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RESEARCH ARTICLE

EFFECTS OF THE GUT MICROBIOME ON THYROID FUNCTION

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Abstract

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The human body is home to numerous microorganisms that colonize the skin, gastrointestinal tract, respiratory tract, genitourinary tract, oral cavity, and other areas. These microorganisms work together to create a complex micro-ecosystem, with the intestinal tract housing the most of them. There are positive effects of a healthy gut micro biota on immune system activity in addition to the thyroid function. Thyroid hormones and thyroid function overall benefited from probiotic supplementation. The effect of gut micro biota on thyroid function and diseases would need to be examined in future human studies with sufficient power.

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Introduction:-

One of the largest interfaces between the host, external factors, and internal antigens in the human body is the gastrointestinal (GI) tract[1].The term "gut microbiota" refers to the assortment of bacteria, archaea, and eukarya that inhabit the GI tract and have co-evolved with the host over thousands of years to develop a complex and beneficial relationship[2,3].The microbiota benefits the host in a variety of physiological ways, including enhancing gut integrity, forming the intestinal epithelium[4], generating energy[5], warding off pathogens[6], and controlling host immunity[7].An altered microbial composition, also known as dysbiosis, has the potential to disrupt these mechanisms[8].The microbiota in the human gut is made up of many trillions of bacterial organisms. Humans have coevolved in a mutually beneficial partnership with the complex, dynamic microbial population[9].It is widely acknowledged that the thyroid hormone can affect gut motility and gastrointestinal structure, and that a healthy gut flora may help thyroid function[10-12].The most important factors in preserving human wellness is the gut microbiota[13].Numerous processes are carried out by the gut bacteria, including the production of vitamins, pathogen defence, induction of immune responses, and food fermentation[14].

Gut Microbiota and Health:

The gut microbiota shows consistency, resiliency, and symbiotic relationships with the host when things are healthy.Viral organisms, yeasts, and bacteria make up the gut microbiota. High taxonomic diversity, high microbial gene richness, and stable core microbiota are frequently found in a healthy microbiota community.It should be noted, though, that the relative distribution of microorganisms varies from person to person and can even differ within the same person. Age and environmental factors can affect the gut microbiota of humans[15]. Additionally, the GI tract's various anatomical regions have different gut microbiota.These variations are primarily caused by the various environments.The small intestine has a short transit time and a high concentration of bile, while the colon

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has a longer transit time, a milder pH, and larger microbial communities, especially anaerobic types, are frequently seen there[16].

Gut microbiota also differs by age. Generally, the microbiota diversity increases in the time between childhood and adulthood and decreases at older age (over 70)[17].Humans are born with a sizable community of pathogenic and symbiotic microbes that live in our gut, skin, and mucosal passages and are resistant to external pathogens[18]. In the GI tract, proteins and sugars from food are both digested. Numerous enzymes produced by various bacteria are needed for the metabolism of polysaccharides and particular proteins[19].Due to the need to compete with foreign bacteria, gut bacteria have evolved different strategies for squelching rivals, such as the secretion of various bacteriocins.

The type 6 secretion system, which is a contact-dependent competitor in the gut and is involved with eukaryotic cells, was first discovered to be important for intraspecies killing[20].The system functions by delivering effectors into the cytoplasm of contact cells, such as membrane, cell wall, and nucleotide degraders[21]. Human diseases and health are closely related to intestinal microbial balance.Human microbiota plays a crucial role in digestion, metabolism, and immunity[22,23].

The gut microbiota is also crucial for the biosynthesis of bioactive molecules like vitamins, amino acids, and lipids[24]. The human microbiota plays an important role in the development of the intestinal mucosa and immune system in addition to protecting the host from external pathogens by producing antimicrobial substances. The idea of a "healthy" gut microbiota and its connection to the physiological processes of the host are the subject of extensive research. [25].

Increasing evidence points to the gut microbiota's ability to control the local intestinal immune system and to modulate the immune system external to the gastrointestinal system by secreting metabolites[26].

Gut microbiota, Thyroid and microelements

Since the primary route of iodine uptake in humans is through the gastrointestinal tract and transfer to the thyroid gland, the trillions of microorganisms in the gut play a crucial role in regulating iodine metabolism[27].As a supplementary micronutrient for the synthesis of thyroid hormones, the thyroid gland needs iodine.

Potentially connected to microbial metabolism is the immunological system that leads to thyroiditis development. The main producers of short chain fatty acids, which are primarily butyrate, acetate, and propionate, are the bacteria Bacteroidetes, Bifidobacterium, Faecalibacterium, and Enterobacteria, which are abundant sources of energy for the host[26].

According to studies, Lactobacillus transforms intracellular sodium selenite into selenocysteine and selenomethionine, which makes it easier for the body to absorb selenium as organic selenium [28,29].Iron and zinc, which are used to control thyroid hormone synthesis or activity conversion, are microelements that may be affected by microbiota in terms of absorption and utilisation (30).Because some bacteria have improved their heme-catching mechanisms, iron availability affects the microbiota's composition and is necessary for bacterial growth. On the other hand, by lowering pH through the production of short chain fatty acids, microbiota are able to increase iron bioavailability in the colon. In particular in environments where iron is scarce, bacteria have siderophores like enterobactin, which are high-affinity proteins for iron that take up $Fe3+$.[31,32,33].

Despite adequate iodine intake, iron deficiency may contribute to impaired thyroid hormone synthesis, storage, and secretion because it reduces oxygen transport or damages heme-dependent thyroid peroxidase.The enzyme thyroid iodine peroxidase (TPO), which is found at the apical membrane of the thyrocyte, catalyses the iodination of thyroglobulin and the coupling of iodotyrosine molecules, two essential steps in the synthesis of thyroid hormone. Iron deficiency may negatively impact the activity of this iron-dependent enzyme, resulting in low plasma levels of thyroid hormone, increased TSH secretion, and enlarged thyroid[34,35].

By using bacterial sulphate esterase or -glucuronidase, the microbiota can decouple the sulfated glucuronide derivatives of iodothyronine, improving the reabsorption of thyroid hormones in the enterohepatic circulation[36]. Another way that the microbiota is involved in iodothyronine metabolism is through inhibition of 5-deiodinase activity, which has the direct result of reducing the conversion of T4 to T3[37].The enzyme 1,5′-deoidinase, which catalyses the conversion of T4 to T3 and lowers metabolic rate, depends on zinc, a micronutrient that is crucial for thyroid health and homeostasis. Given that hypothyroidism causes zinc deficiency and inadequate zinc supplementation results in hypothyroidism, the relationship between zinc and thyroid disorders appears to be reciprocal. [38,39]

Gut microbiota and thyroid cancer

When compared to the healthy control group, patients with thyroid cancer and thyroid nodules have gut microbiota that is more diverse and rich in microorganisms, suggesting a link between gut microbiota and thyroid cancer and nodules.Streptococcus and Neisseria are relatively more common in thyroid nodules compared to healthy control groups, whereas Clostridiaceae and Neisseria are significantly more common in thyroid cancer. [40].According to studies [41, 42], Streptococcus increases the risk of developing adenomas and carcinomas. Clostridiaceae may also have carcinogenic effects. Diet and gut microbiota interactions may be crucial for tumour aggressiveness, according to a serum metabolomic analysis of patients with thyroid cancer distant metastases [43].

Pro-biotics and thyroid function

Lactobacillaceae and Bifidobacteraceae are frequently decreased in hypothyroidism and hyperthyroidism. Supplementing mice with Lactobacillus reuteri increased free T4, thyroid mass, and physiological factors like more active behaviour, which improved their thyroid function. [44]

In a recent study, pro- and pre-biotic supplementation known as synbiotics had positive effects on patients with hypothyroidism by significantly lowering TSH, levothyroxine dose, and fatigue while raising fT3[45].By attaching T3 to bacterial thyroid-binding hormone, microbes like E. coli serve as a reservoir for T3, which may lessen the need for T4 supplementation by preventing thyroid hormone fluctuations. Given that iodothyronines deconjugation is controlled by the bacterial enzymes sulfatases and ß-glucuronidases, which may be more readily available as a result of probiotics [46,47,48], probiotics have a positive effect on lowering serum hormone fluctuations.

Conclusion:-

A common finding in thyroid disorders is dysbiosis. It modifies the immune response on the one hand by increasing inflammation and decreasing immune tolerance. Microbial dysbiosis may cause fluctuations in the synthesis and metabolism of thyroid hormones that target associated microelements, resulting in abnormal thyroid homeostasis (49). Through the inhibition of TSH and its own deiodinase activity, it can directly affect the levels of thyroid hormones.Additionally, thyroid-related minerals such as iodine, selenium, zinc, and iron—all of which are crucial for thyroid health—are affected by the microbiota in the gut. It is well known that abnormal levels of these minerals are associated with thyroid dysfunction. Incorporating trace elements like selenium, zinc, and copper into organic compounds appears to be possible for probiotics. [48]. For thyroid disorders, probiotics might serve as an adjuvant therapy.

Conflict Of Interest

The authors declare no conflict of interest.

References:-

1. Bengmark S. (1998) Ecological control of the gastrointestinal tract. The role of probiotic flora. Gut 42, 2–7 doi: 10.1136/gut.42.1.2
2. Backhed F. (2005) Host-bacterial mutualism in the human intestine. Science 307, 1915–1920 doi: 10.1126/science.1104816
3. Neish A.S. (2009) Microbes in gastrointestinal health and disease. Gastroenterology 136, 65–80 doi: 10.1053/j.gastro.2008.10.080
4. Natividad J.M.M. and Verdu E.F. (2013) Modulation of intestinal barrier by intestinal microbiota: Pathological and therapeutic implications. Pharmacol. Res. 69, 42–51 doi: 10.1016/j.phrs.2012.10.007
5. den Besten G., van Eunen K., Groen A.K., Venema K., Reijngoud D.-J., Bakker B.M. (2013) The role of short-chain fatty acids in the interplay between diet, gut microbiota, and host energy metabolism. J. Lipid Res. 54, 2325–2340 doi: 10.1194/jlr.R036012
6. Bäumler A.J. and Sperandio V. (2016) Interactions between the microbiota and pathogenic bacteria in the gut. Nature 535, 85–93 doi: 10.1038/nature18849

7. Gensollen T., Iyer S.S., Kasper D.L., Blumberg R.S. (2016) How colonization by microbiota in early life shapes the immune system. Science 352, 539–544 doi: 10.1126/science.aad9378
8. Thursby, Elizabeth, and Nathalie Juge. "Introduction to the human gut microbiota." The Biochemical journal vol. 474,11 1823-1836. 16 May. 2017, doi:10.1042/BCJ20160510
9. G. P. Donaldson, S. M. Lee, and S. K. Mazmanian, "Gut biogeography of the bacterial microbiota," Nature Reviews Microbiology, vol. 14, no. 1, pp. 20–32, 2016.
10. J. Knezevic, "-yroid-Gut-Axis: how does the microbiota influence thyroid function?" Nutrients, vol. 12, no. 6, 2020.
11. X. Su, Y. Zhao, Y. Li, S. Ma, and Z. Wang, "Gut dysbiosis is associated with primary hypothyroidism with interaction ongut-thyroid axis," Clinical Science, vol. 134, no. 12, pp. 1521–1535, 2020.
12. N. R. Shin, S. Bose, J. H. Wang et al., "Chemically or surgically induced thyroid dysfunction altered gut microbiota in ratmodels," -e FASEB Journal, vol. 34, no. 6, pp. 8686–8701, 2020.
13.Shreiner, A. B., Kao, J. Y. & Young, V. B. The gut microbiome in health and in disease. Curr. Opin. Gastroenterol. **31**, 69–75 (2015).
14. Hillman, E. T., Lu, H., Yao, T. & Nakatsu, C. H. Microbial ecology along the gastrointestinal tract. Microbes Environ. **32**, 300–313 (2017).
15.Fan, Y. & Pedersen, O. Gut microbiota in human metabolic health and disease. Nat. Rev. Microbiol. **19**, 55–71 (2021).
16.Milani, C. et al. The first microbial colonizers of the human gut: composition, activities, and health implications of the infant gut microbiota. Microbiol. Mol. Biol. Rev. **81**, e00036–00017 (2017).
17.Rinninella, E. et al. What is the healthy gut microbiota composition? A changing ecosystem across age, environment, diet, and diseases. Microorganisms. **7**, 14 (2019).
18.Bohnhoff, M., Drake, B. L. & Miller, C. P. The effect of an antibiotic on the susceptibility of the mouse's intestinal tract to Salmonella infection. Antibiotics Annu. **3**, 453–455 (1955).
19.Martens, E. C., Chiang, H. C. & Gordon, J. I. Mucosal glycan foraging enhances fitness and transmission of a saccharolytic human gut bacterial symbiont. Cell Host Microbe **4**, 447–457 (2008).
20.Pukatzki, S. et al. Identification of a conserved bacterial protein secretion system in Vibrio cholerae using the Dictyostelium host model system. Proc. Natl Acad. Sci. USA **103**, 1528–1533 (2006).
21.Russell, A. B. et al. Type VI secretion delivers bacteriolytic effectors to target cells. Nature **475**, 343–347 (2011).
22. Ley, R. E., Turnbaugh, P. J., Klein, S. & Gordon, J. I. Human gut microbes associated with obesity. Nature **444**, 1022–1023 (2006).
23. Bouskra, D. et al. Lymphoid tissue genesis induced by commensals through NOD1 regulates intestinal homeostasis. Nature **456**, 507–510 (2008).
24. Turnbaugh, P. J. et al. An obesity-associated gut microbiome with increased capacity for energy harvest. Nature **444**, 1027–1031 (2006).
25. Hou, K., Wu, ZX., Chen, XY. et al. Microbiota in health and diseases. Sig Transduct Target Ther **7**, 135 (2022). https://doi.org/10.1038/s41392-022-00974-4
26. Fenneman AC, Rampanelli E, Yin YS, Ames J, Blaser MJ, Fliers E, et al. Gut Microbiota and Metabolites in the Pathogenesis of Endocrine Disease.Biochem Soc Trans (2020) 48(3):915–31. doi: 10.1042/bst20190686
27. Jiang, Wen et al. "The relationships between the gut microbiota and its metabolites with thyroid diseases." Frontiers in endocrinology vol. 13 943408. 18 Aug. 2022, doi:10.3389/fendo.2022.943408
28. Calomme M, Hu J, Van den Branden K, Vanden Berghe DA. Seleno-lactobacillus. an organic selenium source. Biol Trace Elem Res (1995) 47(1-3):379–83. doi: 10.1007/BF02790140
29. Pessione E. Lactic acid bacteria contribution to gut microbiota complexity: lights and shadows. Front Cell Infect Microbiol (2012) 2:86. doi: 10.3389/fcimb.2012.00086
30. Frohlich E, Wahl R. Microbiota and thyroid interaction in health and disease. Trends Endocrinol Metab (2019) 30(8):479–90. doi: 10.1016/j.tem.2019.05.008
31. Fröhlich E., Wahl R. Microbiota and thyroid interaction in health and disease. Trends Endocrinol. Metab. 2019;30:479–490. doi: 10.1016/j.tem.2019.05.008
32 Chieppa M., Giannelli G. Immune cells and microbiota response to iron starvation. Front. Med. 2018;5:5–8. doi: 10.3389/fmed.2018.00109.
33 Wu W., Song Y., He C., Liu C., Wu R., Fang L., Cong Y., Miao Y., Liu Z. Divalent metal-ion transporter 1 is decreased in intestinal epithelial cells and contributes to the anemia in inflammatory bowel disease. Sci. Rep. 2015;5:1–12. doi: 10.1038/srep16344.
34. Kawicka A., Regulska-Ilow B. Metabolic disorders and nutritional status in autoimmune thyroid diseases. PostepyHig. Med. Dosw. 2015;69:80–90. doi: 10.5604/17322693.1136383.

35. Zimmermann M.B. The influence of iron status on iodine utilization and thyroid function. Annu. Rev. Nutr. 2006;26:367–389. doi: 10.1146/annurev.nutr.26.061505.111236.
36.Virili C, Centanni M. "With a little help from my friends" - the role of microbiota in thyroid hormone metabolism and enterohepatic recycling. Mol Cell Endocrinol (2017) 458:39–43. doi: 10.1016/j.mce.2017.01.053
37. Nguyen TT, DiStefano JJ, 3rd, Huang LM, Yamada H, Cahnmann HJ. 5'- and 5-deiodinase activities in adult rat cecum and large bowel contents inhibited by intestinal microflora. Am J Physiol (1993) 265(3 Pt 1):E521–4. doi: 10.1152/ajpendo.1993.265.3.E521
38. Fröhlich E., Wahl R. Microbiota and thyroid interaction in health and disease. Trends Endocrinol. Metab. 2019;30:479–490. doi: 10.1016/j.tem.2019.05.008.
39. Arora M. Study of trace elements in patients of hypothyroidism with special reference to zinc and copper. Biomed. J. Sci. Tech. Res. 2018;6:11–16. doi: 10.26717/BJSTR.2018.06.001336.
40. Zhang J., Zhang F., Zhao C., Xu Q., Liang C., Yang Y., Wang H., Shang Y., Wang Y., Mu X., et al. Dysbiosis of the gut microbiome is associated with thyroid cancer and thyroid nodules and correlated with clinical index of thyroid function. Endocrine. 2019;64:564–574. doi: 10.1007/s12020-018-1831-x.
41. Trapani K.M., Boghossian L.J., Caskey E. Clostridium subterminale Septicemia in a Patient with Metastatic Gastrointestinal Adenocarcinoma. Case Rep. Infect. Dis. 2018;2018:1–3. doi: 10.1155/2018/6031510.
42. Dahmus J.D., Kotler D.L., Kastenberg D.M., Kistler C.A. The gut microbiome and colorectal cancer: A review of bacterial pathogenesis. J. Gastrointest. Oncol. 2018;9:769–777. doi: 10.21037/jgo.2018.04.07
43. Shen CT, Zhang Y, Liu YM, Yin S, Zhang XY, Wei WJ, et al.. A distinct serum metabolic signature of distant metastatic papillary thyroid carcinoma. Clin Endocrinol (Oxf) (2017) 87(6):844–52. doi: 10.1111/cen.13437
44. Virili C., Fallahi P., Antonelli A., Benvenga S., Centanni M. Gut microbiota and Hashimoto’s thyroiditis. Rev. Endocr. Metab. Disord. 2018;19:293–300. doi: 10.1007/s11154-018-9467-y.
45. Talebi S., Karimifar M., Heidari Z., Mohammadi H., Askari G. The effects of synbiotic supplementation on thyroid function and inflammation in hypothyroid patients: A randomized, double-blind, placebo-controlled trial. Complement. Ther. Med. 2020;48:102234. doi: 10.1016/j.ctim.2019.102234.
46. Spaggiari G., Brigante G., de Vincentis S., Cattini U., Roli L., de Santis M.C., Baraldi E., Tagliavini S., Varani M., Trenti T., et al. Probiotics ingestion does not directly affect thyroid hormonal parameters in hypothyroid patients on levothyroxine treatment. Front. Endocinol. 2017;8:1–9. doi: 10.3389/fendo.2017.00316
47. Salvatore G. Es hormones thyroidlennes et son mkcanisme ’ Neral Comp. Endocrinol. 1963;3:15–25. doi: 10.1016/0016-6480(63)90042-X.
48. Ren Z., Zhao Z., Wang Y. Preparation of selenium/zinc-enriched probiotics and their effect on blood selenium and zinc concentrations, antioxidant capacities, and intestinal microflora in canine. Biol. Trace Element Res. 2011;141:170–183. doi: 10.1007/s12011-010-8734-x.
49. Knezevic J, Starchl C, Tmava Berisha A, Amrein K. Thyroid-Gut-Axis: How does the microbiota influence thyroid function? Nutrients (2020) 12(6):1769–84. doi: 10.3390/nu12061769.