INVESTIGATING ETIOLOGICAL HETEROGENEITY IN A BANGLADESHI YOUNG-ONSET DIABETES COHORT THROUGH CLINICAL, BIOCHEMICAL, IMAGING AND GENETIC PROFILING

MASHFIQUL HASAN[1*], NUSRAT SULTANA[2], KISHORE KUMAR SHIL[3], SAYAD BIN ABDUS SALAM[4], KOUSHIK ASHRAF[5], ABDULLAH AL NOMAN BHUIYAN[6], MD. OMOR AL MASUD[7], RIFAT HOSSAIN RATUL[8], MUHAMMAD ABUL HASANAT[9]

Background: In South Asian populations, overlapping clinical features often complicate etiological diagnosis of young-onset diabetes, leading to potential misclassification and suboptimal management. **Methods:** This study involved 284 participants (aged 10-34 years) recruited at Bangladesh Medical University (2023-24) through hospital-based and community-based screening. Assessments included fasting C-peptide, islet autoantibodies (GAD65, ZnT8, IA2), and pancreatic imaging. Targeted gene panel sequencing for maturity-onset diabetes of the young (MODY) was performed in cases with suggestive features. **Results:** Low C-peptide (<0.6 ng/mL) was identified in 9.5% (n=27) of the cohort. Among them, only 5 were antibody-positive for one or more islet antibodies [Type 1 Diabetes (T1D)], and the rest were antibody-negative (Hybrid/Idiopathic type 1). Among the 90.5% (n=257) with preserved C-peptide, multi-modal screening identified 6.0% (n=17) with positive islet antibody (LADA), 0.7% (n=2) with pancreatic calcification [fibrocalculous pancreatic diabetes (FCPD)], and 3.5% (n=10) with MODY variants. Further BMI-based categorization revealed 4.9% (n=14) with a 'Type 5' phenotype. Type 2 Diabetes (T2D) was the predominant etiology, representing 75.3% (n=214) of the cohort, including obese, overweight, and normal-weight phenotypes. **Conclusion:** Young-onset diabetes in Bangladesh is highly heterogeneous, with T2D being the most prevalent form. The identification of different proportions of T1D, LADA, MODY, FCPD, hybrid form, and T5D subgroups demonstrates that the etiology of DM in young people is heterogeneous. Incorporating C-peptide, imaging, and genetic testing is essential to achieve diagnostic precision and optimize therapy.

Keywords: Young-onset diabetes, Etiology, Bangladesh

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Affiliations:
1. *Associate Professor (OSD-DGHS), Department of Endocrinology, Bangladesh Medical University, Dhaka, Bangladesh; e-mail: mashfiqul.phd.m22 @bsmmu.edu.bd; ORCID ID: https://orcid.org/0000-0002-1805-5187*
2. *Associate Professor, Department of Endocrinology, Bangladesh Medical University, Dhaka, Bangladesh,*
3. *Resident, Department of Endocrinology, Bangladesh Medical University, Dhaka, Bangladesh,*
4. *Resident, Department of Endocrinology, Bangladesh Medical University, Dhaka, Bangladesh,*
5. *Resident, Department of Endocrinology, Bangladesh Medical University, Dhaka, Bangladesh,*
6. *Resident, Department of Endocrinology, Bangladesh Medical University, Dhaka, Bangladesh,*
7. *Postgraduate trainee, Department of Endocrinology, Bangladesh Medical University, Dhaka, Bangladesh*
8. *Research associate, Department of Endocrinology, Bangladesh Medical University, Dhaka, Bangladesh,*
9. *Professor, Department of Endocrinology, Bangladesh Medical University, Dhaka, Bangladesh*