International Journal of Science and Research (IJSR)
ISSN: 2319-7064
Impact Factor 2025: 7.089

Microbiota and Type 1 Diabetes: An Emerging Connection

Dr. T Karmugil

Junior Resident, Department of Biochemistry, AIIMS Bhopal, India
Email: *karmugil3007[at]gmail.com*

Abstract: ***The body's immune system destroys the pancreatic beta cells that produce insulin in type 1 diabetes mellitus (T1DM), a chronic autoimmune illness. Previously believed to be mostly a genetic condition, T1DM is now recognised to be significantly influenced by environmental factors, with the gut microbiota emerging as one of the most researched. Long before clinical symptoms appear, children who eventually develop type 1 diabetes exhibit altered gut microbial patterns, including decreased microbial diversity and fewer butyrate-producing bacteria such as Faecalibacterium and Roseburia. Several mechanisms have been proposed to link gut dysbiosis to beta-cell destruction, including increased intestinal permeability with translocation of bacterial products, molecular mimicry between microbial and self-peptides, loss of short-chain fatty acids that support regulatory T cells, and altered innate immune responses. The broader hygiene hypothesis is supported by the fact that environmental factors that influence the early microbiota, such as formula feeding, caesarean delivery, and antibiotic exposure, also impact T1DM risk. Probiotics, dietary fibre, prebiotics, and faecal microbiota transplantation are examples of early therapeutic techniques that have demonstrated promising but early outcomes. This review identifies areas that require more research and summarises the available data on the relationship between gut microbiota and type 1 diabetes.***

Keywords: Type 1 diabetes mellitus; Gut microbiota; Dysbiosis; Probiotics; Hygiene hypothesis

1. Introduction

The body's immune system targets and kills the pancreatic beta cells that produce insulin in type 1 diabetes mellitus (T1DM), a chronic autoimmune disease. Patients become reliant on lifelong insulin therapy when blood glucose levels rise substantially in the absence of insulin. Type 1 diabetes typically begins in childhood or adolescence and is not brought on by anything the child or family did incorrectly, in contrast to type 2 diabetes, which is strongly associated with weight and lifestyle choices (1).

Globally, the number of children with type 1 diabetes has been gradually increasing. Children under the age of 15 are diagnosed with roughly 78,000 new cases annually, and in many countries, this number is rising by 3 to 5 percent annually (2). India bears a disproportionate amount of this burden. The Indian Council of Medical Research (ICMR) reports that approximately 16,000 new instances of T1DM are diagnosed annually, and approximately 95,600 children under the age of 14 had the disease in 2022. As a result, India is the nation in South-East Asia with the greatest number of children with T1DM (3). The frequency is around 17.9 per 100,000 children in Karnataka and 10.2 per 100,000 in Karnal, Haryana, with higher rates in urban than in rural areas, according to regional research (4).

Why T1DM is becoming more common is not fully understood. Genetic risk is involved; the strongest known risk factors are variations in HLA class II genes, primarily HLA-DR3 and HLA-DR4. However, since the human gene pool has not changed significantly in a few decades, genes alone cannot account for the increasing numbers. This makes it very evident that a youngster who is genetically predisposed to the condition is affected by environmental circumstances. Although the precise causes are still being determined, early life nutrition, antibiotic exposure, viral infections, and alterations in the gut microbiota have all been proposed (5).

The gut microbiota, the large community of bacteria, viruses, and fungi that live in our intestines, has drawn growing interest in recent years. The gut is home to most of the body's immune cells, and the bacteria that live there help shape how the immune system develops, especially in early childhood. When this microbial community is disturbed, a state called dysbiosis, the immune system may behave abnormally. Several studies have now shown that children who go on to develop T1DM have a different gut microbiota compared to healthy children, often well before clinical symptoms appear (6).

This review brings together current evidence on how the gut microbiota may be involved in the development of T1DM. It looks at what is different about the gut bacteria of T1DM patients, the possible biological pathways linking dysbiosis to beta-cell destruction, the environmental factors that affect both the microbiota and T1DM risk, and the early efforts to use microbiota-based approaches as a way to prevent or treat the disease.

2. The Gut Microbiota in Healthy Children vs T1DM

The human gut is home to trillions of microbes that live alongside us from the moment we are born. In a healthy child, this microbial community is made up mostly of *Firmicutes* and *Bacteroidetes*, with smaller numbers of *Actinobacteria* and *Proteobacteria*. The makeup of the gut microbiota changes a lot during the first three years of life and slowly settles into an adult-like pattern by around age three (7). This early window is also the time when the immune system is learning what to attack and what to leave alone, which is why disturbances in the microbiota during this period are thought to matter so much for later autoimmune disease.

Several studies have now compared the gut microbiota of children who develop T1DM with that of healthy children.

One of the most important is the DIABIMMUNE study, which looked at children in Finland, Estonia, and Russia, three countries with very different T1DM rates. The researchers found that children from Finland, where T1DM is most common, had a different microbial pattern early in life, with more *Bacteroides* and fewer *Bifidobacterium* species compared to Russian children, who have the lowest rates of T1DM (8). The TEDDY study (The Environmental Determinants of Diabetes in the Young), one of the largest birth cohort studies in this area, also showed reduced microbial diversity in children who later developed islet autoimmunity (9).

Kostic and associates monitored the intestinal flora of a small group of infants from birth. They found that there was a significant decrease in microbial diversity and an increase in microorganisms associated with inflammation prior to the development of T1DM (10). According to other research, Bacteroides species are frequently more prevalent in T1DM patients than butyrate-producing bacteria such as Faecalibacterium prausnitzii and Roseburia species (11). Reducing butyrate intake may be very important because it is a short-chain fatty acid that promotes anti-inflammatory immune responses and helps maintain gut lining health.

Overall, the pattern that emerges from these studies is fairly consistent: children who develop T1DM tend to have lower microbial diversity, fewer beneficial bacteria, and more pro-inflammatory species, and these changes often appear well before any clinical signs of diabetes.

3. How Microbiota May Trigger T1DM (Mechanisms)

What role do gut microorganisms play in pancreatic damage? Over the past ten years, this question has been the subject of extensive investigation, and a number of potential avenues have emerged. The microbiota most likely influences T1DM through a variety of pathways that cooperate in a child who is genetically predisposed; no single mechanism most likely operates alone.

1) Leaky Gut and Immune Activation

Like a tight wall, a healthy gut lining allows nutrients to enter the bloodstream while preventing bacteria and their byproducts from doing so. This wall becomes more permeable in T1DM, a condition known as "leaky gut." Studies have demonstrated that children with T1DM, and even those who are still in the pre-diabetic stage with islet autoantibodies, have higher amounts of zonulin, a protein that controls the openings between gut cells (12). Bacterial compounds like lipopolysaccharide (LPS) can enter the bloodstream when the gut becomes leaky and activate immune cells via toll-like receptors. The autoimmune assault on beta cells may be initiated by this low-grade inflammation(13).

2) Molecular Mimicry

Another idea is molecular mimicry- the immune system attacks a bacterial protein, but because that protein looks similar to one in the body, it ends up attacking the body too. Certain gut bacteria carry peptides that resemble parts of the insulin molecule or other beta-cell proteins. T cells trained against these bacterial peptides may then cross-react with the pancreas (14). This idea has been supported by both animal studies and human data, though it is not yet fully proven.

3) Loss of Short-Chain Fatty Acids and Treg Cells

Short-chain fatty acids (SCFAs), especially butyrate, are produced when gut bacteria ferment dietary fibre. Butyrate has a calming effect on the immune system: it feeds the gut lining, supports regulatory T cells (Tregs) that suppress autoimmune responses, and lowers production of inflammatory cytokines (15). In children who develop T1DM, butyrate-producing bacteria are reduced, which means less butyrate is available to keep the immune system in check. The result is fewer Tregs and a tilt toward inflammation, both of which favour autoimmune destruction of beta cells.

4) Disturbed Innate Immunity

The microbiota also shapes how innate immune cells like dendritic cells and macrophages behave. In germ-free mice, which have no gut bacteria, the development of T1DM in the non-obese diabetic (NOD) mouse model is altered, showing that gut microbes directly influence the disease course (16). In NOD mice given certain commensal bacteria, the rate of diabetes development drops, while exposure to other bacteria speeds it up. These animal findings, although not perfectly translatable to humans, point to a direct role for gut microbes in shaping autoimmune attack on the pancreas.

Taken together, the gut microbiota seems to influence T1DM through several connected routes: gut barrier breakdown, immune cross-reactivity, loss of anti-inflammatory metabolites, and direct effects on immune cells. These pathways do not act in isolation, and the relative importance of each is still being worked out.

4. Environmental Factors Affecting Microbiota and T1DM Risk

If the gut microbiota plays a role in T1DM, then anything that shapes the microbiota in early life could, in turn, affect disease risk. A number of such environmental factors have been studied, and many of them line up with the rise in T1DM cases seen over the past few decades.

1) Mode of Delivery

The way a baby is born has a strong influence on the first set of microbes that colonise the gut. Babies born by vaginal delivery are exposed to the mother's vaginal and gut flora, while those born by caesarean section pick up skin and hospital-associated bacteria instead (17). Several studies have reported that children born by caesarean section have a slightly higher risk of developing T1DM, though the effect is modest and not seen in every population.

2) Breastfeeding and Early Diet

Breast milk supports the growth of *Bifidobacterium* species and contains immune-protective factors that help the gut mature. Longer breastfeeding has been linked to lower T1DM risk in some studies. Early introduction of cow's milk and gluten (before 3–4 months of age) has been linked to a higher risk, possibly because these foods can disturb the developing microbiota and trigger early immune sensitisation (18).

3) Antibiotic Exposure

One of the most potent changes to the gut microbiota is frequent use of antibiotics during infancy. Many beneficial bacteria are eliminated by antibiotics, which also decreases the variety and can have long-lasting effects. Early-life antibiotic exposure raises the incidence of diabetes, according to studies in NOD mice and some human cohorts, albeit the results are conflicting (19).

4) The Hygiene Hypothesis

The broader theory underlying these findings is the hygiene hypothesis, which holds that early life exposure to fewer microorganisms due to cleaner surroundings, fewer diseases, smaller families, and increased antibiotic usage leaves the immune system underdeveloped and more prone to target the body's own tissues (20).

5. Microbiota- Based Approaches for T1DM

If gut dysbiosis contributes to T1DM, then correcting it may help prevent or slow the disease. This idea is still in early stages, but several approaches are being explored.

1) Probiotics

Live bacteria are administered as probiotics to rebalance the gut. Certain strains of Lactobacillus and Bifidobacterium have been demonstrated to postpone or prevent diabetes in NOD mice (21). There are fewer and smaller human trials. Early probiotic supplementation (before 27 days of life) was associated with a lower rate of islet autoimmunity, according to the PRODIA trial and the Trial to Reduce IDDM in the Genetically at Risk (TRIGR) research, which examined probiotic usage in infants at high genetic risk (22). Even these results are encouraging, more extensive research is required before probiotics may be suggested as a preventative measure.

2) Diet and Prebiotics

One of the main factors influencing the gut microbiota is diet. A diet high in fibre promotes a healthy gut lining by feeding bacteria that generate short-chain fatty acids. Beneficial bacteria are specifically fed by prebiotics, which are non-digestible carbohydrates like fructo-oligosaccharides and inulin. Although there is little evidence to prevent T1DM, prebiotic-rich and high fibre diets may help lower inflammation in those with the condition, according to preliminary findings (23).

3) Faecal Microbiota Transplantation (FMT)

During FMT, a healthy donor's stool is put into the patient's stomach. It is already used to treat recurrent Clostridium difficile infections. A small study in newly diagnosed adult T1DM patients in the Netherlands revealed that FMT could preserve residual beta-cell function for up to 12 months, despite uneven results (24). Since FMT is still experimental for T1DM, it should only be utilised in clinical trials.

6. Future Directions

Other approaches under study include postbiotics (purified bacterial metabolites such as butyrate), engineered probiotics designed to deliver insulin-protective signals, and dietary interventions starting in pregnancy or infancy. Most of these are years away from routine clinical use, but they reflect a growing belief that the gut microbiota will become a real therapeutic target in T1DM in the coming years (25).

7. Conclusion

It is no longer believed that type 1 diabetes solely affects the pancreas. The development and course of the illness seem to be significantly influenced by the gut and the microbes that live there. Many routes, such as leaky gut, molecular mimicry, loss of short-chain fatty acids, and altered innate immunity, relate these microbial changes to beta-cell destruction. Children who go on to develop type 1 diabetes typically exhibit changes in their gut bacteria even before clinical symptoms manifest. The broader hygiene hypothesis is supported by the fact that environmental factors like newborn feeding, mode of delivery, and antibiotic use can influence both the microbiota and T1DM risk. Probiotics, dietary modifications, and faecal microbiota transplantation are examples of microbiota-based treatments that are still in their infancy yet have great potential. To translate these early findings into effective prevention and treatment efforts, larger and longer research is now required, particularly in Indian children, where the burden is substantial.

References

[1] DiMeglio LA, Evans-Molina C, Oram RA. Type 1 diabetes. Lancet. 2018 Jun 16;391(10138):2449–62. doi:10.1016/S0140-6736(18)31320-5 PubMed PMID: 29916386; PubMed Central PMCID: PMC6661119.

[2] Patterson CC, Karuranga S, Salpea P, Saeedi P, Dahlquist G, Soltesz G, et al. Worldwide estimates of incidence, prevalence and mortality of type 1 diabetes in children and adolescents: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. Diabetes Res Clin Pract. 2019 Nov;157:107842. doi:10.1016/j.diabres.2019.107842 PubMed PMID: 31518658.

[3] Indian Council of Medical Research. ICMR Guidelines for Management of Type 1 Diabetes. New Delhi: ICMR; 2022. Available from: https://www.icmr.gov.in

[4] Kumar KMP. Incidence trends for childhood type 1 diabetes in India. Indian J Endocrinol Metab. 2015 Apr;19(Suppl 1): S34–5. doi:10.4103/2230-8210.155378 PubMed PMID: 25941647; PubMed Central PMCID: PMC4413384.

[5] Knip M, Siljander H. The role of the intestinal microbiota in type 1 diabetes mellitus. Nat Rev Endocrinol. 2016 Mar;12(3):154–67. doi:10.1038/nrendo.2015.218 PubMed PMID: 26729037.

[6] Zheng P, Li Z, Zhou Z. Gut microbiome in type 1 diabetes: A comprehensive review. Diabetes Metab Res Rev. 2018 Oct;34(7):e3043. doi:10.1002/dmrr.3043 PubMed PMID: 29929213.

[7] Yatsunenko T, Rey FE, Manary MJ, Trehan I, Dominguez-Bello MG, Contreras M, et al. Human gut microbiome viewed across age and geography. Nature. 2012 May 9;486(7402):222–7. doi:10.1038/nature11053 PubMed PMID: 22699611; PubMed Central PMCID: PMC3376388.

[8] Vatanen T, Kostic AD, d'Hennezel E, Siljander H, Franzosa EA, Yassour M, et al. Variation in microbiome LPS immunogenicity contributes to autoimmunity in humans. Cell. 2016 May 5;165(4):842–53. doi:10.1016/j.cell.2016.04.007 PubMed PMID: 27133167; PubMed Central PMCID: PMC4950857.

[9] Vatanen T, Franzosa EA, Schwager R, Tripathi S, Arthur TD, Vehik K, et al. The human gut microbiome in early-onset type 1 diabetes from the TEDDY study. Nature. 2018 Oct;562(7728):589–94. doi:10.1038/s41586-018-0620-2 PubMed PMID: 30356183; PubMed Central PMCID: PMC6296767.

[10] Kostic AD, Gevers D, Siljander H, Vatanen T, Hyötyläinen T, Hämäläinen AM, et al. The dynamics of the human infant gut microbiome in development and in progression toward type 1 diabetes. Cell Host Microbe. 2015 Feb 11;17(2):260–73. doi:10.1016/j.chom.2015.01.001 PubMed PMID: 25662751; PubMed Central PMCID: PMC4689191.

[11] de Goffau MC, Luopajärvi K, Knip M, Ilonen J, Ruohtula T, Härkönen T, et al. Fecal microbiota composition differs between children with β-cell autoimmunity and those without. Diabetes. 2013 Apr;62(4):1238–44. doi:10.2337/db12-0526 PubMed PMID: 23274889; PubMed Central PMCID: PMC3609577.

[12] Sapone A, de Magistris L, Pietzak M, Clemente MG, Tripathi A, Cucca F, et al. Zonulin upregulation is associated with increased gut permeability in subjects with type 1 diabetes and their relatives. Diabetes. 2006 May;55(5):1443–9. doi:10.2337/db05-1593 PubMed PMID: 16644703.

[13] Vaarala O. Is the origin of type 1 diabetes in the gut? Immunol Cell Biol. 2012 Mar;90(3):271–6. doi:10.1038/icb.2011.115 PubMed PMID: 22290506.

[14] Tai N, Wong FS, Wen L. The role of gut microbiota in the development of type 1, type 2 diabetes mellitus and obesity. Rev Endocr Metab Disord. 2015 Mar;16(1):55–65. doi:10.1007/s11154-015-9309-0 PubMed PMID: 25619480; PubMed Central PMCID: PMC4474723.

[15] Mariño E, Richards JL, McLeod KH, Stanley D, Yap YA, Knight J, et al. Gut microbial metabolites limit the frequency of autoimmune T cells and protect against type 1 diabetes. Nat Immunol. 2017 May;18(5):552–62. doi:10.1038/ni.3713 PubMed PMID: 28346408.

[16] Wen L, Ley RE, Volchkov PY, Stranges PB, Avanesyan L, Stonebraker AC, et al. Innate immunity and intestinal microbiota in the development of type 1 diabetes. Nature. 2008 Oct 23;455(7216):1109–13. doi:10.1038/nature07336 PubMed PMID: 18806780; PubMed Central PMCID: PMC2574766.

[17] Dominguez-Bello MG, Costello EK, Contreras M, Magris M, Hidalgo G, Fierer N, et al. Delivery mode shapes the acquisition and structure of the initial microbiota across multiple body habitats in newborns. Proc Natl Acad Sci U S A. 2010 Jun 29;107(26):11971–5. doi:10.1073/pnas.1002601107 PubMed PMID: 20566857; PubMed Central PMCID: PMC2900693.

[18] Virtanen SM, Kenward MG, Erkkola M, Kautiainen S, Kronberg-Kippilä C, Hakulinen T, et al. Age at introduction of new foods and advanced beta cell autoimmunity in young children with HLA-conferred susceptibility to type 1 diabetes. Diabetologia. 2006 Jul;49(7):1512–21. doi:10.1007/s00125-006-0236-1 PubMed PMID: 16596359.

[19] Livanos AE, Greiner TU, Vangay P, Pathmasiri W, Stewart D, McRitchie S, et al. Antibiotic-mediated gut microbiome perturbation accelerates development of type 1 diabetes in mice. Nat Microbiol. 2016 Aug 22;1(11):16140. doi:10.1038/nmicrobiol.2016.140 PubMed PMID: 27782139; PubMed Central PMCID: PMC5076472.

[20] Bach JF. The effect of infections on susceptibility to autoimmune and allergic diseases. N Engl J Med. 2002 Sep 19;347(12):911–20. doi:10.1056/NEJMra020100 PubMed PMID: 12239261.

[21] Calcinaro F, Dionisi S, Marinaro M, Candeloro P, Bonato V, Marzotti S, et al. Oral probiotic administration induces interleukin-10 production and prevents spontaneous autoimmune diabetes in the non-obese diabetic mouse. Diabetologia. 2005 Aug;48(8):1565–75. doi:10.1007/s00125-005-1831-2 PubMed PMID: 15986236.

[22] Uusitalo U, Liu X, Yang J, Aronsson CA, Hummel S, Butterworth M, et al. Association of early exposure of probiotics and islet autoimmunity in the TEDDY study. JAMA Pediatr. 2016 Jan;170(1):20–8. doi:10.1001/jamapediatrics.2015.2757 PubMed PMID: 26552054; PubMed Central PMCID: PMC4803028.

[23] Ho J, Nicolucci AC, Virtanen H, Schick A, Meddings J, Reimer RA, et al. Effect of prebiotic on microbiota, intestinal permeability, and glycemic control in children with type 1 diabetes. J Clin Endocrinol Metab. 2019 Oct 1;104(10):4427–40. doi:10.1210/jc.2019-00481 PubMed PMID: 31188437.

[24] de Groot P, Nikolic T, Pellegrini S, Sordi V, Imangaliyev S, Rampanelli E, et al. Faecal microbiota transplantation halts progression of human new-onset type 1 diabetes in a randomised controlled trial. Gut. 2021 Jan;70(1):92–105. doi:10.1136/gutjnl-2020-322630 PubMed PMID: 33106354; PubMed Central PMCID: PMC7813091.

[25] Del Chierico F, Conta G, Matteoli MC, Fierabracci A, Reddel S, Macari G, et al. Gut microbiota functional traits, blood pH, and anti-GAD antibodies concur in the clinical characterization of T1D at onset. Int J Mol Sci. 2022 Sep 22;23(19):10256. doi:10.3390/ijms231910256 PubMed PMID: 36232556; PubMed Central PMCID: PMC9569488.