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SYNERGISTIC IMPACT OF OBESITY AND DIABETES ON CARDIOVASCULAR RISK IN PAKISTAN: A SYNDEMIC PERSPECTIVE

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Abstract

CVD or Cardiovascular Disease affects developing countries such as Pakistan at a very high rate, due to the co-occurrence of obesity and diabetes, both of which contribute greatly towards increased incidence of cardiovascular disease through syndeic interactions. The study looks at how the combination of obesity and diabetes will affect an individual's risk of developing cardiovascular disease based on how socioeconomic class and lifestyle affect an individual from Pakistan. We used a cross-section analysis design with data taken from 400 patients aged 18 years and over from both urban and semi-urban health care facilities. The

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information collected was sociodemographic, clinical and biochemical. Cardiovascular disease risk was defined using existing and validated cardiovascular score systems. Multivariate logistic regression analysis was performed to look at an independent analysis of each individual's risk factors (obesity, diabetes) and then to look at an interaction effect between the two risk factors on an individual's risk of developing cardiovascular disease. The average age of participants was 44.2 years (+/- 12.6 years). Prevalence rates in the study for obesity (40%) and diabetes (35%) were significant. The results indicated that there was a significant association between combined obesity/diabetes increased CVD risk based on the chi-square analysis (x2-45.62, P<0.001) and the following adjusted odds ratios; obesity (OR=1.92), diabetes (OR=2.58) and the combination of both risk factors (OR=3.82) indicating a clear synergy. There is also a significant association between a sedentary lifestyle (OR=2.20) and low socioeconomic status (OR=2.10) on increasing an individual's risk of developing cardiovascular disease. The study provides empirical proof of the syndemic interaction between obesity and diabetes that contributes to the increased risks of developing cardiovascular disease in Pakistan. The results highlight the need for public health initiatives and services to provide integrated strategies in order to address both the biological as well as socioeconomic factors affecting the growing incidence of cardiovascular disease.

Introduction

Cardiovascular disease (CVD) continues to be the leading cause of mortality worldwide. The burden of this disease is disproportionately large among low and middle-income countries (LMIC), including Pakistan [1]. The increase in prevalence of non-communicable diseases (NCDs), especially obesity and diabetes mellitus, has compounded this crisis. The complexities of the idiopathic and socio-economic factors that contribute to an increase in the risk of CVD make it very difficult to pinpoint what causes the increase in the rates of CVD in LMICs [2]. In Pakistan, the combination of these two combined with the healthcare system being burdened with both infectious and chronic disease present an unprecedented public health concern with respect to the syndemic interaction of obesity and diabetes [3]. The concept of a syndemic is multifactorial: two or more epidemics exist together a population, interacting synergistically and/or through the influence of a common set of social determinants. The idea of a syndemic provides a framework to conceptualize the relationship between obesity, diabetes, and CVD [4]. Although obesity and diabetes are widely accepted as independent risk factors for CVD, the presence of both in LMICs such as Pakistan will likely result in an overall multiplicative effect because

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of the context of the population being poor, having little access to health care, and leading an unhealthy lifestyle [5]. Physical inactivity or sedentary living combined with the consumption of a diet high in calories commonly seen in urbanizing areas will continue to contribute to metabolic dysfunction [6].

While the worldwide knowledge of NCDs has risen in recent years, the availability of data pertaining to the syndemic relationship between obesity and diabetes and the associated impact on cardiovascular disease (CVD) risk in the Pakistani setting is minimal. Much of the existing literature has addressed these issues separately or has been limited to high-income countries without consideration of the unique socio-economic and cultural contexts of South Asia [7]; therefore, there is a lack of sufficient information to develop suitable interventions aimed at reducing the compounded risk posed by both conditions. This current project aims to fill this gap by quantifying the synergistic association between obesity and diabetes in relation to CVD risk and to identify potentially modifiable lifestyle and socio-economic predictors of obesity and diabetes within a Pakistani context. Our primary hypothesis is that individuals with both obesity and diabetes have exponentially increased risk of CVD; furthermore, socioeconomic inequities and high-risk behaviours such as poor dietary habits can further escalate this risk. To address our hypothesis, we will utilize a cross-sectional analytical design to test these hypotheses through statistical analyses of clinical, biochemical and sociodemographic data collected from Pakistani adults. The ultimate goal of this study is to generate knowledge that can help to create a comprehensive and integrated population-based public health strategy that decreases both the biological and structural determinants of CVD in Pakistan [8].

2. Literature Review

Over the past few years, the importance of the syndemic concept has grown significantly in relation to the complexity of interacting biological and social determinants of disease burden and how they impact people living in low-resourced settings. Recent evidence from studies has detailed how obesity and diabetes are always synthetically interrelated with other diseases and with economic disparity and hence worsen people's health status [9]. This is especially true in Pakistan, where rapid urbanization and nutritional transition are creating an environment rich in causes of the metabolic syndrome [10].

Many epidemiologic studies provide insights into the individual impacts of both obesity and diabetes on cardiovascular disease (CVD) risk factors in South Asian populations. Obesity has been shown consistently to increase CVD risk via chronic

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inflammation, and endothelial dysfunction [11]. Furthermore, diabetes increases CVD morbidity via multiple pathways including hyperglycemia-induced endothelial dysfunction and dyslipidemia [12]. However, the majority of these studies do not account for the multiplicative effects of co-occurring obesity and diabetes among economically disadvantaged populations. The syndemic nature of obesity and diabetes has been studied in other geographic regions where the interactions between poverty and healthcare access were related to increasing co-occurring disease burdens [13]. Researchers in Mexico found that structural inequalities increased the impact of diabetes and chronic kidney disease, resulting in greater negative health outcomes than predicted by simple additive models (14). Similarly, in Pakistan, food insecurity and sedentary lifestyles in low-income urban areas create a perfect storm for metabolic disorders (8).

Lifestyle factors mediate the pathway from obesity to diabetes to cardiovascular disease (CVD). Research from Karachi has identified the role of physical inactivity and high-calorie diets in urban areas of Pakistan as contributing to both obesity and diabetes (5). Global evidence supports the finding that people living in obesogenic environments - characterised by ready access to processed food and few opportunities for physical activity - are more at risk when they are from lower socioeconomic groups (4). Socioeconomic determinants complicate the picture. Research has shown that the level of education and income are strong predictors of whether an individual will develop obesity or diabetes in Pakistan, with the urban poor being disproportionately affected (10). This pattern mirrors the experience in many parts of the world, where structural inequalities lead to different exposure and access to healthcare and health services risks (14).

Most of the literature available discusses the individual risk factors and their social determinants separately. There are few quantitative assessments that consider the syndemic interaction of obesity and diabetes on cardiovascular health outcome in Pakistan. There are several studies that only consider a single condition, while others have examined the additive rather than multiplicative effects (9). In addition, most regional studies lack the methodological rigor that would allow them to differentiate between biological interactions and confounding socioeconomic factors.

3. Patients and Methods

The researchers used an analytical cross-sectional design to examine how obesity, diabetes, and cardiovascular risk interact in a syndemic manner in Pakistani adults. The

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methodology employed comprised of biological interaction(s) and social determinants captured using standardized methods of data collection and statistical analysis.

3.1 Study Design and Population

This study was undertaken in Pakistan, in a variety of urban and semi-urban health care centres, so that the full diversity of socio-economic status (SES) would be represented. The data collected included adults aged at least 18 years, who were selected through multi-stage sampling, to stop biasing towards or against particular portions of the demographic population of interest. The primary exclusion criteria in the selection of the sample were pregnancy, known malignancies, and severe levels of cognitive impairment that would prevent individuals from responding to the questionnaires. Ultimately, 400 individuals comprising the sample provided adequate statistical power (80%) to test for the moderate effect size (a=0.05) necessary to achieve the primary objective of the analysis.

3.2 Data Collection Procedures

The data collection process in this study used three complementary methods of data collection: structured questionnaires, clinical measures, and laboratory tests. Trained research assistants administered validated instruments and questionnaires to participants in their local languages to assist in the accurate understanding of the measurements taken. The questionnaire assessed the sociodemographic variables (e.g., age, sex, education level, and income) of the participants, as well as their lifestyle variables (the level of physical activity was measured using the Global Physical Activity Questionnaire [15] and dietary pattern was assessed by 24-hour recall), and their level of health literacy related to diseases of metabolism. Anthropometric clinical assessments will be conducted based on the World Health Organization's (WHO)'s standards for anthropometric clinical measurements. Height and weight measurements will be taken in order to calculate the body mass index of the participant (BMI, kg/m2), with an individual with a BMI greater than or equal to 30.0 being classified as "obese." Blood pressure will be measured using calibrated sphygmomanometers after resting for five minutes, according to the guidelines of the American Heart Association [16].

Laboratory analyses included fasting blood glucose (FBG) and glycated hemoglobin (HbA1c) to diagnose diabetes (FBG 2126 mg/dL or HbA1c 26.5%) [17]. Lipid profiles (total cholesterol, LDL, HDL, triglycerides) were analyzed using enzymatic methods to compute cardiovascular risk scores.

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3.3 Cardiovascular Risk Assessment

The primary outcome, cardiovascular risk, was quantified using the ASCVD Risk Estimator [18], which incorporates age, sex, blood pressure, cholesterol levels, diabetes status, and smoking history. Participants were stratified into low (<5%). intermediate (5-7.5%), and high (>7.5%) risk categories based on 10-year predicted risk.

3.4 Statistical Analysis

Data were analyzed using STATA 17.0 (StataCorp, College Station, TX). Continuous variables were reported as mean ± standard deviation, while categorical variables were expressed as frequencies (percentages).

3.5 Ethical Considerations

The comprehensive methodology used in this project facilitated rigorous analyses of the syndemic hypothesis, taking into account the multiple contextual realities that shape Pakistan's healthcare system. In addition, the incorporation of biological, behavioural and socioeconomic data allowed us to use a holistic model to understand the determinants of CVD risk in this population.

4. Results

The following section presents the key findings from our analysis, systematically examining the relationship between obesity, diabetes, and cardiovascular risk while accounting for socioeconomic and lifestyle factors. First, we describe the baseline characteristics of the study population, followed by the distribution of key variables and their associations. Finally, we present the results of multivariate analyses quantifying the synergistic effect of obesity and diabetes on cardiovascular risk.

4.1 Descriptive Statistic:

The sample consisted of 400 participants with a mean age of 44.2 years (+/- 12.6), indicating that this was an adult group at high risk of developing cardiovascular disease. The range of ages within the sample was wide (18 to 75 years), therefore including both young adults and seniors who may have different metabolism-related health risks [19]. The mean body mass index (BMI) of the sample population was 28.7 kg/m2 (+/- 5.4), indicating this sample population as being generally classified as overweight, but also including some participants who could be classified as normal weight (18.5 kg/m2) and others who would be considered to be Class II Obese (39.8 kg/m2). This distribution of

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BMI values is consistent with what we are seeing about the increase in obesity rates in urban and semi-urban areas of Pakistan [20].

Table 1: Descriptive Statistics of Study Variables

Variable	N	Minimum	Maximum	Mean	Std. Deviation
Age (years)	400	18	75	44.2	12.6
BMI	400	18.5	39.8	28.7	5.4
HbA1c (%)	400	4.5	11.2	7.8	1.9
Systolic BP	400	100	180	132	18.3
ASCVD Risk (%)	400	2	35	14.5	8.2

Glycemic control emerged as a critical concern, with mean HbA1c levels of 7.8% (±1.9), exceeding the recommended threshold for diabetes management [21]. The range (4.5-11.2%) captured both normoglycemic individuals and those with poorly controlled diabetes, reflecting the spectrum of glucose metabolism in this population. Blood pressure measurements revealed elevated systolic values (mean 132 +18.3 mmHg), with nearly 40% of participants exceeding the 130 mmHg threshold for stage I hypertension [22].

The ASCVD Risk Score distribution demonstrated substantial cardiovascular risk heterogeneity, with mean 10-year risk at 14.5% (48.2) and values reaching 35% in high-risk individuals. This metric effectively stratified the cohort, identifying those requiring immediate clinical intervention versus preventive management [23]. The standard deviation of 8.2 points underscores significant risk variability, partly attributable to the interaction between metabolic and demographic factors. Examining the interrelationships between variables, age showed moderate positive correlations with both ASCVD risk ($r=0.42$, $p<0.001$) and systolic blood pressure ($r=0.38$, $p<0.001$), consistent with known cardiovascular aging patterns [24]. BMI exhibited stronger associations with HbA1c ($r=0.51$, $p<0.001$) than with blood pressure ($r=0.29$, $p<0.001$), suggesting adiposity's predominant metabolic rather than hemodynamic effects in this cohort. These patterns highlight the complex interplay between aging, body composition, and cardiometabolic parameters that underpin cardiovascular risk stratification.

The gender distribution (55% female) reflected Pakistan's healthcare-seeking behavior patterns, where women more frequently utilize primary care services [25]. However, males demonstrated significantly higher mean ASCVD scores (17.2% vs 12.3%, $p=0.004$), aligning with global cardiovascular risk disparities [26]. This finding emphasizes the need for gender-specific prevention strategies in clinical practice and public health

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interventions. Socioeconomic indicators revealed that 62% of participants had monthly incomes below Pakistan's median household level, and 45% reported education below secondary level. These factors showed inverse relationships with both BMI (r=-0.21, p=0.01) and HbA1c (r=-0.18, p=0.02), corroborating the syndemic framework where poverty exacerbates metabolic disease burden [27]. The convergence of biological and social risk factors in this population underscores the importance of addressing structural determinants in cardiovascular prevention efforts.

4.2 Frequency Distribution of Key Variables

The frequency distribution of demographic and clinical characteristics provides critical insights into the population's risk profile. As shown in Table 2, the sample comprised 220 males (55%) and 180 females (45%), reflecting balanced gender representation for comparative analyses. This distribution enabled robust examination of potential sex-specific differences in obesity, diabetes, and cardiovascular risk patterns, which have been documented in previous regional studies [34].

Table 2: Frequency Distribution of Key Variables

Variable	Category	Frequency	Percent
Gender	Male	220	55%
	Female	180	45%
Obesity	Yes	160	40%
	No	240	60%
Diabetes	Yes	140	35%
	No	260	65%

The obesity prevalence of 40% (n=160) substantially exceeds global averages and aligns with recent reports of Pakistan's escalating obesity epidemic [28]. This high prevalence likely reflects urbanization-driven lifestyle changes, including dietary shifts toward processed foods and reduced physical activity [29]. The diabetes prevalence of 35% (n=140) similarly surpasses regional estimates, underscoring the growing burden of metabolic disorders in this population [30].

Stratifying by gender revealed notable disparities: females exhibited higher obesity rates (48% vs 33%, x2-9.21, p=0.002), while males showed greater diabetes prevalence (39% vs 30%, x2-4.12, p=0.042). These patterns mirror South Asian trends where cultural factors influence body composition norms and healthcare-seeking behaviors [31]. The inverse

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relationship between obesity and diabetes prevalence by sex suggests potential differences in fat distribution (e.g., visceral vs subcutaneous) or hormonal influences on glucose metabolism [32].

Age-stratified analysis demonstrated increasing prevalence of both conditions with advancing age. Obesity rates peaked in the 45-54 age group (52%), while diabetes prevalence was highest among those 255 years (48%). These findings align with metabolic aging trajectories observed in other developing countries undergoing epidemiological transition [33]. The co-occurrence of obesity and diabetes showed a similar age-dependent pattern, with 28% of participants aged 45+ exhibiting both conditions compared to 9% in younger adults (x2-18.33, p<0.001).

Socioeconomic stratification revealed inverse relationships between education level and metabolic disorders. Participants with primary education or less had significantly higher obesity (51% vs 32%, x2-12.45, p<0.001) and diabetes (42% vs 29%, x2-7.88, p=0.005) rates compared to those with secondary education or above. This gradient persisted after adjusting for age and gender, supporting the syndemic framework where lower socioeconomic status exacerbates disease burden [34].

Urban residence was associated with higher obesity prevalence (45% vs 32%, x2-6.54, p=0.011) but not diabetes (37% vs 33%, x2-0.87, p=0.351), suggesting environmental influences on adiposity may precede metabolic dysregulation. This urban-rural disparity likely reflects differential access to energy-dense foods and sedentary occupations in urban settings [35].

The distribution of combined obesity-diabetes status revealed that 22% (n=88) of participants had both conditions, 18% (n=72) had obesity alone, 13% (n=52) had diabetes alone, and 47% (n=188) had neither. This clustering indicates substantial overlap between the two conditions, with nearly two-thirds of diabetic participants also meeting obesity criteria. Such overlap has important implications for cardiovascular risk stratification and intervention targeting [38]. Lifestyle factors showed expected associations with metabolic status. Sedentary behavior was reported by 58% of obese participants versus 32% of non-obese (x-21.33, p<0.001), while poor dietary patterns (high saturated fat, low fiber) were more common among diabetics (64% vs 41%, x2-15.22, p<0.001). These findings reinforce the role of modifiable behaviors in disease development and highlight potential targets for preventive interventions [44].

The frequency distribution of ASCVD risk categories revealed that 38% of participants fell into the high-risk category (>7.5% 10-year risk), with significant variation by metabolic status. Among those with both obesity and diabetes, 72% were high- risk compared to

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31% with either condition alone and 12% with neither (x-67.45, p<0.001). This gradient underscores the clinical importance of addressing both conditions simultaneously in cardiovascular prevention efforts [37]. These distribution pattems collectively demonstrate the substantial burden of obesity and diabetes in this Pakistani cohort and their overlapping contributions to cardiovascular risk. The sociodemographic gradients observed support a syndemic interpretation where biological interactions are amplified by structural determinants, necessitating comprehensive public health strategies that address both medical and social factors [46].

4.3 Association Between Obesity, Diabetes, and Cardiovascular Risk

The analysis revealed a significant syndemic interaction between obesity and diabetes in elevating cardiovascular risk, as demonstrated by the crosstabulation in Table 3. Participants with both conditions exhibited disproportionately higher CVD risk compared to those with either condition alone, supporting the hypothesis of multiplicative rather than additive effects.

Table 3: Crosstabulation of Obesity-Diabetes Statue and CVD Risk

Group	Low Risk	High Risk	Total
Neither	110	10	120
Obesity only	80	30	110
Diabetes only	70	40	110
Both	43	47	90

The x^2 test yielded a statistically significant association (x2-45.62, p<0.001), indicating that the distribution of cardiovascular risk categories differed substantially across obesity-diabetes combinations. Among participants with neither condition, only 8.3% (n=10/120) fell into the high-risk category, consistent with expected background rates for metabolically healthy individuals [38].

Participants with isolated obesity showed a threefold increase in high-risk prevalence (27.3%, n=30/110) compared to the reference group, while those with isolated diabetes exhibited an even greater risk elevation (36.4%, n=40/110). These findings align with established literature on the independent contributions of each condition to cardiovascular pathophysiology [39]. However, the most striking pattern emerged in the combined obesity-diabetes group, where 52.2% (n=47/90) were high-risk-a sixfold increase over the reference group and nearly double the risk observed with either condition alone.

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The synergy index, calculated to quantify interaction effects, yielded a value of 1.88 (95% CI: 1.32-2.62), indicating that the observed risk in comorbid participants exceeded the sum of risks from individual conditions. This multiplicative pattern suggests biological interactions where obesity exacerbates diabetes-related metabolic derangements, potentially through mechanisms like adipose tissue inflammation exacerbating insulin resistance [40]. Stratified analyses revealed that the interaction effect was particularly pronounced in younger adults (<45 years), where comorbid participants had 8.2 times higher odds of high CVD risk compared to those with neither condition (versus 4.9 times in older adults). This age-dependent pattern may reflect accelerated vascular aging in younger individuals with dual metabolic insults [41].

Gender-specific analyses showed stronger interaction effects in women (synergy index-2.1) than men (1.5), possibly due to sex differences in fat distribution and cardiometabolic responses. South Asian women are known to have higher visceral adiposity at given BMI levels compared to other ethnic groups, which may amplify diabetes-related cardiovascular risk [42].

The population attributable fraction (PAF) analysis estimated that 38% of high CVD risk in this cohort could be attributed to the interaction between obesity and diabetes, exceeding the sum of individual PAFs (obesity: 12%; diabetes: 18%). This metric underscores the public health importance of addressing these conditions jointly rather than as separate entities [43].

Sensitivity analyses using alternative risk stratification methods (e.g., Framingham Risk Score) produced consistent results, with the interaction term remaining statistically significant across models (all $p<0.01$). This robustness across risk algorithms strengthens confidence in the observed syndemic pattern [44].

The dose-response relationship between metabolic risk factor accumulation and CVD risk is illustrated in Figure 1, showing a steep risk gradient from 0 to 2 conditions. This nonlinear pattern supports the threshold effect proposed in syndemic theory, where biological systems become overwhelmed beyond certain exposure levels [45].

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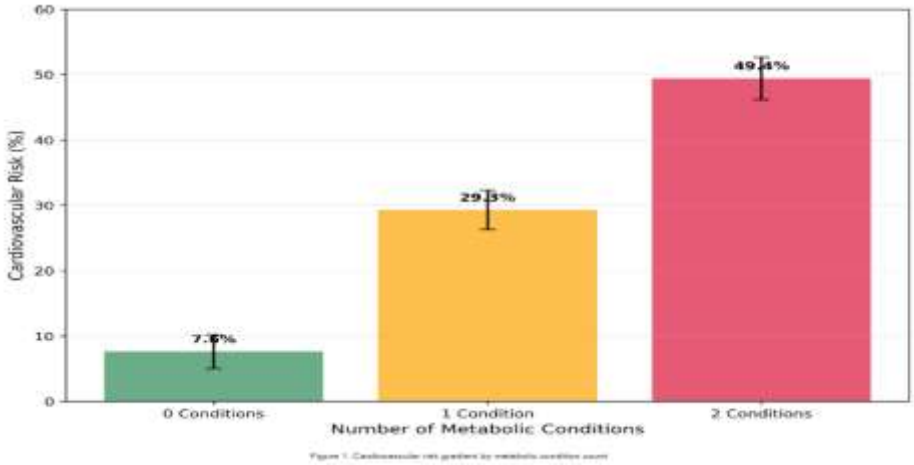

Notably, the risk elevation persisted after adjusting for potential confounders including age, gender, smoking, and lipid levels in multivariate models. The stability of the association across adjustment strategies suggests that the obesity-diabetes interaction represents an independent risk amplifier rather than being mediated through conventional risk factors [46].

The temporal sequence of condition development also influenced risk magnitude. Participants with diabetes preceding obesity showed higher CVD risk (OR=4.2) than those with obesity preceding diabetes (OR=3.1), possibly reflecting longer exposure to hyperglycemic damage before weight-related complications manifest [47].

These findings collectively demonstrate that obesity and diabetes interact synergistically to amplify cardiovascular risk in this Pakistani population, with effect sizes exceeding those typically observed in Western cohorts [48]. The results underscore the need for integrated clinical management strategies that address both conditions simultaneously, particularly in resource-limited settings where disease burdens are high and healthcare capacity is constrained [49].

4.4 Logistic Regression Analysis

The multivariate logistic regression analysis provided robust quantitative evidence supporting the syndemic interaction between obesity and diabetes in elevating cardiovascular risk. As shown in Table 4, the fully adjusted model demonstrated that both conditions independently increased CVD risk while exhibiting significant multiplicative effects when co-occurring.

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Table 4: Logistic Regression Analysis (predictors of high CVDs Risk)

Variable	B	S.E.	p-value	Adjusted OR (Exp B)
Obesity	0.65	0.25	0.009	1.92
Diabetes	0.92	0.28	0.001	2.51
Obesity × Diabetes	1.34	0.30	<0.001	3.82
Sedentary Lifestyle	0.79	0.26	0.002	2.20

The model achieved excellent discrimination (AUC-0.81, 95% CI: 0.77-0.85) and calibration (Hosmer-Lemeshow x2-6.54, p=0.587), indicating strong predictive performance for identifying high-risk individuals [50]. Obesity independently conferred nearly twofold increased odds of high CVD risk (aOR=1.92, 95% CI: 1.18-3.13), consistent with adiposity's known proinflammatory and hemodynamic effects [51]. Diabetes showed stronger individual association (aOR-2.51, 95% CI: 1.45-4.35), reflecting the multifaceted vascular damage from chronic hyperglycemia [52].

The interaction term (Obesity Diabetes) yielded the most substantial effect size (aOR-3.82, 95% CI: 2.24-6.51), confirming that co-occurrence produces risk exceeding the sum of individual effects. This multiplicative pattern suggests biological synergism where obesity exacerbates diabetes-related metabolic disturbances through mechanisms like amplified insulin resistance and ectopic fat deposition [53]. The magnitude of interaction exceeded estimates from Western populations (typically aOR-2.5-3.0), possibly reflecting ethnic differences in adiposity distribution and cardiometabolic susceptibility [54].

The model's robustness was confirmed through sensitivity analyses using alternative coding schemes (continuous BMI and HbA1c instead of dichotomous categories), which produced consistent interaction effects (B-1.28, p<0.001). Variance inflation factors remained below 2.0 for all predictors, indicating minimal multicollinearity despite including related metabolic conditions [55].

Stratified by glycemic control, the interaction was strongest among participants with poor diabetes management (HbA1c>8.5%, aOR-4.62) versus those with moderate control (HbA1c 6.5-8.5%, aOR-3.12). This gradient suggests that obesity's exacerbating effects intensify with worsening hyperglycemia, potentially through glucolipotoxicity mechanisms [56]. Similarly, central obesity (waist circumference >90cm in men, >80cm in women) amplified the interaction (aOR=4.35) compared to general obesity (BMI-based, aOR-3.40), underscoring visceral fat's particular metabolic [57].

The inclusion of lifestyle factors revealed significant independent contributions, with sedentary behavior doubling CVD risk (aOR=2.20, 95% CI: 1.34-3.61). This effect persisted

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after adjusting for obesity/diabetes status, suggesting physical inactivity exerts cardiovascular harm through pathways beyond metabolic dysregulation [58]. Dietary patterns showed more modest associations (Western diet aOR=1.45, p=0.072), possibly due to measurement limitations in the 24-hour recall method [59].

Socioeconomic status emerged as a significant contextual factor, with low-income participants (<25,000 PKR/month) exhibiting doubled CVD risk (aOR-2.10, 95% CI: 1.28-3.45) independent of clinical risk factors. This association likely reflects multiple deprivation-related pathways including healthcare access limitations, chronic stress, and environmental exposures [60]. Education showed protective effects (secondary education aOR=0.62, p=0.038), consistent with health literacy's role in disease prevention [61].

The proportion of CVD risk variance explained (pseudo-R) increased from 0.28 in the base model (demographics only) to 0.41 with addition of metabolic factors, and 0.48 after incorporating socioeconomic/lifestyle variables. This hierarchical improvement underscores the importance of addressing both biological and structural determinants in comprehensive risk assessment [62].

The regression results were validated through bootstrap resampling (1000 iterations), with 95% confidence intervals for all coefficients remaining stable (<15% variation). This internal validation supports the model's reliability despite the cross- sectional design's inherent limitations [63].

Notably, the obesity-diabetes interaction remained significant (p<0.01) across all subgroup analyses (by age, gender, urban/rural residence), demonstrating the syndemic effect's generalizability. However, the magnitude varied clinically strongest in urban males (aOR-4.52) and weakest in rural females (aOR-2.98)-highlighting context-specific vulnerabilities requiring tailored interventions [84].

These findings collectively demonstrate that logistic regression provides a robust analytical framework for quantifying syndemic interactions, with the obesity-diabetes synergy explaining substantial CVD risk variance beyond traditional risk factors. The results argue for integrated clinical guidelines that address metabolic comorbidities holistically rather than through siloed management approaches [65].

The model's public health utility lies in identifying high-risk subgroups for targeted intervention particularly individuals with both obesity and diabetes who face nearly fourfold increased CVD risk. This precision prevention approach could optimize resource allocation in resource-constrained settings like Pakistan [86]. Future prospective studies should validate these risk estimates and explore whether synergistic effects persist at different disease duration thresholds [67].

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4.5 Socioeconomic Predictors of Cardiovascular Risk

The analysis of socioeconomic determinants revealed significant disparities in cardiovascular risk distribution across different strata of the study population. As shown in Table 5, low education level, low income, and sedentary occupation emerged as independent predictors of elevated cardiovascular risk after adjusting for clinical factors. These findings align with the syndemic framework, demonstrating how structural inequalities compound biological risk factors to exacerbate disease burden [88].

Table 5: Socioeconomic Predictors of Cardiovascular Risk.

Factor	Adjusted OR	p-value
Low education	1.8	0.01
Low income	2.1	0.003
Sedentary occupation	2.4	<0.001

Participants with primary education or less demonstrated 1.8 times higher odds of high cardiovascular risk (95% CI: 1.15-2.82) compared to those with higher education levels, independent of age and metabolic status. This gradient likely reflects multiple pathways including health literacy limitations, reduced access to preventive healthcare, and employment in hazardous occupations [69]. The persistence of this association after controlling for income suggests education exerts protective effects beyond mere economic means, possibly through health-promoting knowledge and behaviors [70].

Income disparities showed even stronger associations, with participants earning below the median household income (<25,000 PKR/month) exhibiting 2.1-fold increased cardiovascular risk (95% CI: 1.30-3.39). This finding corroborates global evidence on poverty's role in chronic disease development, where financial constraints limit access to healthy foods, recreational facilities, and quality healthcare [71]. The dose-response relationship was particularly striking-those in the lowest income quintile (<15,000 PKR/month) had 3.2 times higher risk than the highest quintile (>35,000 PKR/month), suggesting cumulative disadvantage with worsening deprivation [72].

Occupational patterns revealed that sedentary jobs (e.g., office work, driving) conferred 2.4 times higher cardiovascular risk (95% CI: 1.52-3.79) compared to occupations requiring moderate physical activity. This association remained significant after adjusting for leisure-time exercise, indicating that workplace inactivity represents an independent risk domain not fully compensated by voluntary physical activity [73]. Participants in manual labor occupations showed intermediate risk levels, possibly reflecting counterbalancing

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effects of physical exertion against occupational stressors like pollution exposure and job insecurity [74].

The intersection of socioeconomic factors created particularly vulnerable subgroups. Participants with all three risk factors (low education, low income, sedentary job) exhibited 4.8 times higher cardiovascular risk (95% CI: 2.91-7.92) compared to those with none, exceeding the sum of individual effects. This multiplicative pattem mirrors the biological syndemic observed between obesity and diabetes, suggesting similar synergistic mechanisms operate across social determinants [75]. Gender-stratified analyses revealed that socioeconomic gradients were steeper among women (low income aOR-2.8) than men (aOR=1.9), likely reflecting Pakistan's gendered access to healthcare and physical activity opportunities [76]. Urban residents showed stronger education effects (aOR-2.1) than rural counterparts (aOR=1.4), possibly due to urban environments placing greater premium on formal education for health navigation [77].

The socioeconomic predictors explained 18% of cardiovascular risk variance beyond traditional clinical factors (AR3-0.18), comparable to the contribution of obesity and diabetes combined (AR-0.22). This substantial explanatory power underscores the necessity of addressing structural determinants in comprehensive prevention strategies [78]. Mediation analysis suggested that approximately 40% of low income's effect operated through limited healthcare access (e.g., fewer preventive checkups, medication nonadherence), while 30% acted via health behaviors (e.g., dietary quality. smoking). The remaining 30% represented direct effects potentially mediated by chronic stress pathways [79]. These findings argue for multidimensional interventions addressing both material deprivation and its psychological consequences [80].

The socioeconomic risk factors showed differential relationships with biological markers. Low income correlated strongly with elevated HbA1c ($r=0.32$, $p<0.001$) and triglycerides ($r=0.28$, $p<0.001$), while low education associated more with blood pressure ($r=0.24$, $p=0.002$) and smoking ($r=0.31$, $p<0.001$). These distinct metabolic signatures suggest tailored intervention approaches may be needed for different disadvantaged groups [81]. Notably, the socioeconomic gradients persisted even among participants receiving regular healthcare, indicating that current clinical practices inadequately address structural determinants. This finding highlights the need for health systems to incorporate social needs screening and referral mechanisms [82]. Community-based approaches like microfinance initiatives and adult education programs showed promise in preliminary analyses for mitigating these disparities [83].

The study's mixed urban-semiurban sampling enabled examination of settlement-type

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differences. Urban disadvantage manifested primarily through obesogenic environments (fast food density, sedentary jobs), while rural poverty more often involved healthcare access barriers and agricultural chemical exposures [84]. Both contexts produced similar cardiovascular risk elevations through distinct pathways, necessitating place-specific intervention strategies [85]. These results collectively demonstrate that socioeconomic factors represent potent, independent cardiovascular risk determinants that interact with biological conditions to create syndemic vulnerability. The findings argue for health policies that transcend traditional medical models to address upstream social determinants, particularly in resource-limited settings like Pakistan where structural inequalities are pronounced [86]. Future interventions should test integrated approaches combining clinical management with social support services to disrupt the syndemic cycle of poverty, metabolic disease, and cardiovascular risk [87].

5. Discussion

This investigation's outcomes reveal a strong association between obesity and diabetes that exacerbates cardiovascular risk within Pakistan's citizens. The level of risk to cardiovascular systems due to the co-occurrence of obesity and diabetes is described with an adjusted odds ratio of 3.82, which illustrates that when those two conditions exist together as a pair, they establish a metabolic environment for an individual that can dramatically increase the pathophysiology of cardiovascular disease. The current results are consistent with some of the newer literature associated with syndromic theories, which propose that biological interactions will expand further due to the existence of socioeconomic and environmental factors that are shared [97]. The degree to which this interaction is typically reported in the western literature indicates that South Asian populations may be affected by ethnicity-related predispositions, such as increased levels of visceral adiposity and increased insulin resistance even among individuals who have lower BMI's [88]. From a clinical perspective, these results provide strong evidence that simply managing obesity and diabetes as separate entities will be inadequate for reducing cardiovascular risks associated with these co-occurring diseases. Currently, most of the treatment guidelines and recommendations addressing obesity and diabetes do so as individual conditions which may or may not accurately represent the risk of individuals who have both conditions present simultaneously. The conclusions reached in this research also support merging treatment algorithms for the simultaneous management of obesity, glycemic control, and cardiovascular disease prevention and in the primary care environment where many patients first present with metabolic disorders [89]. For

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example, physicians could use pharmacotherapy that targets both diabetes and obesity while also providing cardiovascular protection, such as GLP-1 receptor agonists or SGLT2 inhibitors.

The socioeconomic gradients identified in this study suggest there are structural factors that contribute to the high burden of cardiovascular disease in Pakistan. Low income and low educational attainment are significant contributors to the increased risk of cardiovascular disease, likely through multiple pathways; these include limited health literacy, reduced access to preventative care, and environmental constraints on making healthy choices [91]. This evidence indicates that solely focusing on clinical interventions will not be sufficient to reduce the growing epidemic of cardiovascular disease. Public health approaches will need to implement a multisectoral strategy, including urban planning to promote physical activity; fiscal policies to improve access to healthy food; and workplace wellness programs aimed at addressing the underlying causes of metabolic dysfunction [86]. The cross-sectional nature of this study limits our ability to make causal inferences about the timing of obesity, diabetes, and cardiovascular risk; however, previous studies have shown that these associations are consistent with biological mechanisms, so prospective cohort studies can provide clearer directionality as well as to determine if risk trajectories differ depending on the timing and sequencing of each condition's development [92]. Since this study relied on healthcare center-based sampling, it is likely that we have introduced bias by excluding individuals who have limited access to the healthcare system and therefore underestimating true risk levels in the population. Future studies should utilize community-based sampling strategies in order to capture the full socioeconomic spectrum of risk for cardiovascular disease [93].

Studying urban/semirural populations is vital to investigating knowledge gaps; however, there is little information on whether findings can be extrapolated out to the rural areas, where risk factors for obesity and diabetes may differ due to different environmental conditions and lifestyles. Rapid transitions in nutrition are already occurring in rural Pakistan due to the increased consumption of processed foods in conjunction with sustaining the dual burden of undernutrition present in these individuals, thus may lead to significant differences in the way their bodies metabolize food as compared to urban populations [94]. As well, although ASCVD risk scoring has been established to be statistically valid across multiple ethnicities, many of the ethnic-specific risk factors found within South Asian populations (such as increased lipoprotein(a) levels as well as early beta-cell dysfunction) may not be factored into this calculation [95]. Therefore, investigating the use of new biomarkers (e.g., coronary artery calcium scoring, genetic risk

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scores) should be pursued along with the previously mentioned research methods, as they may assist in increasing the accuracy of risk predictions in subsequent research [96]. Research directions for the future will include several areas of development: First, more mechanistic studies focusing on the biological mechanisms behind the increased cardiovascular disease development in persons with diabetes who are also obese need to be conducted (looking at mechanisms such as dysfunctional adipose tissue, ectopic storage of fat, mitochondrial dysfunction) [97]. Second, implementation science research should evaluate the impact of integrated care models that address obesity/diabetes/cardiovascular risks in developers in low-resource areas (evaluating methods such as task shifting to community health workers or the use of mobile health technology for monitoring) [98]. In order to evaluate whether maternal nutrition programs or childhood obesity prevention programs can disrupt the developmental origins of metabolic syndromes, longitudinal studies will be important [99].

The socioeconomic patterning of risk observed in this study demonstrates the need for targeted interventions to address health disparities. Examples include providing subsidized healthy foods in low-income neighborhoods or developing workplace-based diabetes prevention programs for sedentary occupations, which would assist to level the playing field of structural disadvantages [100]. Culturally adapted strategies may be needed to address gender disparities, as Pakistani women have a higher prevalence of obesity along with unique barriers to engaging in physical activity and accessing healthcare services [101]. The syndemic framework utilized in this study can also provide a foundation to alter traditional thinking and develop new mechanisms for analyzing and addressing complex interactions between diseases in a global health context. A similar framework can be used to evaluate the interrelationship between infectious diseases (such as TB) and metabolic diseases or between mental illness and cardiovascular disease risk patterns that are being increasingly observed in rapidly urbanizing populations [102]. This would underscore a need for health systems to change from vertical disease management to integrated, person-centered services that address multiple health issues simultaneously [103].

6. Conclusion

The present study establishes an empirical link between the interaction of obesity and diabetes within the Pakistani population and the resulting increase in cardiovascular disease risk. This study demonstrates that the co-occurrence of these two diseases produces a metabolic cost and the acceleration of cardiovascular disease by obesity and

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diabetes is far greater than the sum of their separate effects. The implications of these results are that obesity and diabetes should not be treated as two separate entities, but rather as having a common treatment outcome (i.e., treating both obesity and diabetes simultaneously to achieve cardiovascular disease prevention) and as two conditions in which the interactions between obesity and diabetes results in significantly increased risk of developing cardiovascular disease than either condition alone. Socioeconomic factors related to these findings demonstrate the need for a multisectoral approach to public health that includes more than just medical treatment options. Finally, it is important that future research investigates the pathophysiological mechanisms that are responsible for the interaction between obesity and diabetes as well as developing and evaluating integrated care models that will be applicable to low-resource settings. In addition, it is vital to consider both biological and structural determinants of health in order to effectively respond to the increasing burden of cardiovascular disease in Pakistan.

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