

Research Article

Big Data and Diabetes: Seven-Year Data from Pakistan's Nation-Wide Laboratory Network

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Article Info

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Abstract

Introduction: Diabetes has become a prominent worldwide public health issue, with its prevalence notably higher in lower middle-income countries. Pakistan ranks third globally in terms of number of individuals diagnosed with Type 2 Diabetes Mellitus and have highest prevalence of diabetes throughout the world. The objective of current study was to assess the frequency of diabetes in relation to demographics utilizing laboratory data of individuals residing in Pakistan.

Methods: Biochemical data of HbA1c, fasting and random plasma glucose, and oral glucose tolerance test were retrieved from Laboratory Information System analyzed in Pathology and Laboratory Medicine department from Jan 2016 to Dec 2022. Specimens were received from Aga Khan University laboratories' network, which is spread over the country. For interpretation of biochemical tests' values American Diabetes Association (ADA) criteria was applied.

Results: After removal of duplicates and missing data, the final sample included 4,260,171 unique individuals. Diabetes was present in 35.9% of the overall population, with the highest incidence (55.6%) recorded in males aged 35 to 59 years. Diabetes was significantly associated with advancing age and gender ($p < 0.001$). Individuals who had the fasting blood glucose ≥ 126 mg/dl were ($n=372,050$), HbA1c exceeding 6.5% were ($n=762,940$) the random blood glucose ≥ 200 mg/dl were ($n=128,820$), OGTT level ≥ 200 mg/dl were ($n=487$) and diabetes confirmed with more than one diagnostic test were ($n=505,609$).

Conclusion: The study, based on dataset of around 4.2 million individuals, revealed an overall diabetes frequency of 35.9%, with highest prevalence in middle-aged group (55.6%), and significant associations with both advancing age and gender.

Introduction

Globally, diabetes affected an estimated 463 million people in 2019, and the figure is expected to rise to around 700 million by 2045 [1]. It is a major public health concern worldwide, is more prevalent in low and middle -income countries (LMICs) such as Pakistan [2]. The International Diabetes Federation (IDF) reports that more than one in every four adults (26.7%) in Pakistan, a South Asian LMIC with a population of over 220 million, have Type 2 Diabetes Mellitus (T2DM) and has the highest national prevalence of diabetes throughout the world [3, 4]. Pakistan is expected to top the list in the near future, having surpassed China and India in terms of the number of people with T2DM globally [5].

The high prevalence of T2DM in LMICs is due to a complex interaction of socioeconomic, lifestyle, and environmental factors [6]. Rapid urbanization in LMICs has made a significant contribution to the rising T2DM rate. These changes include decreased physical activity, increased consumption of processed and high-calorie foods, and sedentary behaviors [7]. Traditional diets are frequently replaced by processed foods and high-fat, sugar-rich diets as countries transition economically. This nutritional shift increases the risk of obesity and, as a result, T2DM [8]. Genetic predisposition and family history are important factors in increasing diabetes risk in these populations [9, 10]. Furthermore, limited access to healthcare, lower education levels, and cultural norms that promote higher body weight aggravate the problem, making early detection and management of diabetes difficult [11]. Several developed countries, including the United States, Canada, Germany, Finland, Denmark, and Australia, have established diabetes registries; however, no such database exists in Pakistan. While global estimates exist, there is a lack of comprehensive national electronic registries to track real time diabetes prevalence in Pakistan. In the absence of comprehensive data, analyzing high-volume biochemical lab data could provide a preliminary understanding of diabetes burden in the country. The aim of this study involved utilizing the Aga Khan University Hospital's extensive laboratory network across Pakistan to examine

the period prevalence and gender distribution of diabetes and prediabetes across various age groups within the Pakistani populace.

Methodology

We curated and studied data of HemoglobinA1C (HbA1c), fasting and random blood glucose (FBG and RBG respectively) and Oral Glucose Tolerance Test (OGTT) in blood samples analyzed in the Section of Chemical Pathology, Department of Pathology and Laboratory Medicine. Data were extracted from the Laboratory Information System (LIS) of the Aga Khan University Hospital (AKUH). Presently, AKUH has a vast clinical laboratory network, serving the AKU health system, patients, and clinicians across Pakistan. The network includes laboratories on campuses and multiple collecting stations in over 90 districts with more than three hundred collection units, covering Pakistan's diverse population. The study was approved as an exemption by AKU's Ethical review committee (ERC number 2023-8559-24624). The data collection spanned from January 2016 to December 2022. Cases with missing or incomplete information and duplicate cases were removed. To maintain confidentiality, data encryption of patient identities was executed. Throughout the study, all HbA1c and glucose samples were tested using an ADVIA 1800, Siemens analyzer, New York, USA. The HbA1c assay has been certified by the National Glycohemoglobin Standardization Programme (NGSP), and its results can be directly linked or compared to those obtained using the Diabetes Control and Complications Trial (DCCT) reference method (for diagnostic purposes). Throughout the study, the laboratory was subject to proficiency testing by the College of American Pathologists. FBG, RBG and OGTT were performed by hexokinase method while HbA1c was analyzed using enzymatic assay method. In all biochemical analysis systems, performance was evaluated using three levels of quality control materials: low, medium, and high. The 75-g OGTT was performed according to international protocol with fasting and timed plasma glucose samples analyzed using validated analytical laboratory methods. Table 1 describes the cutoff values for HbA1c, FBG, RBG, and OGTT, as per the ADA guidelines [12,13]

Table 1: Prediabetes and Diabetes Diagnostic Criteria as per American Diabetes Association.

Diagnostic Test	Normal	Prediabetes	Diabetes
FBG, mg/dl	≤ 99	100 – 125	≥ 126
HbA1C, %	≤ 5.7	5.8 - 6.4	≥ 6.5
RBG, mg/dl	≤ 139		≥ 200
OGTT, mg/dl	≤ 139	140 – 199	≥ 200

Fasting is defined as no caloric intake for at least 8 hours. A1C tests should be performed in a laboratory using a method that is NGSP certified and standardised to the DCCT assay. RBG is not used to diagnose Prediabetes.

Statistical analysis

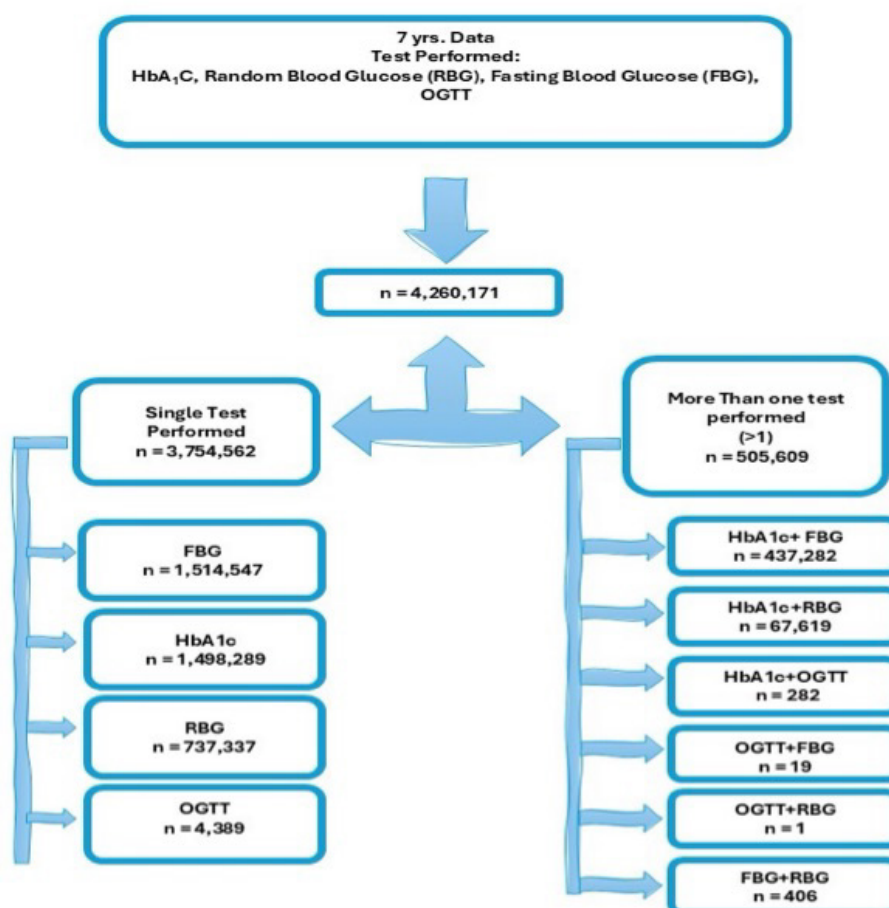
All data cleaning and analyses were performed on the software Stata version 17 (StataCorp LLC). Continuous variables values (FBG, HbA1c, RBG, OGTT) were reported using descriptive statistics, mean and standard deviation (SD). Using the ADA criteria above, age and gender variables were also grouped to construct a categorical variable. Categorical variables, including gender, were reported as frequencies and percentages. Age was categorized into four groups as follows: <18 years, 18 to 38 years, 39 to 59 years and >60 years. Chi-square test was used to calculate the statistical significance of difference in proportions amongst the categorical variables. Values were considered statistically significant when p value was <0.05. Additionally, Pakistan-specific spatial coordinates and divisions were found using the Global Administrative Areas Database (GADM) (www.gadm.org). The laboratory and hospital databases were used to construct spatial coordinates for collection sites where blood specimens were

given for analysis. Google Maps was used to gather correct spatial information in circumstances where details were absent, or verification was required. The study used Power BI software to create a provincial level choropleth map by aggregating frequencies and individual counts based on GADM's map and spatial subdivision of provinces.

Results

In this study, a total of 4,260,171 laboratory tests (HbA1c, FBG, RBG and OGTT) were studied. Figure 1 illustrates the sample categorization according to number of biochemical tests requested per individual. Out of the total biochemical tests analyzed, 88.1% were single tests and 11.9% were combination tests with the majority being single testing of HbA1c ($n=1,498,289$). The study included a total of 4,174,967 adult samples, accounting for approximately 98.0% of the total, with 85,204 children (<18 years) included, constituting about 2.0% of the samples.

Figure 1: Seven years data sample flow categorized according to diabetes diagnostic tests performed as part of panel and solo.



This flowchart illustrates the distribution of clinical samples over a seven-year period. Samples are categorized based on whether diabetes diagnostic tests were performed as individual (solo) assays or as part of a multitest panel. Classifications follow the ADA diagnostic criteria detailed in Table 1.

Out of the total ($n=4,260,171$), 35.9% ($n=1,533,523$) had increased levels of biochemical markers encompassing cases through either a single positive marker or a combination of elevated HbA1c, RBG, FBG, and OGTT results indicating diabetes as described in Table 2. Out of the total tests

conducted 20.4% ($n=872,024$) were identified as prediabetes either through either a single positive marker or a combination of elevated HbA1c, FBG, and OGTT results using ADA cutoffs. Out of total biochemical tests studied including the combination testing of the studied population had prediabetes. The majority

of diabetes cases were identified through HbA1c testing (49.7%), followed by FBG testing (24.2%). The mean adult age among diabetes cases was 48 ± 14.9 years and mean age of children were 10.2 ± 5.4 years. Age emerged as a crucial factor, with the highest frequency of diabetes and prediabetes observed in the 39-59 years age group as described in Table 3. Statistical analysis demonstrated a significant association between diabetes and both advancing age and gender, with p -values less than 0.001, highlighting the multifaceted nature of this disease's epidemiology. Frequency of diabetes and prediabetes was more in males (40.3% and 22% respectively) as compared to females (31.5% and 18.8% respectively); p value <0.001. Table 4 denotes the Multinomial

regression of diabetes and prediabetes showing significant correlation between age and gender for this cohort. For diabetes, the factor Age (RRR = 1.0562): One unit of age increases the relative risk of diabetes by 5.62%, compared to the normal group ($p < 0.001$) while in factor gender for Male (RRR = 1.4445) indicating, Males have a 44.45% higher risk of diabetes compared to females, controlling for age ($p < 0.001$). Similarly for Prediabetic category, for Age (RRR = 1.0439): One unit increase in age is associated with a 4.39% increase in the relative risk of being in the prediabetes group compared to the normal group ($p < 0.001$). As for the gender, Males (RRR = 1.1998): have a 19.98% higher relative risk of prediabetes than females.

Table 2: Total number of diabetes tests (HbA1C, OGTT, RBG, FBG) ordered categorized based on number of normal, prediabetes and diabetes ratio.

Biochemical Test	Overall n (%)	Normal n (%)	Prediabetes n (%)	Diabetes n (%)
Overall	4,260,171	1,854,624 (43.5)	872,024 (20.4)	1,533,523 (35.9)
FBG	1,514,547 (35.5)	767,648 (41.3)	374,849 (42.9)	372,050 (24.2)
HbA1C	1,498,289 (35.1)	374,052 (20.1)	361,297 (41.4)	762,940 (49.7)
RBG	737,337 (17.3)	608,517 (32.8)		128,820 (8.4)
OGTT	4,389 (0.1)	2,690 (0.14)	1,212 (0.13)	487 (0.03)
More than 1 test	505,609 (11.8)	101,717 (5.4)	134,666 (15.4)	269,226 (17.5)

For single-test evaluations, FBG, OGTT, HbA1c were treated as standard diagnostic markers. Whereas n is the number of test performed or total number of normal, diabetic and prediabetic results and % is total number of test (HbA1C/ OGTT/ RBG/ FBG) / overall test performed and total number of normal, diabetic and prediabetic results / total number of HbA1C/ OGTT/ RBG/ FBG performed respectively.

Table 3: Distribution of Prediabetes and Diabetes by Age and Gender in Clinical Laboratory Data Over Seven Years.

Age Category	Female	Female	Female	Male	Male	Male	p- value
Age Category	Total n(%)	Prediabetes n(%)	Diabetes n(%)	Total n(%)	Prediabetes n(%)	Diabetes n(%)	p- value
Overall	2,091,598 (49.0)	394,416 (18.8)	659,544 (31.5)	2,168,573 (50.9)	477,608 (22)	873,979 (40.3)	<.001
Adolescent (<18)	35,762 (1.7)	2,277 (0.57)	5,633 (0.85)	37,909 (1.7)	2,758 (0.57)	6,018 (0.6)	<0.001
Early Adulthood (18-38)	676,243 (32.3)	60,109 (15.2)	69,700 (10.5)	448,742 (20.7)	77,215 (16.1)	105,555 (12.0)	<0.001
Middle Age (39-59)	877,922 (41.9)	196,147 (49.7)	354,054 (53.6)	1,097,456 (50.6)	252,271 (52.8)	486,543 (55.6)	<0.001
Old Age (≥ 60)	501,671 (23.9)	122,570 (31.0)	230,157 (34.9)	584,466 (26.9)	145,364 (30.4)	275,863 (31.5)	<0.001

Chi square test significant association ($p < 0.001$) is used, in female, diabetes and prediabetes are significantly associated with age categories. As well as male also show significant difference between age categories with prediabetes and diabetes

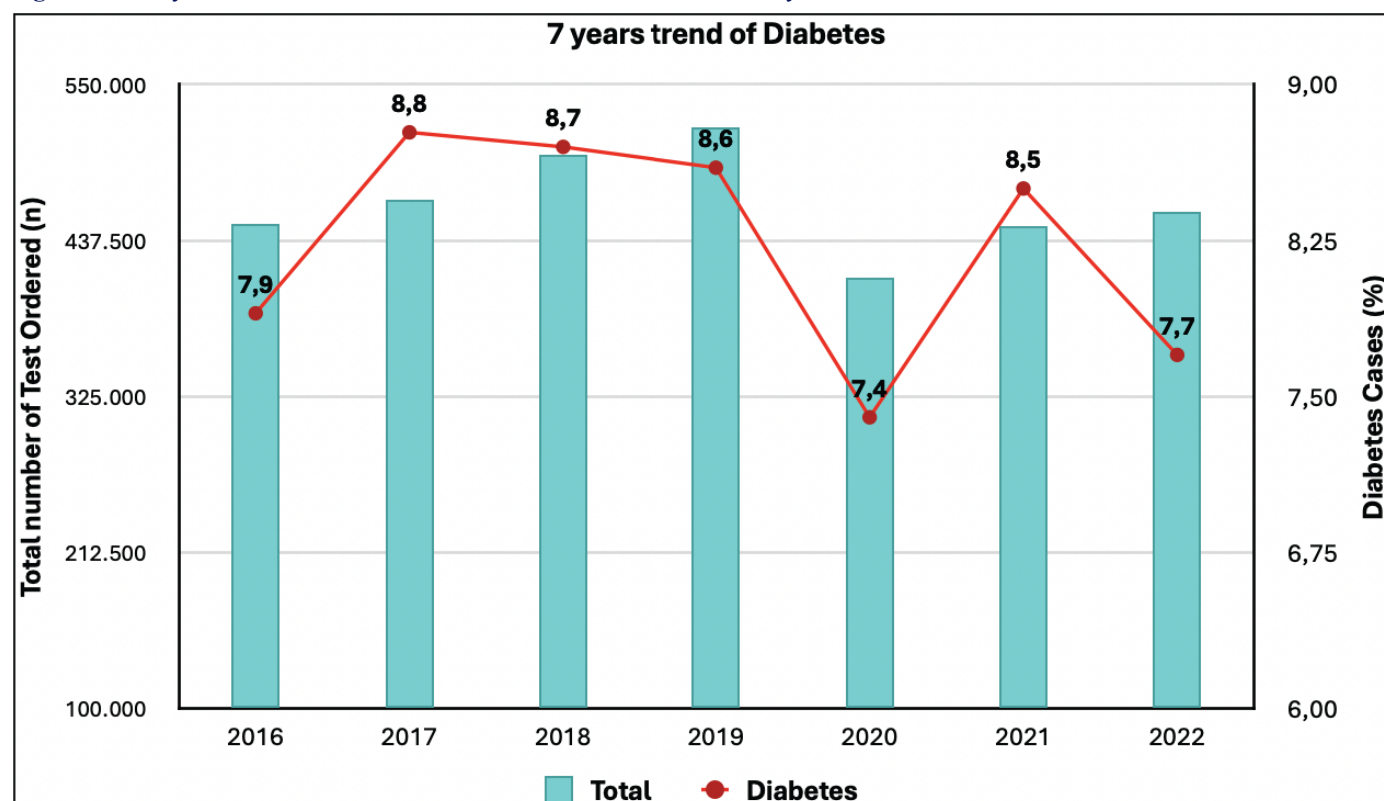
Table 4: Multinomial Regression of Diabetes and Prediabetes Data, Showing Significance between Age and Gender.

Outcome Category	Variable	RRR	Std. Error	z-value	p-value	95% CI Lower	95% CI Upper
Prediabetes	Age	1.044	0.000	251.100	<0.001	1.044	1.044
	Male (ref: Female)	1.200	0.006	37.980	<0.001	1.189	1.211
	Constant	0.119	0.001	-247.05	<0.001	0.117	0.121
Diabetes	Age	1.056	0.000	356.020	<0.001	1.056	1.057
	Male (ref: Female)	1.445	0.006	87.080	<0.001	1.433	1.457
	Constant	0.123	0.001	-272.59	<0.001	0.121	0.125

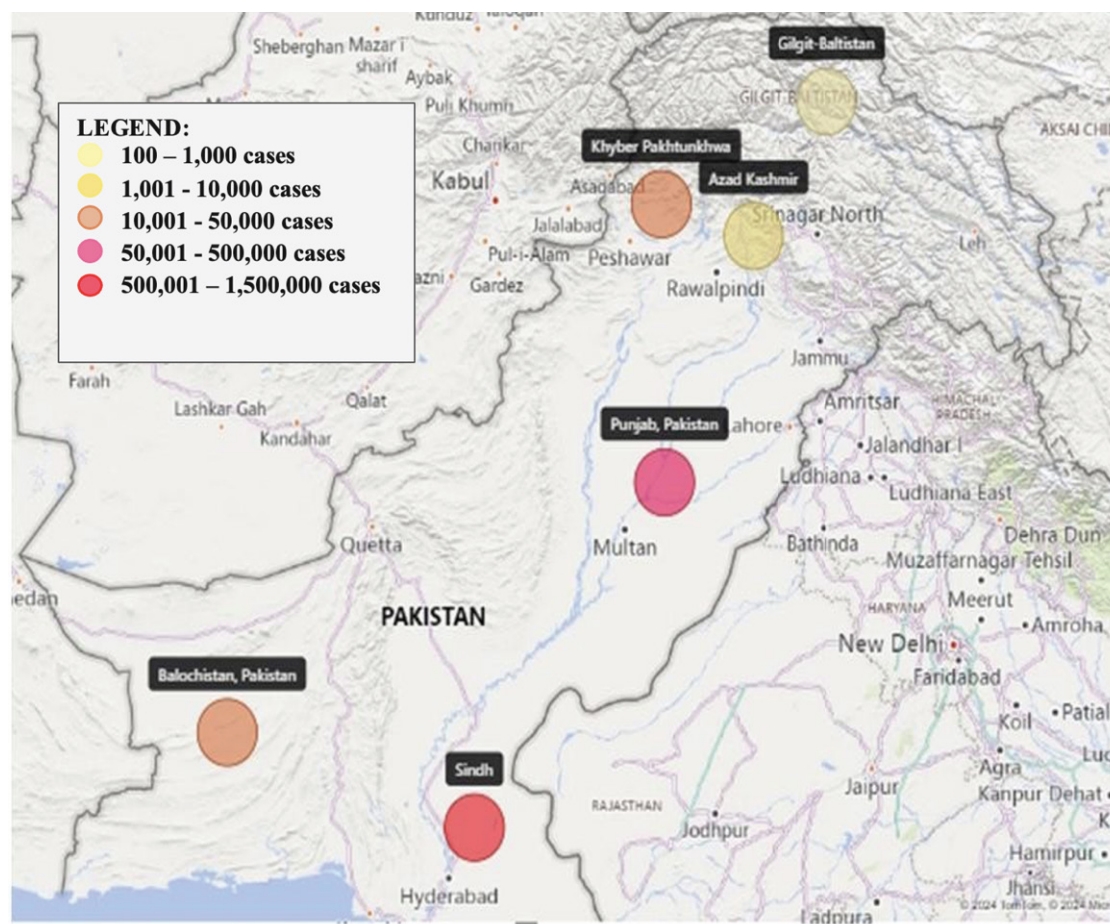
Age significantly increases the risk of both prediabetes and diabetes. Males are significantly higher risk than females for both conditions. All predictors are statistically significant at $p < 0.001$.

Figure 2 denotes the trend of diabetes within country; the graph shows the constant rise of the diabetes case till 2019 maintaining the fluctuation and hike at least from recent years. The choropleth map (Figure 3) shows the cases with diabetes from different regions of Pakistan indicating 214 cases of diabetes were reported from Gilgit-Baltistan, 4,918

cases from Azad Jammu Kashmir (AJK), 46,905 cases from Balochistan, 45,952 cases from Khyber Pakhtunkhwa (KPK), 351,221 cases from Punjab and 1084,313 cases from Sindh. There were additional samples with missing or inadequate location data that could not be traced.

Figure 2: Yearly Pattern of Diabetes Cases Identified in Clinical Laboratory Data Over Seven Years.

Cases in Figure 2 were identified from clinical samples across Pakistan and analyzed at a central laboratory. Classification was based on American Diabetes Association (ADA) diagnostic criteria, as detailed in Table 1.

Figure 3: Choropleth Map Showing Distribution of Diabetes Cases by Province in Clinical Laboratory Data Over Seven Years.

This map illustrates the prevalence of diabetes across provinces based on clinical laboratory records. Cases were identified using ADA diagnostic criteria: Color intensity represents the concentration of cases, with darker shading indicating a higher volume of identified individuals. Data were processed in a central clinical laboratory from samples collected nationwide.

Discussion

In this study, conducted on a sample set of approximately 4.2 million laboratory specimens, the period prevalence of diabetes emerged as a significant health concern, with 35.9% of the cases affected. Our data depicted that males are at higher diabetes rate (40.3%) than female while in terms of age, a higher rate of diabetes was observed in middle-aged men (55.6%) as compared to middle aged females (53.6%). In prediabetics, similar ratio was observed with males having slightly higher ratio than females with the highest prediabetic ratio seen in middle-aged male group. This data analysis found that gender and age were significant predictors of hyperglycemia and prediabetes, which can be considered a risk factor for diabetes. The COVID-19 pandemic most likely attributed to a temporary drop in the trend line of diabetes prevalence in 2020 when routine screening rates declined followed by an unstable recovery.

The IDF Diabetes Atlas 2022, Pakistan ranks number one, with highest prevalence of diabetes 31%, with projection of prevalence over 34% keeping it at the top position in 2045 (3). The Pakistan National Diabetes Survey showed that in urban areas 9.83% of women and 12.14% of men had diabetes. Furthermore, impaired glucose tolerance was present in 9.54% of females and 4.54% of males [14]. Studies indicated that the prevalence of glucose intolerance is high in the Pakistani population. Local data

assessed from current studies also showed that Sindh and Punjab have the highest reported diabetes cases and similarly have higher risk prevalence of diabetes [15]. According to studies prevalence of diabetes was 26.3%, with 19.2% known and 7.1% newly diagnosed. Urban areas have 28.3% prevalence, while pre-diabetes is 14.4%, the reported mean age (greater than or equal to 43 years) was similar coinciding with our studies [16]. Key factors for higher period prevalence of diabetes in Sindh and Punjab include urbanization causing sedentary lifestyles and unhealthy diets, high obesity rates, and the shift to urbanization. Cities like Karachi, Hyderabad, Lahore, Islamabad, Multan and Faisalabad have better access to healthcare facilities and clinical laboratories. A larger middle and upper class in these provinces can afford health check-ups, and many health awareness programs are active in the region.

The National Diabetes Survey shows an increase in type 2 diabetes and Impaired Glucose Tolerance (IGT) prevalence with age in both sexes, consistent with other South Asian studies [17] it further indicates that at national level while the prevalence of impaired glucose tolerance (IGT) is higher in women than in men, the prevalence of diabetes is higher in men. Diabetes in Pakistan women presents a complex, multidimensional scenario.

Sociocultural barriers, limited healthcare access, and the metabolic stress of multiparity risk higher morbidity and mortality rates. Gestational Diabetes Mellitus (GDM) can serve as a blessing in disguise for early diagnosis and intervention. It shall sensitize multi-stakeholders for prevention of T2DM focusing on a healthy lifestyle at comparatively younger age group, and in turn also addressing interventions for child hood obesity, GDM shall be integrated into maternal and child health (MCH) care programs [18, 19].

Subsequently, the laboratory data showed that even children (<18) were also diagnosed with diabetes and at-risk status (pre diabetes) was also observed, though the data availability was limited but it was still indicative of the impelled effects of diabetes. A study conducted in 2010 estimated that though the actual number of diabetic children within the country is unknown still it was approximated that around 61,196 children are affected with an increment in this figure in every passing year [20]. Diabetes risk in children increases with high BMI, blood pressure, and larger waists, influenced by factors like genetic predisposition, urbanization, lifestyle changes, obesity, malnutrition, depression, and socio-cultural issues [21,22]. The country's choropleth map for diabetes highlights significant regional disparities in the reported cases of diabetes. This geographic distribution emphasizes the importance of focused public health measures for diabetes, including healthy diet, regular exercise, diabetes education, screenings, and healthcare access in the most affected areas, primarily in Sindh and Punjab. These findings raise important questions about the underlying factors contributing to the regional disparities in diabetes prevalence. More large-scale longitudinal research is needed to answer the question of whether environmental, socioeconomic, or lifestyle factors are driving these developments in various provinces of Pakistan.

The study conducted has its own limitations as it is a cross sectional study, anthropometric measurements, clinical history, lifestyle factors and dietary intake were not available and no follow up was carried out on these individuals. The fact that this article includes a significant number of patients who represent both urban and rural populations makes it possible to generalize the findings throughout Pakistan, which is one of its strengths. The choropleth map also clearly illustrates the disease burden, emphasizing the necessity of focused interventions. The absence of a specific database or registry is still a drawback, though.

Conclusion and Call to Action

According to the data, age is positively associated with both prediabetes and diabetes. Males are at significantly higher risk for both prediabetes and diabetes compared to females. Middle-aged men reported more positive cases, which means they are at higher prevalence of risk. Nonetheless, the percentage of females is not far behind, and a significant number of cases have also been reported among women. Sindh and Punjab showed the higher risk of diabetes while may be due to data unavailability from their provinces the Pakistan population tendency to become diabetic cannot be ruled out. As age increases, non-communicable diseases increase, necessitating efficient and diligent treatment.

Human resources and evidence-based solutions are crucial, prompting multi-stakeholder action.

The current study highlights the need for establishing a national multi-center diabetes database using identical, consistent definitions and data collection methods for prevalence and incidence of diabetes across different times, locations, and standardized frequency measures. To facilitate robust cross-study comparisons and ensure the validity of longitudinal analyses, it is imperative to establish a standardized diabetes reporting framework for prevalence and incidence. A key component of the creation of a comprehensive digital database for both pre-diabetics and diabetics, can also be promoting active, real-time management and facilitating personalized lifestyle modifications and care.

Authors' contributions

YS substantially contributed to the conception, design of the work, data acquisition, analysis and interpretation, and drafted and revised the paper. LJ designed and conceptualized the work, acquired the data, and contributed to drafting and revising the paper. SA, ZN, AS substantively analyzed and made significant contributions to the revision of the work. BH, SBZN revised the data analysis and manuscript. AS primarily works on data decoding and statistical analysis. AH, IS and HM contributed to manuscript revision. All authors read and approved the final manuscript.

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Disclosure of Ethical Statements

Approval of the research protocol: An exemption has been acquired from the institutional ethical review committee (Exemption number 2023-8559-24624).

Informed Consent: N/A

Approval date of Registry and the Registration No. of the study/trial: N/A Animal Studies: N/A

Disclosure

The authors declare that they have no competing interests, and No funding was received for conducting this study.

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