Intersecting Genetic Risk, Central Adiposity, and Sociocultural Determinants of Type 2 Diabetes in South Asians

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Introduction

South Asians represent a large portion of the world's population, around 1.9 billion. This accounts for nearly 24% of the world's population.[1] The South Asian population is affected by a disproportionately high rate of Type 2 Diabetes (T2D). In New York City alone, foreign-born South Asians are nearly twice as likely to have diabetes compared to other foreign-born Asians.[2] Additionally, despite having lower Body Mass Index (BMI) levels, South Asians face an early onset and higher prevalence of metabolic disease compared to their international Western counterparts. While recent work has brought forward information on the South Asian community, little work exists to discuss the multifactorial contributions to the high prevalence of T2D in South Asians and effective solution mechanisms for this group. Existing studies focus on isolated factors like BMI or migration, but not integrated frameworks.[3,4] In this paper, I will explore how the South Asian T2D crisis is driven by unique biological, genetic, and environmental factors that may render standard clinical interventions ineffective, suggesting a need for ethnic-specific diagnostic guidelines and culturally tailored interventions.

Methods

A comprehensive search of peer-reviewed literature from 2011 to 2026 was conducted using PubMed and Google Scholar. Inclusion criteria required a primary focus on South Asian-origin populations, including specific subgroups such as Punjabi Sikhs and Bangladeshi immigrants, or South Asian Americans. Given the relative scarcity of literature dedicated solely to South Asian cohorts, research involving broader Asian American populations was included when South Asian or Asian Indian subgroups were specifically disaggregated. This selection strategy acknowledges that South Asians are frequently aggregated into general "Asian American" or "Other Asian" categories in existing studies, a research practice that can mask significant ethnic-specific disparities in metabolic risk and diabetes prevalence. Exclusion criteria included studies published prior to 2011, non-English language publications, non-peer-reviewed literature, and studies lacking South Asian-specific or disaggregated subgroup data. Studies without relevance to T2D risk, diagnosis, prevention, or management were also excluded. Limitations include database limitations, potential publication bias, English

[1] Shifa Puri and Vikram Anumakonda, "A Review of Obesity, Metabolic Syndrome and Epigenetics in South Asian (SA) Communities," *Recent Advances in Clinical Trials* 4, no. 4 (2024): 1.
[2] Leena S. Gupta et al., "Prevalence of Diabetes in New York City, 2002–2008: Comparing Foreign-Born South Asians and Other Asians with U.S.-Born Whites, Blacks, and Hispanics," *Diabetes Care* 34, no. 8 (2011): 1791
[3] Puri and Anumakonda, "A Review of Obesity," 1
[4] Unjali P. Gujral et al., "Comparing Type 2 Diabetes, Prediabetes, and Their Associated Risk Factors in Asian Indians in India and in the U.S.: The CARRS and MASALA Studies," *Diabetes Care* 38, no. 7 (2015): 1312.

language restrictions, as well as substantial heterogeneity in the classification of South Asian populations across studies. Additionally, the inclusion of broader Asian American studies with disaggregated South Asian data may limit the generalizability of these findings to specific South Asian communities. Priority was given to studies examining unique biological, genetic, and environmental drivers or the efficacy of community-focused intervention models for T2D prevention or treatment. A narrative synthesis approach was employed to compare studies for recurrent patterns and grouped according to their primary focus, including biological drivers, population heterogeneity, diagnostic standards, and culturally adapted community care. When findings differed across studies, differences in population, geographic setting, study design, and measured outcomes were considered. Considering some studies addressed multiple issues, the thematic categories were used as organizational guides as opposed to mutually exclusive categories a specific study must be sorted into.

Key terms: "thin-fat phenotype," "South Asian metabolic syndrome," "epigenetics," "BMI cut-points," "ectopic adiposity," and "culturally tailored interventions"

Biological and Epigenetic Drivers of Metabolic Risk

The South Asian population demonstrates a unique biological susceptibility to T2D that is often not captured by standard clinical measures.[5] Advancements in molecular and genomic research have identified specific biomarkers that provide a deeper understanding of this risk.[6]

The "Thin-Fat" Phenotype, Epigenetics, and Ectopic Adiposity

Obesity continues to be a rising health issue among various global populations. In fact, since 1975, the worldwide prevalence of obesity has tripled.[7] This growth has been primarily attributed to an increasingly sedentary lifestyle and reduced consumption of healthy diets. Obesity is both a chronic disease and a global epidemic. Indeed, the American and European regions are home to the highest prevalence of obesity.[8] Studies have shown an association between high body mass index (BMI) and multiple chronic diseases. These include, but are not limited to, "Non Alcoholic Fatty Liver (NAFL), cardiovascular disease, diabetes mellitus, several malignancies, musculoskeletal diseases, chronic kidney disease, and mental disorders."[9]

Subsequently, obesity continues to grow rapidly as a global health issue among South Asians. South Asians often appear lean by traditional physical standards, but carry high levels of excess visceral fat. This, in turn, leads to higher cardiovascular risk.[10] Central obesity, excessive levels of visceral fat in the abdomen and stomach, leads to metabolic issues such as "insulin resistance and hypertension, even at lower body mass index (BMI) levels than seen in Western populations."[11]

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[5] Puri and Anumakonda, "A Review of Obesity," 1
[6] Richa Saxena et al., "Genome-Wide Association Study Identifies a Novel Locus Contributing to Type 2 Diabetes Susceptibility in Sikhs of Punjabi Origin From India," *Diabetes* 62, no. 5 (2013): 1746
[7] Puri and Anumakonda, "A Review of Obesity," 1
[8] Chrysoula Boutari and Christos S. Mantzoros, "A 2022 Update on the Epidemiology of Obesity and a Call to Action: As Its Twin COVID-19 Pandemic Appears to Be Receding, the Obesity and Dysmetabolism Pandemic Continues to Rage On," *Metabolism* 133 (August 2022): 155217, https://doi.org/10.1016/j.metabol.2022.155217.
[9] Boutari and Mantzoros, "2022 Update," 155217.
[10] Puri and Anumakonda, "A Review of Obesity," 1
[11] Puri and Anumakonda, "A Review of Obesity," 1

Additionally, the high rates of metabolic disorders are driven by a combination of both genetic and environmental factors against a "background of genetics."[12] This may lead to an increased tendency for fat storage and lower lean muscle mass in the population. Even at low BMI levels, South Asians experience significant levels of intrahepatic (liver) fat and pericardial fat.[13] BMI is considered an "inadequate measure of metabolically risky adiposity," especially in South Asians. Thus, intrahepatic (liver) fat and pericardial fat serve as stronger predictors of T2D compared to BMI alone.[14]

Molecular and Genetic Biomarkers

South Asia includes many ethnic populations, such as the Punjabi Sikh community. A genome-wide association study (GWAS) and multistage analysis of type 2 diabetes (T2D) of this group revealed a novel population-specific signal in the *SGCG* gene (rs9552911) located at the l3q12 locus.[15] This intronic SNP was found to be significantly associated with T2D susceptibility in this population. It is important to note that statistical association does not imply causation, and further replication in diverse South Asian populations and functional studies are needed to determine whether this variant directly contributes to the development of T2D. Functionally, the *SGCG* gene is expressed in skeletal and vascular smooth muscle. Research in knockout mice suggests that a deficiency in the sarcoglycan complex, which includes *SGCG*, leads to whole-body insulin resistance and glucose intolerance. This is due to impaired glucose uptake in the muscles.[16]

Beyond fixed genetic markers, circulating microRNAs (miRs), small molecules that regulate gene expression, may serve as epigenetic indicators of T2D risk in Asian Indians. A research study identified that miR-191 is positively associated with prevalent glycemic impairment, functioning as a marker for those already exhibiting metabolic dysfunction.[17] Nonetheless, a separate set of miRs, including miR-15a, miR-122, and miR-486, was found to be inversely associated with glycemic progression over a 2.5-year period. Further investigation is needed to evaluate whether miR(s) might serve as useful clinical biomarkers for incident T2D in the Asian Indian population and the potential for early detection.[18]

Novel scores (MET-Liver and MET-Visc) can signal elevated T2D risk independent of measured adiposity, and before fasting glucose is elevated, capturing these initial signals of disrupted processes before clinically relevant aberrations in glycemic control are present.[19] They may even detect before these ectopic fat stores may be measured radiographically. In this way, metabolites could serve as biomarkers for intrahepatic fat and visceral adiposity as early biomarkers of T2D risk.[20] These scores are particularly valuable because they can signal T2D risk independent of measured adiposity and, crucially, before fasting glucose levels become elevated. By capturing these initial signals of disrupted metabolic processes, these biomarkers

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[12] Puri and Anumakonda, "A Review of Obesity," 1

[13] Meghana D. Gadgil et al., "Adipose Tissue-Derived Metabolite Risk Scores and Risk for Type 2 Diabetes in South Asians," *International Journal of Obesity* (2024): 1.

[14] Gadgil et al., "Adipose Tissue-Derived Metabolite Risk Scores," 1.

[15] Saxena et al., "Genome-Wide Association Study," 1747.

[16] Saxena et al., "Genome-Wide Association Study," 1747.

[17] Elena Flowers et al., "Circulating microRNAs Associated with Glycemic Impairment and Progression in Asian Indians," *Biomarker Research* 3, no. 22 (2015): 2.

[18] Flowers et al., "Circulating microRNAs," 2.

[19] Gadgil et al., "Adipose Tissue-Derived Metabolite Risk Scores," 1.

[20] Gadgil et al., "Adipose Tissue-Derived Metabolite Risk Scores," 1.

offer a means of detecting pre-clinical metabolic abnormalities even before they can be measured through other avenues. As the research group stated, “use of a metabolite risk score as a biomarker of visceral and intrahepatic fat can signal elevated risk for T2D regardless of the presence of BMI-defined overweight or obesity.”[21]

Population Heterogeneity and Specific Vulnerabilities

South Asian is a diverse group where metabolic risk is influenced by geographic location, specific cultural practices, and life stages. Understanding these nuances is critical for moving beyond aggregated data that often masks the higher disease burden in specific subgroups.

The Migration Paradox

Contrary to historical assumptions that migration to Western countries inherently increases disease risk, current evidence highlights a “migration paradox” regarding diabetes prevalence. T2D prevalence is significantly higher in urban India (38%) than among Asian Indians in the U.S. (24%).[22] Conversely, the prevalence of prediabetes is higher among Asian Indians in the U.S. (33%) than among Indians living in urban India (24%). This suggests rapid economic and nutritional transitions in India may contribute to the higher diabetes prevalence exceeding the risk found in immigrant populations. Additionally, the higher prediabetes rates in the U.S. may reflect a "healthy migrant effect,” wherein individuals with higher access to education, along with early maternal and childhood nutrition, were “more likely to have the means for migration.”[23] Indeed, further studies are needed in this area.

Subgroup Diversity: Sikh and Bangladeshi Communities

Distinct cultural and religious subgroups within the South Asian diaspora exhibit unique risk profiles that may differ from some traditional clinical assumptions.

In the Punjabi Sikh community, high disease rates persist despite "nontraditional" risk profiles. Specifically, high rates of T2D and coronary artery disease persist despite the absence of conventional risk factors. Such risk factors include smoking and a meat-rich diet; however, many Sikhs do not smoke or chew tobacco due to religious and cultural reasons. Along with this, approximately 50% of Punjabi Sikhs are lifelong vegetarians.[24] Despite such behaviors, metabolic diseases have reached epidemic proportions in this group, stressing the powerful role of population-specific genetic drivers like the *SGCG* gene.

In the Bangladeshi immigrant population, a pilot study identified significant gaps in diabetes health literacy and unique cultural barriers to prevention.[25] Although participants of the study recognized family history as a risk, there was low awareness regarding hypertension and pregnancy history as diabetes risk factors. Moreover, the study also found that lifestyle modification was hindered by cultural and practical barriers. For example, 30.8% of participants cited a lack of culturally appropriate exercise clothing as a barrier to physical activity, while

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[21] Gadgil et al., "Adipose Tissue-Derived Metabolite Risk Scores," 1.
[22] Gujral et al., "Comparing Type 2 Diabetes," 1312.
[23] Gujral et al., "Comparing Type 2 Diabetes," 1312.
[24] Saxena et al., "Genome-Wide Association Study," 1747.
[25] Evangel Sarwar, Brittny Bol, and Monideepa B. Becerra, "Exploratory Pilot Study on Diabetes Health Literacy (DaHL) Among Bangladeshi Immigrants in the United States," *The Journal of Healthcare Ethics & Administration* 11, no. 3 (2025): 25.

15.4% expressed resistance to modifying traditional diets because they feared that reducing sweets would limit their participation in cultural activities.[26]

Maternal Health: The Impact of Gestational Diabetes (GDM)

For South Asian women, a history of gestational diabetes (GDM) represents a critical window of vulnerability. South Asian women in the MASALA cohort with a history of gestational diabetes (GDM) were found to have a 3.2-fold increased risk of developing T2D even after adjusting for age, weight, and family history.[27] Notably, these findings underscore that the elevated risk of GDM in this population compounds an already high genetic predisposition for metabolic impairment. Since this risk is modifiable through behavior change, the study urges the importance of early postpartum screening and lifestyle alterations to delay or prevent the onset of T2D in South Asian women.[28]

Re-evaluating Diagnostic Standards and Clinical Gaps

Current universal diagnostic standards often fail to account for the unique physiological profile of South Asians, leading to significant rates of underdiagnosis and clinical mismanagement. Addressing these gaps requires a re-evaluation of standard body mass index (BMI) thresholds and the reliance on specific glycemic markers.

The BMI Threshold Problem

Traditional clinical guidelines leverage a BMI cut-point of $\geq$25 kg/m^2 in order to trigger diabetes screening. However, this cut point is significantly under-sensitive for the Asian American population. Specifically, research consolidating data from community-based studies, including the MASALA study, suggests that standard cut-point guidelines miss approximately 36% of Asian Americans with T2D. This evidence demonstrates that lowering the screening cut-point to $\geq$23 kg/m^2 increases sensitivity to 84.7%, facilitating earlier intervention.[29] This revised methodology may facilitate earlier clinical intervention for South Asian patients. Indeed, reducing this cutoff will inevitably lead to more individuals being tested and found to be without the disease. Nevertheless, the identification of at-risk patients at a lower body size is economically and clinically practical. This shift is of note because many South Asians manifest T2D at "normal" BMI levels due to their higher body fat percentage and excess visceral fat accumulation.

Limitations of Isolated HbA1c Testing

Hemoglobin A1c (HbA1c) is increasingly used as a primary diagnostic tool. However, relying on it in isolation may not accurately capture the true prevalence or nature of T2D in Asian Indians, including both Indians living in Chennai and Delhi, India, and Indians in the United States. Findings from the CARRS and MASALA studies indicate that isolated HbA1c testing identifies a specific subgroup of individuals with "milder" glucose intolerance. This subgroup also appears to have a lower cardiometabolic risk profile, characterized by lower blood

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[26] Sarwar, Bol, and Becerra, "Exploratory Pilot Study," 27.
[27] Meghana D. Gadgil et al., "Type 2 Diabetes After Gestational Diabetes Mellitus in South Asian Women in the United States: The MASALA Study," *Diabetes/Metabolism Research and Reviews* 33, no. 6 (2017): e2891.
[28] Gadgil et al., "Type 2 Diabetes After Gestational Diabetes Mellitus," e2891.
[29] Maria Rosario G. Araneta et al., "Optimum BMI Cut Points to Screen Asian Americans for Type 2 Diabetes," *Diabetes Care* 38, no. 5 (2015): 814.

pressure and triglyceride levels. This contrasts with individuals diagnosed by fasting or 2-hour glucose measures.[30] Since the relationship between HbA1c and other glucose measures differs by ethnicity, solely using HbA1c may result in false positives or lead to the over- or under-treatment of patients.[31] These results urge the need for comprehensive studies to examine the "diagnostic accuracy and outcomes" of various glycemic measures within Asian Indian populations.

The Critical Role of the Oral Glucose Tolerance Test (OGTT)

The 2-hour Oral Glucose Tolerance Test (OGTT) remains a meaningful diagnostic tool for the South Asian community. Screening guidelines that limit testing to just HbA1c and Fasting Plasma Glucose (FPG) fail to identify 44% of Asian Americans with T2D, specifically individuals exhibiting isolated post-challenge hyperglycemia.[32] This condition can be described by glucose levels being normal during fasting, but spiking significantly after a glucose challenge. This condition is a common attribution among South Asians. It reflects a severe deficit in late-phase insulin secretion as well as moderate to severe muscle insulin resistance.[33] The 2-hour OGTT serves as a vital tool for the early and accurate diagnosis of type 2 diabetes in this high-risk group when considering such distinct pathophysiological differences.

The Model for Culturally Adapted Intervention

To truly address the high prevalence of T2D in South Asians, we must tailor interventions to the specific needs of individual communities. Some community organizations and institutions, such as the Bhagat Puran Singh Health Initiative (BPSHI) and Project RICE (Reaching Immigrants through Community Empowerment), have adopted this approach in their efforts.

A Model for Culturally Adapted Intervention

Project RICE is a pilot study conducted as part of the New York University (NYU) Prevention Research Center, a center that has roots in Community-Based Participatory Research (CBPR). Project RICE utilizes a quasi-experimental two-arm design, enrolling over 100 participants in a six-workshop intervention led by community health workers.[34] Unlike the traditional Diabetes Prevention Program (DPP), which requires 16–22 sessions, Project RICE condensed the curriculum into six two-hour sessions. The workshops include topics such as nutrition, physical activity, stress and family support, and preparing for a doctor's visit. Workshops even connected the concept of prevention to Sikh core values. The results demonstrated that this model is not only feasible, but highly efficacious as well. The primary outcomes included clinical variables and health behaviors. Clinical variables included weight, body mass index (BMI), waist circumference, blood pressure, glucose, and cholesterol. More specifically, after six months, participants portrayed significant changes in "weight, BMI, waist circumference, blood pressure, glucose, physical activity, food behaviors, and diabetes knowledge, and between-group differences were significant for glucose, diabetes knowledge,

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[30] Unjali P. Gujral et al., "Isolated HbA1c Identifies a Different Subgroup of Individuals with Type 2 Diabetes Compared to Fasting or Post-Challenge Glucose in Asian Indians: The CARRS and MASALA Studies," *Diabetes Research and Clinical Practice* 153 (2019): 93.
[31] Gujral et al., "Isolated HbA1c," 93.
[32] Araneta et al., "Optimum BMI Cut Points," 815.
[33] Araneta et al., "Optimum BMI Cut Points," 815.
[34] Nadia S. Islam et al., "Diabetes Prevention in the New York City Sikh Asian Indian Community: A Pilot Study," *International Journal of Environmental Research and Public Health* 11, no. 5 (2014): 5462.

portion control, and physical activity social interaction." In addition, the study achieved high retention rates, in which 92% of participants completed all sessions.[35] This provides evidence that culturally concordant CHWs foster high levels of trust and engagement with individuals. Ultimately, this pilot study demonstrates the effectiveness of community- and clinic-based interventions.

The literature emphasizes that interventions must provide culturally appropriate recommendations for lifestyle changes rather than attempting to replace traditional habits with Western alternatives. Even with access to high-quality health care, lack of culturally and linguistically appropriate care presents as a barrier.[36] For example, data from the MASALA cohort highlights that a South Asian Mediterranean-style (SAM) diet, which integrates cultural staples like whole grains and legumes, is associated with favorable adiposity measures and lower diabetes risk. [37]

Discussion

The evidence underscores that specific biological traits, such as a high body-fat-to-muscle ratio even at lower weights, are molded by a complex interplay of genetic and epigenetic factors that favor efficient fat storage. As a result of these unique physiological profiles, universal clinical benchmarks, such as standard BMI thresholds, often fail to accurately identify individuals at high metabolic risk within certain populations. Additionally, shifting global health patterns indicate that rapid societal and nutritional transitions can create a higher disease burden in urban centers than in diaspora communities. This suggests that risk factors are evolving rapidly in local and global environments.

The disproportionate prevalence of T2D in South Asian populations may be the result of interacting biological, environmental, and clinical factors. The interactions between the thin-fat phenotype and potential genetic factors may predispose South Asians to insulin resistance and ectopic fat even at low BMI levels. These biological factors, in conjunction with migration, dietary patterns, and sociocultural influences, can further modify this underlying risk. Meanwhile, diagnostic standards based on current BMI thresholds or isolated glycemic measures may fail to identify metabolic dysfunction early enough for preventative interventions.

Emerging research into molecular biomarkers, such as circulating microRNAs and metabolite risk scores, offers significant potential for early detection of metabolic impairment before clinical symptoms manifest. However, clinical risks are often exacerbated by social determinants of health, including gaps in health literacy and cultural barriers to diet and exercise modification. Ultimately, addressing such complex health crises may require moving beyond universal medical models toward specific population-based strategies that integrate both biological insights and culturally concordant community care.

Future research should prioritize large longitudinal studies that examine distinct ethnic and cultural groups rather than solely aggregate data on the South Asian population. Further

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[35] Sahnah Lim et al., "A Culturally Adapted Diabetes Prevention Intervention in the New York City Sikh Asian Indian Community Leads to Improvements in Health Behaviors and Outcomes," *Health Behavior Research* 2, no. 1 (2019): 1.

[36] Maura Eswaradas et al., *Social Determinants of Health Interventions for Diabetes in Black and South Asian-origin Populations: An International Systematic Review* (Toronto, ON: Wellesley Institute, 2025), 1.

[37] Sharan K. Rai et al., "A South Asian Mediterranean-style Diet Is Associated with Favorable Adiposity Measures and Lower Diabetes Risk: The MASALA Cohort," *Obesity* 31, no. 6 (2023): 1697

studies are needed to examine potential replication of emerging genetic and molecular biomarkers across South Asian cohorts, evaluate the effectiveness of population-specific thresholds long-term, and assess culturally adapted interventions in larger communities. Such studies may help clarify how biological susceptibility interacts with environmental and sociocultural factors and determines which approaches are more effective for T2D prevention and management across South Asian populations.

Conclusion

All in all, the disproportionate burden of T2D in South Asian populations results from multiple factors, including a mismatch between their unique biological phenotype and current universal diagnostic standards as well as a lack of culturally appropriate care. To improve clinical sensitivity and mitigate underdiagnosis in the South Asian population, this review provides evidence for adopting an ethnic-specific BMI screening threshold of $\geq$23 kg/m^2 and prioritizing the 2-hour Oral Glucose Tolerance Test (OGTT) to capture isolated post-challenge hyperglycemia. In addition to this, the significant risk identified in South Asian women with a history of gestational diabetes emphasizes the urgent need for early postpartum screening and targeted prevention strategies. Beyond screening, the success of the Community Health Worker (CHW) model reveals that interventions are most efficacious when they are linguistically concordant and culturally adapted. Moving forward, a population health equity approach that integrates population-specific biological research with culturally resonant community care is vital for addressing this global health disparity.

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