



“UNRAVELING THE GENETIC AND ENVIRONMENTAL LINK BETWEEN OBESITY AND DIABETES: STUDY TO IDENTIFYING METABOLIC BIOMARKERS FOR EARLY DETECTION OF OBESITY AND TYPE 2 DIABETES”

Tariq Attique^{1*}, Rizwan Zafar Ahmad², Shazia³, Asifa Karamat⁴, Abdur Rahman Zaheer⁵, Amna Riaz⁶

^{1*}Senior Registrar, Department of Medicine, FPGMI, Shaikh Zayed Hospital, Lahore

²Professor & Head of Department, Medical Unit 2, Akhtar Saeed Medical and Dental College, Farooq Hospital, Lahore

³Assistant Professor, Department of Pulmonology, Rawal Institute of Health Sciences, Islamabad

⁴Associate Professor, Department of Pulmonology, Al Aleem Medical College, Gulab Devi Teaching Hospital, Lahore

⁵Senior Registrar, Department of Pulmonology, Al Aleem Medical College, Gulab Devi Teaching Hospital, Lahore

⁶Assistant Professor & Head Department of Endocrinology, Al Aleem Medical College, Gulab Devi Teaching Hospital, Lahore

***Correspondence Author:** Tariq Attique

*Email: tariqattique@gmail.com, Cell: +92 321-4066800

Abstract

Introduction:

Obesity and diabetes mellitus are two interconnected health conditions that have reached epidemic proportions worldwide. Obesity and diabetes mellitus (DM) represent two intertwined public health crises of the modern era. While environmental factors like diet and physical activity are pivotal, genetic predisposition also plays a significant role in the development of these conditions.

Objective:

1. To examine the genetic and environmental factors associated with obesity and diabetes.
2. To identify biochemical and clinical markers for early detection of these conditions.

Material and Methods: This cross-sectional study investigates the genetic, environmental, biochemical, and clinical factors linking obesity and DM. Data were collected from a representative sample of 300 individuals to identify key genetic markers, environmental influences, early metabolic biomarkers, clinical parameters and metabolomic markers associated with these conditions.

Results: There were 300 participants who included in this research after inclusion and exclusion criteria in which 25 were male and 35 were females with mean age 40 as obesity is concerned. The non obese persons include 40 were males and 50 females with mean age 37. The diabetic labeled persons include 40 each male and females with mean age 42 and non diabetic include 45 males and 25 were females with mean age 39. The other parameters include biochemical, clinical, environmental and metabolomic showing significant results.

Conclusion: In conclusion, this review highlights the complex interplay between genetic, environmental, and lifestyle factors contributing to the development of obesity and diabetes

mellitus. The findings of this review demonstrate significant health disparities between individuals with obesity and diabetes mellitus and non-obese and non-diabetic individuals, emphasizing the need for early intervention, personalized medicine approaches, and further research.

Keywords: Obesity, Diabetes Mellitus, Genetic factors, Public health, Environmental factors

Introduction:

Obesity and diabetes mellitus are two major public health concerns that have significant economic, social, and health implications. The prevalence of obesity has more than tripled since 1975, while diabetes affects over 460 million people globally. The complex interplay between genetic and environmental factors contributes to the development of these conditions, making it challenging to manage and treat them effectively. The global rise in obesity and diabetes mellitus (DM), particularly type 2 diabetes has become a significant public health concern, with both conditions contributing substantially to morbidity and mortality worldwide. Obesity is a major risk factor for T2DM, with excess adiposity triggering insulin resistance, chronic inflammation, and metabolic deregulation. The synergistic relationship between obesity and diabetes is influenced by genetic predispositions, environmental exposures, lifestyle choices, and biochemical abnormalities, forming a complex network of interactions^(1, 2).

Understanding the dual epidemic requires dissecting the genetic factors that predispose individuals to obesity and T2DM, such as polymorphisms in the FTO and TCF7L2 genes, alongside environmental factors like diet, physical activity, and socioeconomic status. Moreover, biochemical parameters, including lipid profiles, inflammatory markers, and metabolic byproducts, offer valuable insights into the path physiological mechanisms underlying these conditions^(3, 4).

The co-occurrence of obesity and diabetes mellitus is not coincidental, as obesity is a major risk factor for the development of type 2 diabetes mellitus (T2DM). The complex interplay between genetic, environmental, and lifestyle factors contributes to the development of these conditions, making it challenging to manage and treat them effectively. Furthermore, obesity and diabetes mellitus are associated with a range of serious health complications, including cardiovascular disease, stroke, kidney disease, and certain types of cancer, resulting in significant morbidity, mortality, and economic burden^(5, 6).

Despite the significant advances in our understanding of the pathophysiology of obesity and diabetes mellitus, there is still a pressing need for further research to elucidate the complex relationships between genetic, environmental, and lifestyle factors and to develop effective prevention and treatment strategies. This research aims to contribute to the existing body of knowledge by providing a comprehensive review of the current literature on the genetic and environmental factors contributing to the development of obesity and diabetes mellitus, as well as the effective management strategies for these conditions^(7, 8).

Recent advances in genomics, metabolomics, and precision medicine have paved the way for identifying biomarkers that enable early detection and targeted interventions. This study seeks to unravel the multi factorial links between obesity and diabetes, offering insights into their shared etiological pathways and highlighting the potential for personalized prevention and treatment strategies^(9, 10).

Material and Methods:

This cross-sectional study investigates the genetic, environmental, biochemical, and clinical factors linking obesity and DM. Data were collected from a representative sample of 500 individuals from Shaikh Zayed Hospital to identify key genetic markers, environmental influences, early metabolic biomarkers, and clinical parameters associated with these conditions. A comprehensive literature search was conducted using major databases, including Pub Med, Scopus, and Web of Science.

Inclusion Criteria:

The adults aged between 18-65 years were included in the research and no history of chronic illnesses unrelated to metabolic health.

Exclusion Criteria:

As far exclusion criteria is concerned Pregnancy and diagnosed genetic syndromes associated with obesity or diabetes were excluded from the research

Data Collection:

The data collection procedure includes demographic male to female ratio both in obese and non obese persons and diabetic and non diabetic ration in urban residency. The other parameters as far anthropometric concern waist to hip ratio (WHR), blood tests include fasting glucose level along with HbA1C, lipid profile, C-reactive protein (CRP), liver function tests and creatinine levels. Dietary intake, physical activity levels, and socioeconomic status were assessed using validated questionnaires as far environmental factor concerned. Systolic and diastolic blood pressure along with heart also calculated.

Results:

There were 300 participants who included in this research after inclusion and exclusion criteria in which 25 were male and 35 were females with mean age 40 as obesity is concerned. The non obese persons include 40 were males and 50 females with mean age 37. The diabetic labeled persons include 40 each male and females with mean age 42 and non diabetic include 45 males and 25 were females with mean age 39 as discussed in table 01. The biochemical parameters include waist to hip ratio high in obese and diabetic individuals while normal in non obese and non diabetic individuals. Other parameters include C-reactive protein, total cholesterol, LDL, Triglycerides, creatinine, ALT, AST, FBS and HbA1c showed elevated levels in Obese and Diabetic individuals while non obese and non diabetic individuals showing downward trend as showed in table 02. HDL level increased in non obese and non diabetic individuals as good cholesterol while in diabetic and obese individuals having downward trend as discussed in table 02. The clinical parameters include systolic, diastolic blood pressure, heart rate, eGFR and Albuminuria showing elevated values in obese and diabetic individuals and lower values in non obese and non diabetic as discussed in table 03. It is also noted that ultra processed food is highly associated with obesity and diabetic individuals. Physical inactivity is at high risk associated to insulin resistance.

Demographics:

Table 01

Sr. #	Demographic Variable	Obese	Non-Obese	Diabetic	Non-Diabetic
1	Gender (Male/Female)	25/35	40/50	40/40	45/25
2	Mean Age (Years)	40	37	42	39

Biochemical Parameters:

Table 02

Sr. #	Parameter	Obese Individuals	Non-Obese Individuals	Diabetic Individuals	Non-Diabetic Individuals
1	Waist-to-Hip Ratio (WHR)	High	Normal	High	Normal
	Male	>0.96	<0.84	>0.95	<0.83
	Female	>0.87	<0.74	>0.85	<0.74
2	C-Reactive Protein (CRP)	High	Low	High	Low
3	Total Cholesterol (mg/dL)	225	150	240	180
4	HDL (mg/dL)	37	56	35	60
5	LDL (mg/dL)	135	95	147	100
6	Triglycerides (mg/dL)	220	115	255	112
7	Creatinine (mg/dL)	1.2	0.8	1.3	0.9
8	ALT (U/L)	45	25	45	30
9	AST (U/L)	35	22	40	25
10	Fasting blood sugar	128	84	148	85
11	HbA1c	6.3	5.4	7.9	5.2

Clinical Parameters:

Table 03

Sr. #	Clinical Parameter	Obese Individuals	Non-Obese Individuals	Diabetic Individuals	Non-Diabetic Individuals
1	Systolic BP (mmHg)	140	120	145	122
2	Diastolic BP (mmHg)	92	80	95	84
3	Heart Rate (bpm)	82	74	85	78
4	eGFR (mL/min/1.73m ²)	72	91	67	86
5	Albuminuria (mg/g)	115	30	150	28

Environmental Influences:

It is noted that high intake of ultra-processed foods was strongly associated with obesity and T2DM while Physical inactivity contributed to increased insulin resistance.

Metabolomic Biomarkers:

Table 04

Sr. #	Biomarker	Obese Individuals	Non-Obese Individuals	Diabetic Individuals	Non-Diabetic Individuals
1	Branched-Chain Amino Acids (BCAAs)	Elevated	Normal	Elevated	Normal
2	Lipid Metabolites	Dysregulated	Normal	Dysregulated	Normal
3	Oxidative Stress Markers	High	Normal	High	Normal

Discussion:

The current study aimed to unravel the genetic and environmental link between obesity and diabetes, with a focus on identifying metabolic biomarkers for early detection of obesity and type 2 diabetes mellitus. The findings of this study provide valuable insights into the complex relationships between genetic, environmental, and metabolic factors contributing to the development of these conditions^(11, 12).

The findings highlight the significant role of genetic predisposition, environmental factors, biochemical dysregulation, and clinical parameters in the development of obesity and T2DM. Elevated WHR, CRP, dyslipidemia, liver function abnormalities, and kidney dysfunction were observed in obese and diabetic individuals, suggesting their utility as key markers for early detection. The metabolomic analysis identified biomarkers such as elevated BCAAs and oxidative stress markers, which may serve as early indicators of metabolic dysfunction^(13, 14).

Lifestyle factors, including diet and physical inactivity, exacerbate these risks, demonstrating the importance of comprehensive prevention strategies. The integration of genetic, biochemical, clinical and environmental profiles in risk assessment can enhance personalized interventions.

The study's large, diverse sample strengthens the generalizability of findings, but it also highlights the necessity for longitudinal studies to establish causal relationships. Addressing disparities in access to healthcare and healthy food options will be vital in reducing the burden of these conditions^(9, 15, 16).

Conclusion:

This study underscores the complex interplay between genetic, environmental, biochemical and clinical factors in the obesity-diabetes nexus. Early identification of at-risk individuals through genetic screening, WHR assessment, CRP measurement, lipid profiling and clinical parameter evaluation can enhance prevention efforts. Public health strategies should prioritize dietary modifications, increased physical activity and early intervention to curb the rising tide of obesity and diabetes. The results also suggest that metabolomics and genetic profiling offer transformative opportunities for personalized medicine, enabling early detection and tailored therapeutic approaches. However, translating these findings into clinical practice requires validation across diverse populations, improved accessibility to diagnostic tools and ethical consideration of genetic data.

Implications:

The findings of this review have significant implications for public health policy, clinical practice and future research specifically

- Early intervention and prevention strategies are critical for reducing the risk of obesity and diabetes mellitus
- Personalized medicine approaches, tailored to an individual's genetic and environmental profile, may be effective in managing these conditions
- Further research is needed to elucidate the complex relationships between genetic, environmental, and lifestyle factors and to develop effective prevention and treatment strategies

Limitations:

Research on obesity and diabetes mellitus is constrained by several limitations that affect the robustness and generalizability of findings. A key challenge is the heterogeneity of study populations, with differences in genetic predispositions, environmental exposures, and socioeconomic factors often overlooked, limiting the applicability of results across diverse groups.

References:

1. Chobot A, Górowska-Kowolik K, Sokołowska M, Jarosz-Chobot P. Obesity and diabetes—Not only a simple link between two epidemics. *Diabetes/metabolism research and reviews*. 2018;34(7):e3042.
2. Estampador AC, Franks PW. Precision medicine in obesity and type 2 diabetes: the relevance of early-life exposures. *Clinical chemistry*. 2018;64(1):130-41.
3. Satheesh G, Ramachandran S, Jaleel A. Metabolomics-based prospective studies and prediction of type 2 diabetes mellitus risks. *Metabolic Syndrome and Related Disorders*. 2020;18(1):1-9.
4. Yaghootkar H, Whitcher B, Bell J, Thomas E. Ethnic differences in adiposity and diabetes risk—insights from genetic studies. *Journal of internal medicine*. 2020;288(3):271-83.
5. Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB, et al. Pathophysiology of type 2 diabetes mellitus. *International journal of molecular sciences*. 2020;21(17):6275.
6. Inge TH, Laffel LM, Jenkins TM, Marcus MD, Leibel NI, Brandt ML, et al. Comparison of surgical and medical therapy for type 2 diabetes in severely obese adolescents. *JAMA pediatrics*. 2018;172(5):452-60.
7. Bellary S, Kyrou I, Brown JE, Bailey CJ. Type 2 diabetes mellitus in older adults: clinical considerations and management. *Nature Reviews Endocrinology*. 2021;17(9):534-48.
8. Ma Q, Li Y, Wang M, Tang Z, Wang T, Liu C, et al. Progress in metabonomics of type 2 diabetes mellitus. *Molecules*. 2018;23(7):1834.
9. Malone JJ, Hansen BC. Does obesity cause type 2 diabetes mellitus (T2DM)? Or is it the opposite? *Pediatric diabetes*. 2019;20(1):5-9.
10. Al-Sulaiti H, Diboun I, Agha MV, Mohamed FF, Atkin S, Dömling AS, et al. Metabolic signature of obesity-associated insulin resistance and type 2 diabetes. *Journal of translational medicine*. 2019;17:1-11.
11. Tremblay J, Hamet P. Environmental and genetic contributions to diabetes. *Metabolism*. 2019;100:153952.
12. Pilon NJ, Loos RJ, Marshall SM, Zierath JR. Metabolic consequences of obesity and type 2 diabetes: Balancing genes and environment for personalized care. *Cell*. 2021;184(6):1530-44.
13. De Rosa S, Arcidiacono B, Chiefari E, Brunetti A, Indolfi C, Foti DP. Type 2 diabetes mellitus and cardiovascular disease: genetic and epigenetic links. *Frontiers in endocrinology*. 2018;9:2.
14. Goodarzi MO. Genetics of obesity: what genetic association studies have taught us about the biology of obesity and its complications. *The lancet Diabetes & endocrinology*. 2018;6(3):223-36.

15. Veit M, van Asten R, Olie A, Prinz P. The role of dietary sugars, overweight, and obesity in type 2 diabetes mellitus: a narrative review. *European journal of clinical nutrition*. 2022;76(11):1497-501.
16. Schnurr TM, Jakupović H, Carrasquilla GD, Ängquist L, Grarup N, Sørensen TI, et al. Obesity, unfavourable lifestyle and genetic risk of type 2 diabetes: a case-cohort study. *Diabetologia*. 2020;63:1324-32.