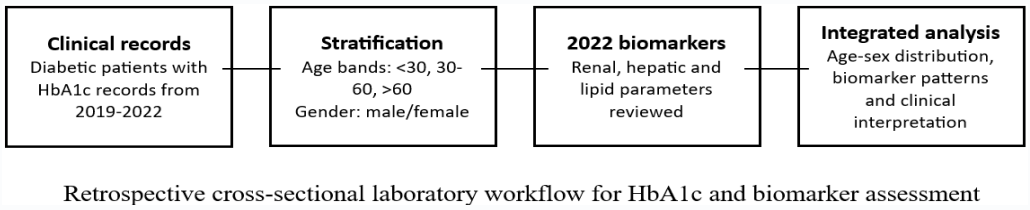

Figure 1: Study workflow for retrospective analysis of HbA1c and associated biomarkers. The dataset was structured by year, age group, sex, and available biomarker status.

HbA1c reflects the nonenzymatic glycation of hemoglobin and approximates average blood glucose exposure over the preceding two to three months. It is widely used for diagnosis, risk stratification, therapeutic monitoring, and long-term assessment of diabetes control. Current professional guidance recognizes HbA1c values of >=6.5% (>=48 mmol/mol) as compatible with diabetes diagnosis when confirmed appropriately, while HbA1c targets for established diabetes should be individualized according to age, comorbidities, hypoglycemia risk, and patient-specific priorities [2, 3].

The clinical importance of HbA1c extends beyond diagnosis. The Diabetes Control and Complications Trial and the United Kingdom Prospective Diabetes Study demonstrated that sustained improvement in glycemic control reduces the risk of microvascular complications and may influence long-term cardiovascular outcomes [4, 5]. These landmark findings established the principle that chronic glycemic exposure is biologically linked to kidney injury, retinal disease, neuropathy, and vascular risk. However, HbA1c alone cannot fully describe the multisystem metabolic phenotype of a patient with diabetes.

Diabetes-related kidney disease is commonly assessed through estimated GFR and albuminuria or albumin-creatinine ratio, while dyslipidemia is evaluated through cholesterol, triglycerides, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and related lipid fractions. Consensus recommendations from the American Diabetes Association and Kidney Disease: Improving Global Outcomes highlight the need for integrated assessment of glycemia, kidney function, cardiovascular risk, and medication safety in patients with diabetes and chronic kidney disease [6]. Similarly, diabetic dyslipidemia, typically characterized by hypertriglyceridemia, low high-density lipoprotein cholesterol, and atherogenic low-density lipoprotein particles, is an important contributor to cardiovascular morbidity [7, 8].

The present study was designed to transform an available routine-laboratory dataset into a structured clinical manuscript. Specifically, it aimed to summarize year-wise HbA1c distribution across age and sex groups from 2019-2022 and to describe the 2022 biomarker profile associated with elevated HbA1c. By presenting renal, hepatic, and lipid biomarkers alongside HbA1c, this study provides a practical framework for comprehensive diabetes monitoring in a tertiary diagnostic setting.

Materials and Methods

Study design and setting

This was a retrospective cross-sectional laboratory-based study using anonymized records of patients with diabetes who underwent HbA1c testing between 2019 and 2022. The analysis was designed to describe age- and sex-specific patterns in HbA1c-tested patients and to explore biomarker abnormalities in the 2022 dataset.

Study population

Eligible records included patients with available HbA1c data and recorded age and sex. Patients were grouped into three age categories: <30 years, 30-60 years, and >60 years. Records with missing essential demographic or HbA1c information were excluded from subgroup analysis. The source dataset reported annual totals of 331 patients in 2019, 289 in 2020, 309 in 2021, and 262 in 2022; however, the visible age-sex cell counts for 2019 summed to 300. Therefore, the manuscript reports the analyzable strata-level counts while recommending source-database verification before final journal submission.

Laboratory variables

HbA1c was used as the principal glycemic marker. For 2022, additional laboratory parameters included micro-creatinine ratio, urea, creatinine/GFR ratio, uric acid, total bilirubin, alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, gamma-glutamyl transferase, albumin, total protein, total cholesterol, triglycerides, low-density lipoprotein, high-density lipoprotein, and very-low-density lipoprotein. The source dataset classified results into normal and abnormal categories according to laboratory reference ranges.

Statistical analysis

Data were summarized using frequencies and percentages. Age- and sex-specific counts were tabulated by year. In the biomarker subset, the percentage of abnormal results was calculated for each marker where normal and abnormal counts were available. Given the summary-level nature of the dataset, the analysis was primarily descriptive. No causal inference was attempted.

Table 1: Age- and sex-stratified HbA1c-tested records from 2019 to 2022.

Year	Age group	Male (n)	Female (n)	Total (n)
2019	<30	28	21	49
2019	30-60	99	32	131
2019	>60	71	49	120
2020	<30	15	10	25
2020	30-60	67	78	145
2020	>60	60	59	119
2021	<30	25	10	35
2021	30-60	77	82	159
2021	>60	60	55	115
2022	<30	29	27	56
2022	30-60	42	33	75
2022	>60	79	52	131

Abbreviation: HbA1c: Glycated hemoglobin Counts reflect analyzable age-sex cells from the source dataset

Results

See Figure 1.

Year-wise distribution of HbA1c-tested diabetic records

Across the available age-sex strata, 300 analyzable records were identified in 2019, 289 in 2020, 309 in 2021, and 262 in 2022. In 2019, the 30-60-year group represented the largest analyzable stratum (n = 131), followed by the >60-year group (n = 120). In 2020 and 2021, the 30-60-year group remained dominant, with 145 and 159 records, respectively. In 2022, the >60-year group accounted for the largest share of records (n = 131), suggesting a shift toward an older monitored diabetic population (Table 1 and Figure 2 & 3).

Biomarker abnormalities in the 2022 younger-patient subset

In the 2022 dataset, additional laboratory parameters were available for biomarker profiling. In patients younger than 30 years, elevated HbA1c was accompanied by heterogeneous renal, hepatic, and lipid biomarker abnormalities. Males showed particularly high abnormal cholesterol and triglyceride proportions (85.71% and 83.33%, respectively), whereas females showed higher abnormal urea (71.43%), uric acid (57.14%), and alanine aminotransferase (55.56%) proportions. Creatinine/GFR, alkaline phosphatase, gamma-glutamyl transferase, albumin, total protein, high-density lipoprotein, and very-low-density lipoprotein were reported as normal in all patients in this younger subset (Table 2 and Figure 4).

Integrated interpretation of HbA1c with organ-system biomarkers

The descriptive pattern suggests that HbA1c abnormalities cluster with organ-system signals relevant to diabetic complications. Renal markers may reflect early kidney stress, lipid abnormalities may signal cardiovascular risk, and liver enzyme changes may reflect metabolic liver involvement or medication-related effects. Although summary-level data prevent patient-level correlation and multivariable modeling, the results support routine integrated monitoring (Figure 5).

Table 2: Proportion of abnormal biomarker results in patients younger than 30 years in the 2022 subset.

Biomarker	Male abnormal (%)	Female abnormal (%)
HbA1c	57.14	47.62
Micro-creatinine ratio	40.00	50.00
Urea	12.50	71.43
Creatinine/GFR	0.00	0.00
Uric acid	25.00	57.14
Total bilirubin	16.67	0.00
Alkaline phosphatase	0.00	0.00
Aspartate aminotransferase	25.00	0.00
Alanine aminotransferase	12.50	55.56
Gamma-glutamyl transferase	0.00	0.00
Albumin	0.00	0.00
Total protein	0.00	0.00
Cholesterol	85.71	37.50
Triglycerides	83.33	28.57
Low-density lipoprotein	0.00	28.57
High-density lipoprotein	0.00	0.00
Very-low-density lipoprotein	0.00	0.00

Abbreviations: GFR: Glomerular Filtration Rate; HbA1c: Glycated hemoglobin

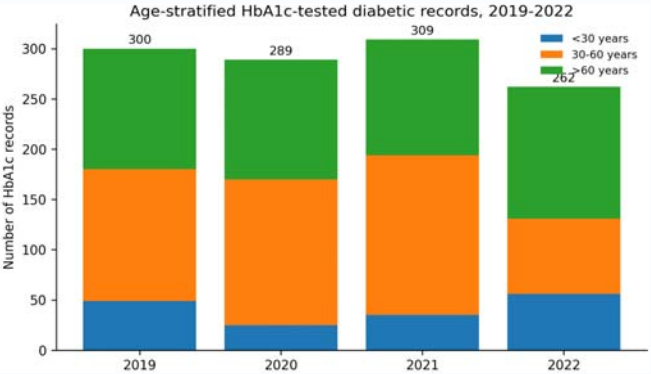

Figure 2: Age-stratified distribution of HbA1c-tested diabetic records from 2019 to 2022. The 30-60-year group predominated in 2020-2021, whereas the >60-year group became more prominent in 2022.

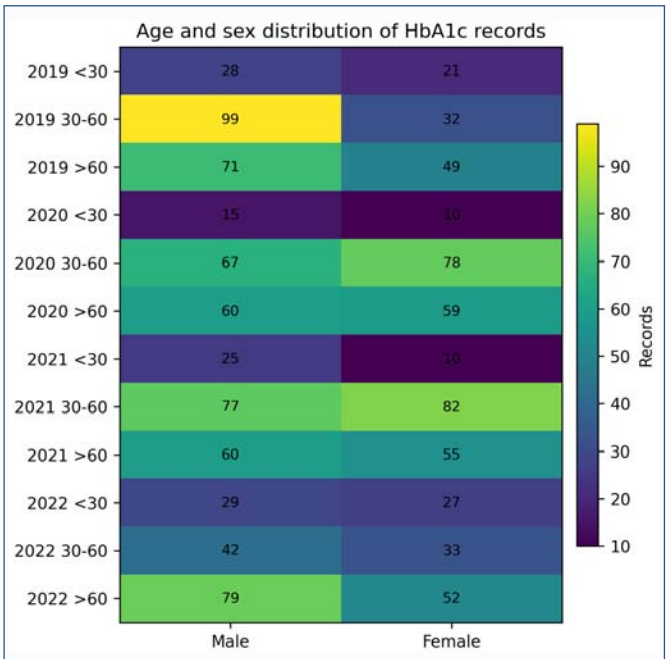

Figure 3: Heat-map summary of age and sex distribution across the four-year dataset. Cell values represent the number of records in each age-sex stratum.

Discussion

This retrospective analysis provides a structured interpretation of a four-year HbA1c dataset with additional 2022 biomarker information. The findings emphasize that glycemic control is not merely a glucose-centered issue but part of a broader metabolic phenotype involving the kidneys, liver, and cardiovascular risk pathways. The year-wise distribution showed a large burden of HbA1c-tested diabetic records in middle-aged adults during 2020-2021 and a greater representation of older adults in 2022. This pattern is clinically meaningful because aging, longer diabetes duration, polypharmacy, and comorbid kidney and cardiovascular disease commonly complicate glycemic management [1, 3, 6].

HbA1c remains a cornerstone marker for diabetes diagnosis and monitoring, but its interpretation requires clinical context. The ADA

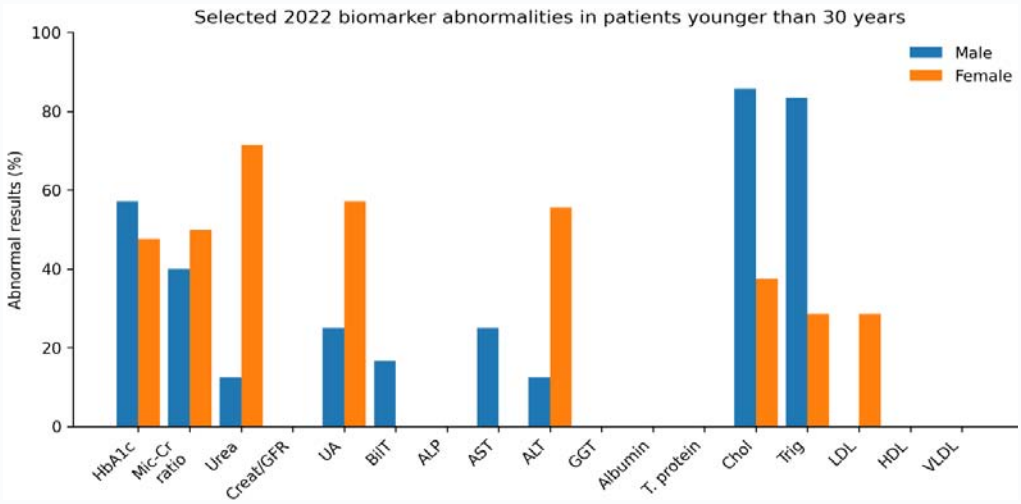

Figure 4: Abnormal biomarker proportions among patients younger than 30 years in the 2022 subset. The plot highlights sex-specific variation in renal, hepatic, and lipid parameters.

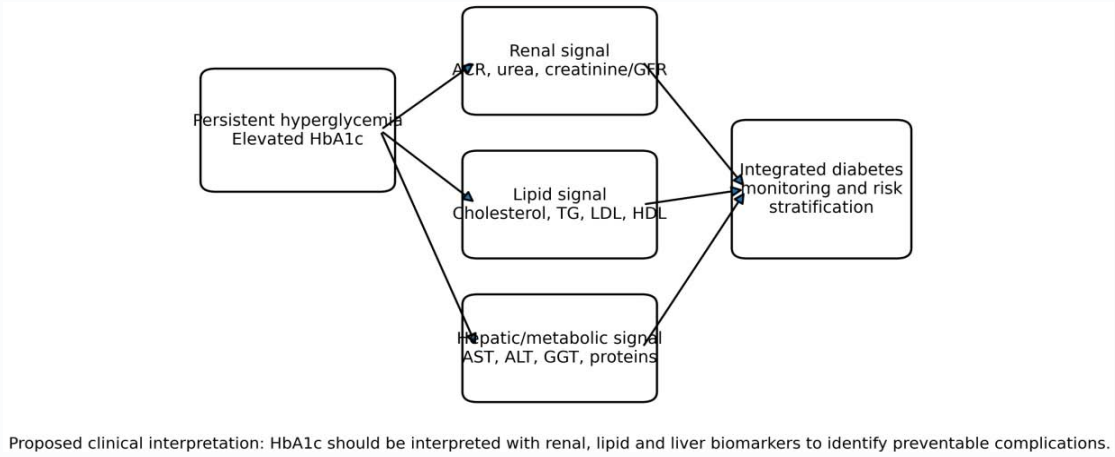

Figure 5: Conceptual model linking elevated HbA1c with renal, lipid, and hepatic biomarker domains. The model supports integrated metabolic risk assessment rather than isolated HbA1c interpretation.

Standards of Care and WHO guidance support HbA1c as a diagnostic and monitoring tool while also recognizing that anemia, kidney disease, hemoglobin variants, recent blood loss, and other conditions can alter interpretation [2, 9]. Therefore, combining HbA1c with renal markers, lipid profile, and liver enzymes offers a more comprehensive view of metabolic status.

The observed renal-marker abnormalities are consistent with the known relationship between hyperglycemia and diabetic kidney disease. Chronic hyperglycemia promotes glomerular hyperfiltration, endothelial dysfunction, oxidative stress, and inflammatory injury, which may eventually present as albuminuria, altered creatinine/GFR ratios, and progressive kidney impairment [6, 10]. In clinical practice, albumin-creatinine ratio and estimated GFR are central tools for early detection and staging of diabetic kidney disease [6].

The lipid findings are also biologically plausible. Poor glycemic control and insulin resistance are associated with increased hepatic very-low-density lipoprotein production, hypertriglyceridemia, altered low-density lipoprotein particle composition, and reduced or dysfunctional high-density lipoprotein cholesterol [7, 8, 11]. Several observational studies have reported significant associations between elevated HbA1c and dyslipidemia among patients with type 2 diabetes [12-16]. This supports the use of lipid monitoring alongside glycemic assessment to guide cardiovascular prevention strategies.

Liver enzyme variation in the dataset suggests another important aspect of diabetes care. Diabetes and insulin resistance are strongly linked with metabolic dysfunction-associated steatotic liver disease, and abnormal alanine aminotransferase, aspartate aminotransferase, or gamma-glutamyl transferase may reflect liver fat accumulation, inflammation, medication effects, or other hepatobiliary conditions. The younger subset showed sex-specific enzyme patterns, but these results require cautious interpretation because the data were summarized rather than modeled at the patient level.

The major strength of this study is its practical use of routine laboratory data to demonstrate how HbA1c may be interpreted with clinically relevant biomarker domains. The main limitations are the summary-level structure of the dataset, incomplete availability of detailed biomarker values for all age groups, and inconsistencies between one reported annual total and the visible age-sex cell counts.

Raw patient-level data would allow correlation analysis, regression modeling, adjustment for diabetes duration, medication exposure, body mass index, blood pressure, and comorbidities. Before journal submission, the underlying database should be audited to confirm denominators and reference-range thresholds.

Conclusion

This study shows that HbA1c monitoring can be strengthened by simultaneous evaluation of renal, hepatic, and lipid biomarkers. The findings support a comprehensive diabetes monitoring model in which elevated HbA1c prompts assessment of kidney function, dyslipidemia, liver enzymes, and protein status. Future studies should use patient-level longitudinal data to quantify risk trajectories and identify clinically actionable biomarker patterns.

Declarations

Ethics approval and consent to participate: The study used anonymized retrospective laboratory records. The exact institutional review board approval number should be inserted before submission.

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No specific funding was reported for this manuscript.

Conflict of Interest

The authors should declare any potential conflicts of interest before submission.

Data Availability

Aggregated data are included in the manuscript. Patient-level data are not publicly available because of privacy considerations.

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