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The Role of high Allostatic Load in the Progression of Type 2 Diabetes

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Ethics approval: Ethical Review: The ethical considerations were approved by the Departmental Doctoral Program Committee (DDPC), Institute of Social and Cultural Studies, Letter No. D/119/ISCS. Punjab University in Lahore. The study's objective was thoroughly clarified and provided information to each participant. All the individuals enrolled in the study provided written informed consent. The recruitment of patients and data collection both adhered to the Helsinki Declaration's ethical principles.

Consent to participate: The purpose of the study was explained to the Diabetic Patients, and those who were given consent to participate were included in the research. The confidentiality of the participants was ensured by concealing their identical information and code numbers used instead of their real names, such as (M1, M2), and deleting identifiable data from the transcript.

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Abstract:

Background: Diabetes mellitus type 2 is a chronic disease characterized by a metabolism disturbance. An allostatic load measures cumulative wear and tear on the body in response to chronic stress and has been linked to the development and progression of T2DM. **Objectives:** This study was to determine the relationship between allostatic load, Dietary pattern, and diabetes. Another purpose was to assess the impact of dietary patterns on allostatic load and diabetes risk. **Methods:** A descriptive observational study based on a questionnaire completed by 350 patients aged 30 to 55 diagnosed with type 2 diabetes mellitus was conducted for three months. Anthropometric measurements and laboratory investigations were conducted to assess primary and secondary outcomes. The statistical analysis used the mean \pm standard deviation and applied logistic regression analysis to determine the association between different risk factors (allostatic load, nutritional status, BMI, CRP, and total cholesterol) and the outcome of uncontrolled diabetes. **Results:** The allostatic load was a significant predictor of uncontrolled diabetes, with a regression coefficient of 0.191 ($p = 0.0017$) and an odds ratio of 2.19. Nutritional status, BMI, CRP, and total cholesterol were insignificant predictors. The odds ratios for these variables were 0.90, 1.09, 0.70, and 1.93, respectively, with wide confidence intervals that included the possibility of no effect. The chi-square test showed a significant association between diabetes control status and allostatic load ($p = 0.0017$).

Keywords: Allostatic Load, Allostasis, Diabetes Mellitus Type 2 (T2DM), Glycaemic Control, Nutritional Status, Chronic Stress, Dietary patterns.

Introduction: Due to its significant morbidity, mortality, and financial burden, type 2 diabetes is becoming more and more prevalent worldwide, raising concerns about public health. Genetic, environmental, and lifestyle factors contribute to T2DM (World Health Organization, 2023). Allostatic load, which describes the cumulative physiological burden of chronic stress on various body systems, is one of the emerging concepts in this study of diabetes.

T2DM and chronic illnesses like cancer and cardiovascular disease have been associated with allostatic load. Allostatic load, diet, and diabetes all have intricately and varied relationships with one another (Macit & Acar-Tek, 2019). On the other hand, dietary elements can influence how the body reacts to stress and may lower the risk of developing diabetes in people with high allostatic loads (Khodarahimi, 2021). Malnutrition and poor dietary habits can increase the risk of developing diabetes by increasing the allostatic load (Gomez, 2022). Stress significantly impacts the endocrine system and can interfere with the body's cortisol release. Cortisol release can be affected by this disturbance, with morning cortisol levels

dropping and evening cortisol levels rising (Edes, 2021). The larger allostasis model, which is based on the regulation and stability reactions of the body to stressful stimuli, includes allostatic load (Wang, 2022).

According to recent research by Sousa (2022), poor lipid profiles, elevated HbA1c, and metabolic disorders like high BMI have all been linked to poor metabolic profiles. Chronic stress can impair physical function, and climate change has also impacted individuals' health impacted by climate change. Scales have been created to determine the allostatic load and metabolic outcomes. Type 2 diabetes mellitus can be avoided by managing obesity through regular exercise and a healthy diet high in fiber and low in sugar. However, medication, such as metformin, is advised when these measures do not sufficiently lower blood sugar levels (Adegoke, 2021).

It is essential to assess past, present, and future research, determine the burden on patients, and develop preventive strategies to lessen the effects of the disease to address the problems brought on by T2DM and its complications. To achieve this, the collaboration between healthcare organizations, academia, and public health policy advocacy organizations this study aims. This study aims to ascertain the relationship between allostatic load, diet, and diabetes. The effect of dietary habits on allostatic load and diabetes risk was a further objective. The authors anticipate that the findings of this study will aid in the search for dietary interventions that could enhance glycaemic control and lessen the complications of diabetes in people with high allostatic load.

Methods

Study design: The participants in this research study with Type 2 Diabetes Mellitus (T2DM) between the ages of 30 and 55 completed questionnaires using a descriptive observational approach.

Sample size: 350 male and female participants represented the study sample, which was selected to ensure a 5% margin of error and a 95% confidence level regarding the prevalence of Type 2 Diabetes Mellitus (T2DM) in this population. $\text{Sample size} = (1.96^2 * 0.5 * (1 - 0.5)) / 0.05^2 = 384$.

Study setting: The most populous and significant metropolitan area in Pakistan, Lahore, receives many referrals for T2DM patients from primary and secondary hospitals. Patients with Type 2 Diabetes Mellitus (T2DM) are referred to tertiary care hospitals by primary and secondary care facilities in Punjab due to their high patient volume. Patients between the ages of 30 and 55 receiving T2DM treatment at different diabetic treatment facilities in Lahore, including Diabetic Medical Centre (DMC) at Services Hospital, Sakina (Begum) Institute of Diabetes and Endocrine Research (SIDER), and Jinnah Allama Iqbal Institute of Diabetes and Endocrinology (JAIDE) at Jinnah Hospital, were included in the study.

Sampling technique: Non-probability Purposive Sampling was the sampling method employed for this study, and it involved purposefully choosing participants who met specific inclusion criteria based on their relevance to the study's objectives.

The inclusion-exclusion criteria: While excluding individuals with cancer and diabetic renal disease, the study's participants for the inclusion criteria were males and females between the ages of 30-55 and were previously diagnosed with type 2 diabetes mellitus.

Data Collection Procedure: Once the study synopsis was approved, information was gathered using a questionnaire from a minimum of 384 patients. Data was gathered using a specially designed questionnaire that had three sections. Three months were dedicated to conducting the study. Questions about diabetes history and sociodemographic information formed the first section. Stress factors and nutritional status were the main topics of the second section. The third section, however, concentrated on quantifying the allostatic load using biomarkers like BSR, HbA1c, BMI, CRP, HDL cholesterol, and total cholesterol. The questionnaire's reliability and validity were evaluated prior to being utilized.

Anthropometric Assessment: Anthropometric measurements were used to calculate BMI using the formula weight in kilograms (or pounds) divided by height in meters squared. The data that emerged was then recorded for analysis.

Stress and Dietary Pattern Assessment: To determine stress levels, The Perceived Stress Scale (PSS), which the researcher filled out in the English version, was used in conjunction with a Likert scale. Participants were asked a series of questions, and their answers were given numerical values. A scale called the Healthy Eating Index (HEI) was used to determine nutritional status. This technique assesses the frequency, intensity, or seriousness of nutrition-related behaviors and the frequency, intensity, or seriousness of stress. An overall score is calculated from the sum of the scores for each question; higher scores denote higher levels of the measured construct.

Allostatic load Scoring: The allostatic load was calculated by scoring biomarkers, with each biomarker assigned a score of 1 for high-risk values, 0.5 for moderate-risk values, and 0 for low-risk values. An allostatic load score above five was considered significant (Liu J., 2021).
Figure 1

Laboratory Assessment: All blood samples from the participants were sent to the pathology department of the Allama Iqbal Medical College, Jinnah Hospital Lahore, where they were tested for BSR, HbA1c, CRP, HDL cholesterol, and total cholesterol using the BECKMAN COULTER AU4800 chemical analyzer. Blood samples were taken from the study population by trained staff with consent.

Statistical analysis: To assess the relationship between various risk factors, such as allostatic load, nutritional status, BMI, CRP, and total cholesterol, and the outcome of uncontrolled diabetes, logistic regression analysis was applied in this study. Regression analysis, chi-square tests, p-values, odds ratios, and 95% confidence intervals were used to investigate the relationship between each risk factor and the result.

Results Table 1. Descriptive Statistics of Socio-demographics of a Population (N=384)

Description: The table presents the percentage and valid percentage of sociodemographic variables such as age, gender, ethnicity, socioeconomic status, and education.

Table 2. Presents the survey results assessing the food behavior and diabetes risk factors for a population. The table includes responses to questions about stress, sleep, physical activity, hunger, food cravings, knowledge of nutritional value, and self-care behaviors related to diabetes management.

Table3. The effect and outcome of food behaviors on controlled and uncontrolled diabetes were evaluated. To correlate diabetes with the dietary pattern of the population

Table 4. Outlines the risk levels, cut-off values, percentage, mean, and standard deviation for various markers used in a study assessing allostatic load and diabetes. The markers include blood sugar level (BSR), glycated hemoglobin (HbA1c), body mass index (BMI), C-reactive protein (CRP), high-density lipoprotein (HDL) cholesterol, and total cholesterol. The scoring of the allostatic load is also included in the table, with risk levels categorized as high, moderate, or low based on the number of risk factors present.

Table 5. Logistic regression analysis of risk factors for uncontrolled diabetes.

Discussion: This research study and research conducted by Abioye et al. (2021) both explored the relationship between allostatic load and diabetes but with different approaches. The higher allostatic load was significantly associated with uncontrolled type 2 diabetes mellitus by Abioye et al. (2021). This current research focused on calculating the allostatic load score using biomarkers, which showed that more than 50% of a strong association was also found load score. Interestingly, it was also discovered a strong association between the prevalence of allostatic load and chronic diseases.

According to Ahmad et al. (2021), patients in Pakistan with uncontrolled type 2 diabetes mellitus had poor nutritional sufficient intakes of protein, energy intake, and micronutrients. This emphasizes the necessity of interventions to enhance patients' nutritional status and health outcomes. The relationship between allostatic load, nutritional status, BMI, CRP, total cholesterol, and uncontrolled diabetes was investigated in this research. In response to our research, allostatic load significantly increases the likelihood of having uncontrolled diabetes by a factor of 2.19 for every unit increase in allostatic load. The other predictor variables, such as nutritional status, BMI, CRP, and total cholesterol, were not reliable indicators of uncontrolled diabetes, on the other hand. The significance of considering allostatic load as a potential marker for identifying patients with uncontrolled diabetes is highlighted by these findings.

Unsupervised machine learning was used in Bej et al. (2022) study to identify subpopulations of type 2 diabetes patients, highlighting the need for tailored interventions to enhance outcomes. BSR, HbA1c, BMI, CRP, HDL cholesterol, and total cholesterol were markers used in the current research to evaluate participant levels of allostatic load and diabetes risk.

It was discovered that a sizeable portion of participants had high or moderate levels of risk for different markers. For example, 15.02% of participants had a high-risk BMI, 40.29% had a high-risk BSR, and 40.28% had a high-risk HbA1c. Additionally, 50.98% of participants had normal-risk levels for CRP, 53.29% had moderate-risk levels for total cholesterol, 47.02% had high-risk levels for CRP, 63.02% for HDL cholesterol, and 35.02% for total cholesterol.

As stated in Chae et al. (2022) research, type 2 diabetes mellitus and its complications, such as diabetic neuropathy and retinopathy, are associated with higher allostatic load. The focus of this research, on the other hand, was depending on several factors related to managing diabetes and nutritional behavior, such as stress, sleep, physical activity, food cravings, confidence in making healthy food choices, frequency study aimedgetables, and consumption of sugary or high-fat foods. The purpose of the study was to assess respondents' knowledge of food nutrition, how frequently they checked their blood sugar levels, and how they cared for themselves living with diabetes.

In contrast, to current research, responses were divided into five categories: always, frequently, occasionally, sometimes, and never. For example, 13.82% of respondents said they were constantly stressed, while 7.09% said they were never stressed. In the same way, 31.07% of respondents said they had never felt overwhelmed, while 5.09% said they had experienced being overwhelmed.

The results highlight the need for improvements in several areas, including raising levels of physical activity and lowering consumption of high-sugar and high-fat foods to improve eating habits and diabetes management. As a risk factor for type 2 diabetes mellitus and its complications, Chae et al. emphasizes the significance of managing allostatic load (Chae, 2022).

In a study published in 2021, Diaz et al. investigated the link between uncontrolled hypertension, uncontrolled glucose, and the risk of developing chronic kidney disease. The study's findings that uncontrolled diabetes and hypertension were significantly associated with chronic kidney disease underscore the significance of managing these risk factors early on (Diaz, 2021). This research utilized BMI as a metabolic indicator. High-risk participants (BMI > 30), moderate-risk participants (BMI 25–30), and low-risk participants (BMI 18–25) were divided into three risk categories. According to the findings, 15.02% of participants were in the high-risk category, 41.34% in the moderate-risk category, and 52.098 in the low-risk category. This suggests that a sizeable portion of the population may be at risk for hypertension linked to high BMI levels. Therefore, to improve o to improve overall health outcomes, interventions to reduce BMI and related risk factors may be required.

It should be acknowledged that the study's three-month duration may not have allowed for a thorough examination of the long-term impacts of dietary habits and other risk factors on the likelihood of developing diabetes. Furthermore, the absence of a control group may make it more challenging to conclude the causal relationships between different risk factors and the likelihood of developing diabetes. It is crucial to recognize that the research was restricted to individuals with Type 2 Diabetes between the ages of 30 and 55, which may limit the applicability of the findings to other age groups. Even though the study had some limitations, future researchers can address these problems by modifying the study design and adding more variables.

The study's strengths include its analysis of how dietary habits and other risk factors affect Type 2 Diabetes, a serious affecting millions of individuals worldwide. In addition, 350 participants represented a sizable sample, and a wide range of measurements were used to evaluate various risk factors. The study's prospective design further minimizes any potential biases that may develop in retrospective studies. The study's importance for future research and potential impact on public health is highlighted in part by its potential implications for public health policies and interventions that aim to manage or prevent Type 2 Diabetes.

Conclusion: Allostatic load and diabetes control status seemed to be significantly correlated. This research emphasized the need for interventions to lower the risk of diabetes and enhance general health. Dietary habits, allostatic load, and diabetes risk are related, which may help guide future interventions to manage and prevent type 2 diabetes. Allostatic load results can be lowered by eating a nutritious diet that complies with the guidance of lowering body weight, waist/hip ratio, blood pressure, and fasting blood glucose—long-term malnutrition in T2Dso help to mitigate the detrimental effects of stress on metabolic functions.

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Figure 1

Clinically relevant biomarkers and their values			
System	Markers	High Moderate low risk	Scores
Cardiovascular	Total cholesterol	>=240 mg/dl	1
		200 to 239 mg/dl	0.5
		<200 mg/dl	0
	HDL cholesterol	>=40 md/dl	1
		40 to 59 mg/dl	0.5
		<60 mg/dl	0
Total/ HDL	>=6,5	1	
	<6	0.5	

		<5	0
	Glycated hem	>= 6.5%	1
		5.7 to <6.5%	0.5
		< 5.7%	0
Metabolic	Waist-hip ratio (women)	>=0.85m	1
		>0.80 to <0.85	0.5
		<=0.80m	0
	Waist-hip ratio (men)	>=1.0	1
		>0.95 to < 1.0	0.5
		<=0.95	0
	Body mass index	>= 30 kg/m ²	1
		25 to < 30 kg/m ²	0.5
		18 to <25 kg/m ²	0
	Albumin	<3%	1
		3 to 3.8%	0.5
		>=3.8%	0
Inflammatory	C-reactive protein	>3 mg/L	1
		1 to 3 mg/L	0.5
		< 1mg/L	0

Table 1. Socio-demographics of the population

Descriptive statistics of socio-demographics of population, N=350		
	N	percent
Age		

	30-40	53	15.001
	40 above	297	85.018
Gender			
	Male	243	69.571
	Female	107	30.833
Ethnicity			
	Rural	159	45.428
	Urban	191	55.571
Socioeconomic status			
	Upper	41	11.666
	Middle	114	32.500
	Low	195	55.833
Education			
	Uneducated	128	36.666
	Primary	109	30.833
	Secondary	113	32.500

Note: This table provided information on the sociodemographic characteristics of a population sample of 384 individuals. It included data on age, gender, ethnicity, socioeconomic status, and education.

Table 2. Dietary pattern assessment and Correlation of Stress and food behaviors

Assessment of food behavior of the population for the regulation of diabetes					
	Always	Often	Sometimes	Occasional	Never
How often do you experience stress in	13.82	10.98	40.14	20.97	7.09

your daily life?					
How often do you feel overwhelmed by your responsibilities or obligations?	5.09	25.075	22.09	38.96	31.07
How often do you have trouble falling or staying asleep?	34.08	21.97	19.03	20.87	3.01
How physically active are you regularly?	6.02	13.73	48.01	38.09	2.07
How often do you feel tired during the day?	54.09	12.09	10.65	7.15	3.10
How often do you feel hungry or crave certain foods?	17.08	15.02	56.38	14.03	2.09
How confident are you in your ability to make healthy food choices?	53.08	17.09	12.76	7.09	--
How often do you eat fruits and vegetables?	70.17	13.02	--	--	--
How often do you consume sugary or high-fat foods?	4.09	13.02	10.98	38.02	39.21
how knowledgeable do you feel about the nutritional value of the foods you eat	20.98	40.91	13.26	--	--
how often do you monitor your blood sugar levels (for those who have been diagnosed with diabetes	60.12	28.91	12.01	9.1	2.19
How often do you engage in self-care behaviors such as monitoring your blood sugar levels, taking medications, or attending appointments with	30.18	20.92	18.94	19.02	--

healthcare providers (for those diagnosed with diabetes)?					
How confident are you in your ability to manage your diabetes or prevent the development of diabetes?	11.09	9.02	15.03	34.02	29.01
How much do you think stress, sleep, and physical activity impact your risk for developing type 2 diabetes?	2.02	3.19	17.02	74.01	6.01

Note: The survey covered various aspects, including stress, sleep, physical activity, food cravings, confidence in making healthy food choices, frequency of eating fruits and vegetables, and consumption of sugary or high-fat foods. It also evaluated respondents' knowledge about the nutritional value of foods, frequency of monitoring blood sugar levels, and self-care behaviors for those with diabetes. The survey categorized responses into five levels: always, often, sometimes, occasionally, and never. For instance, 13.82% of respondents reported experiencing stress constantly, while 7.09% reported never experiencing stress. Similarly, 5.09% of respondents reported feeling overwhelmed by responsibilities, while 31.07% reported never feeling overwhelmed. The survey findings suggest areas for improvement, such as increasing physical activity levels, and reducing sugary and high-fat food consumption, to improve food behavior concerning diabetes regulation.

Table3. Effect and outcome of food behaviors on controlled and uncontrolled diabetes

Inferential statistics for nutritional status and diabetes control					
Dietary pattern	percent	Diabetes	Percent	Chi-square X²	p-value
Good to average	62.198	Controlled	41.985	82.91	0.001
		Uncontrolled	20.231		
poor	38.032	Controlled	11.382		
		Uncontrolled	26.47		

Note: The survey finalized that the population with good nutritional status tend to have a more stable control of diabetes mellitus type 2

Table 4. Calculation of risk levels of biomarkers and allostatic load scoring

The markers included in the study for the assessment of allostatic load and diabetes					
Risk factor	Risk level	Cut off value	Percentage	Mean	SD
BSR					
	High	(BSR > 140)	37.714	40.29	3.10
	Moderate	(BSR 100-140 mg/dl)	18.998	25.01	3.92
	Low	(BSR 80 – 100 mg/dl)	42.285	50.28	4.23
HbA1c					
	High risk	>= 6.5%	39.238	40.28	3.23
	Moderate risk	5.7 to <6.5%	40.432	40.92	4.21
	Low risk	>= 5.7%	42.991	40.12	3.98
BMI					

	High risk	Obese (BMI > 30)	11.710	15.02	3.19
	Moderate risk	Overweight (BMI 25 - 30)	37.560	41.34	4.19
	Low risk	Normal (BMI 18 - 25)	52.098		
CRP					
	High	(CRP>1)	36.780	47.02	5.17
	Normal	(0.9 g/dl)	64.090	50.98	4.29
HDL cholesterol					
	High risk	<60 mg/dl	52.078	63.02	3.19
	Moderate risk	40 to 59 mg/dl	37.765	37.17	3.82
	Low risk	>=40 mg/dl	9.238	20.91	4.02
Total cholesterol					
	High risk	>=240 mg/dl	31.0	35.02	3.10
	Moderate risk	200 to 239 mg/dl	47.0	53.29	4.19
	Low risk	<200 mg/dl	22.089	25.92	5.29
Scoring of allostatic load					
	High risk	< 5	53.142	50.24	3.91
	Moderate risk	<3 or >5 or 5	25.428	30.19	3.45
	low risk	> 3	21.428	28.18	3.10

Note: The markers included in the study were BSR, HbA1c, BMI, CRP, HDL cholesterol, and total cholesterol. Results indicated many participants were at high or moderate risk for

diabetes and allostatic load. For BSR, 40.29% of participants had a high-risk level. Regarding HbA1c, 40.28% of participants were at a high-risk level, while 40.92% were at a moderate-risk level, and in interpreting BMI, 15.02% were at a high-risk level. Concerning CRP, 47.02% of participants were at a high-risk level, while 50.98% were at a normal-risk level. For HDL cholesterol, 63.02% of participants were at a high-risk level, and for total cholesterol, 35.02% of participants were at a high-risk level, while 53.29% were at a moderate-risk level. The allostatic load was scored based on the sum of risk factors, with 50.24% of participants at the high-risk level. These results indicate a need for interventions to reduce diabetes risk and improve overall health.

Table 5. Regression Model Analysis, And Calculation Of Chi-Square Test, P Vales, And Odds Ratio With CI 95%

Outcome (uncontrolled diabetes)	Regression coefficient	Chi-square X²	P value	Odds ratio (95% CI)
Intercept	-3.017	40.32	0.031	
Allostatic load	0.191	63.09	0.0017	2.19 (0.56, 12.640)
Dietary pattern	-0.170	82.91	0.146	0.90 (0.217, 3.241)
BMI	0.051	38.621	0.761	1.09 (0.23, 2.171)
CRP	0.061	32.513	0.346	0.70 (0.81, 3.109)
Total cholesterol	-0.0261	11.0029	0.567	1.93 (0.898, 1.023)

Note: The table presents the results of a logistic regression analysis examining the relationship between allostatic load, Dietary pattern, BMI, CRP, total cholesterol, and the outcome of uncontrolled diabetes. The results show that allostatic load is a statistically significant predictor of uncontrolled diabetes (p=0.0017), with a positive regression coefficient of 0.191. This means that, for each one-unit increase in allostatic load, the odds of having uncontrolled diabetes increase by a factor of 2.19, although the 95% confidence interval (0.56, 12.64) is quite broad. The other predictor variables (nutritional status, BMI, CRP, and total cholesterol) are not statistically significant predictors of uncontrolled diabetes (p>0.05). However, the wide confidence intervals for the odds ratios suggest that caution should be exercised when interpreting these results.