



A CASE SERIES: MOOD, MICROBES AND GUT BRAIN AXIS

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ABSTRACT Humans have abundant bacteria in the intestinal tract and they are considered a part of the neuro-endocrine-immune pathways and can be associated with various mood disorders and affect mental health. The intestinal flora comprises approximately 1014 microbial cells, predominantly characterized by two principal bacterial phyla: Bacteroidetes and Firmicutes which collectively represent 75–80% of the total gut microbiome. Others are phyla Proteobacteria, Actinobacteria, Fusobacteria, and Verrucomicrobiota which constitutes smaller fraction of the gut microbiome. Out of which, some are beneficial (Clostridium scindens and Clostridium cluster IV–XIVa, Bacteroides thetaiotaomicron, Bacteroides uniformis) and some are non-beneficial (Clostridium difficile, pathogenic Streptococci and pathogenic Enterococci, Bacteroides fragilis). The Firmicutes/Bacteroidetes (F/B) ratio is widely accepted to have an important influence in maintaining normal intestinal homeostasis. Alteration in F/B ratio is regarded as dysbiosis, responsible for obesity and inflammatory bowel disease (IBD). These interactions play a pivotal role in human health- modulating the functions of the immune and nervous systems and has an integral role in context of human physiological processes. In this paper, we aim to highlight the role of gut microbiota in causing mental health problems. We have included three case studies of irritable bowel syndrome. All the three cases presented with both depressive and somatic symptoms. Two cases improved with combined psychiatric management and treatment of gastro-intestinal symptoms while the third case improved with treatment of GI symptoms alone. There is a link between gut microbiota and the brain, though it was difficult to distinguish temporal causality through just the symptomatology. Timely diagnosis and prompt treatment of functional gastro intestinal disorders are of utmost importance to prevent adverse mental health consequences such as depression, somatic symptom, and others.

KEYWORDS : Gut-brain axis, Microbiota in gut, mental health

INTRODUCTION

Gut-brain axis (GBA) is the two-way biochemical signaling that takes place between gastrointestinal tract (GI tract) and central nervous system (CNS) [1]. It plays a role in regulating our mood and related disorders. Major Depressive Disorder (MDD), Anxiety are primarily mind disorders, influenced by alterations of GBA and affects mood, cognition, and mental health [2]. GBA works through vagus nerve, HPA axis, neurotransmitters, and products of microbiota [2]. Microbiota can secrete many kinds of neurotransmitters, for example Lactobacillus subspecies can secrete acetylcholine (regulating memory, attention, learning and mood), Candida, Streptococcus, Escherichia coli and Enterococcus can secrete serotonin, Bacilli and Serratia can secrete dopamine [3]. Probiotics are good bacteria, or yeasts, that are beneficial for our health [9]. Mechanism of action of probiotics is closely linked to the role of prebiotics. Prebiotics are primarily polysaccharides, that the human body cannot digest or absorb. They contribute to the growth or activity of beneficial microorganisms within the host. These substances are known for their roles in enhancing immune regulation, combating pathogens, impacting metabolism, increasing mineral absorption, and overall health promotion. They regulate the capacity of intestinal microbiota, preserving the integrity of the intestinal barrier, preventing bacteria translocation, and regulating local inflammatory reaction through intestinal related immune system [4]. Irritable bowel syndrome (IBS) is a disorder of gut-brain interaction in which individuals experience symptoms of abdominal pain, altered bowel habits and bloating [5]. In this paper we have included a series of 3 cases who had presented with depressive and somatic symptoms along with IBS symptoms.

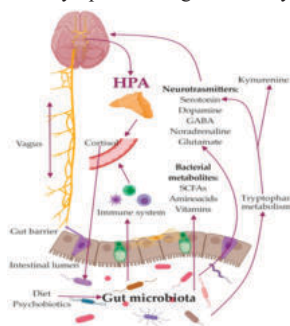


Figure 1. Figure shows that interactions occurring locally between the

gut microbiota and the intestinal cells or the enteric nervous system (ENS) and between this microbial community and the brain via neuroendocrine and metabolic pathways. Bacteria can synthesize neuromodulators, regulate the release of neurotransmitters, can produce the neurotransmitters-GABA, serotonin, dopamine, and acetylcholine which can affect the emotional state by binding to specific receptors on nerve and immune cells in the central and peripheral nervous systems. Vagus nerve and HPA axis facilitate interaction between gut and brain [2].

Case 1

A 45-year-old married female patient presented to OPD with complaints of sadness of mood most of the day, lack of interest in previously pleasurable activities, easy irritability, feeling of decreased energy in body, restlessness, occasional sleep disturbance, decreased appetite, and guilt about not being able to do proper house hold work as she was doing previously. These symptoms present since the preceding 1 to 1.5 months, have been increasing gradually. Along with these symptoms, she had recurrent complaints of abdominal pain, diarrhea, frequent urge for defecation, passing mucus in stool for 3 months and for these symptoms she had been taking medication from nearby medical store whenever such symptoms worsened as prescribed by a doctor, she had previously consulted 3 times in the past. Such symptoms had preceded the onset of depressive symptoms as per the patient's verbal report though records were not available for the same at the time of presentation. She was prescribed Tab. Escitalopram 10 mg in the morning with Tab. Clonazepam 0.5mg at night time and physician opinion was done. After 20 days it was found that she was diagnosed as IBS by physician and was prescribed probiotics - Cap. Enterogermina 2 billion CFU 3 times daily and Rifaximin 400 mg 3 times daily. But she had not taken these medications prescribed by physician and reported no improvement in depressive symptoms. Compliance was well maintained by patient for psychiatric medication. She was continued on same dose of Escitalopram and Clonazepam and need for medication compliance was explained. After 10 days she consulted again because of worsening depressive symptoms. She was taking only psychiatric medication for 10 days and had taken probiotics and Rifaximin only for 2 to 3 days due to concern about taking both medications simultaneously. She was continued again on the same dose of psychiatric medication and psychoeducation was done about maintaining compliance. In subsequent follow ups,

compliance was ensured and her depressive symptoms started to improve gradually. Within 2 months of taking probiotics regularly along with 10 mg of Escitalopram, she achieved 100% improvement in both depressive as well as GI symptoms and antidepressants were down titrated within the next 2 months.

Case 2

A 27-year-old unmarried male patient, an engineer by profession and doing work from home presented to OPD with complaints of headache, occasionally body pain, abdominal pain, weakness, not able to concentrate properly in work, impaired work performance, sleep disturbance, frequent mistakes in work, forgetfulness, diarrhea, which started around 4 months back but worsened since last 1.5 months. He had excessive concern for symptoms particularly headache which resulted in impaired work performance for which he had checked for refractive errors as he already wore prescription spectacles for myopia since childhood. He had consulted multiple physicians for headache and even an MRI was done at patient's insistence, (which was found to be normal) and for diarrhea he took ORS and Tab. Metronidazole 400 mg from medical store by himself in between. He reported frequent urge to defecate, passing excessive gas and abdominal cramping particularly after food and these symptoms preceded previously reported complaints. Such complaints have been present sporadically since around 4 months. He had similar complaints 2 year ago which resolved by itself within 2 to 3 months. He was prescribed Tab. Duloxetine 40 mg; Tab. Clonazepam 0.5 mg and psychoeducation was done about gastrointestinal symptoms and physician consultation was done. After 20 days, it was found that he was diagnosed as IBS and was prescribed probiotics- Cap. Lactogut 5 billion CFU twice a day and Tablet Rifaximin 400 mg thrice a day and anti-spasmodic (Dicyclomine) by his physician and reported some improvement in somatic symptoms. He was continued on the same dose of Duloxetine. After 30 days, he reported some improvement in somatic symptoms and gastrointestinal symptoms, so Tab. Duloxetine was hiked up to 80 mg for somatic complaints and psychoeducation was done about stress management for his busy work schedule. In further follow-ups, within 1 month, he had reported improvement in both somatic and gastrointestinal symptoms simultaneously. Then, Duloxetine was down titrated and omitted gradually within 1 month with no worsening thereafter.

Case 3

A 28-year-old married female patient, a business woman by profession came with complaints of low mood, loss of interest, lack of energy, lack of concentration and reduced appetite and weight gain in the last 1 month. Prior to the onset of above symptoms patient had two bouts of food poisoning, 2 weeks apart following which the patient had developed recurrent and persistent diarrhea and the urge to pass stools after every meal. For the above complaints she had first consulted physician and then was referred to psychiatrist. Physician had already diagnosed her as IBS and prescribed probiotics- Sachet Uno Biotics 30 billion CFU once daily. We advised for Tablet Escitalopram 10 mg and stress management. She returned after 5 days and followed only the advice of physician and she noticed significant improvement within 5 days [in both GIT symptoms and mood symptoms], even without antidepressant. She was advised to continue physician advice and to not take Escitalopram and to consult us after 20 days. In further follow-ups, it was noted that depressive symptoms completely resolved with gradual improvement in GI symptoms. She never started any antidepressant and continued to improve with probiotics and dietary modifications alone.

DISCUSSION

The cases described in this study were comparable to the existing literatures in many aspects. We have found that after starting on probiotics, there was improvement in gastrointestinal symptoms along with depressive and somatic symptoms though the temporal relationship was not properly established.

Probiotics play a role in the development of a healthy intestinal mucosal layer, thereby enhancing the intestinal barrier function and improving immunity [6,7]. Emerging probiotic sources include yogurt, whole grains wheat, whole grain corn, fruit juices, peels, seeds, garlic, onions, and green vegetables [8].

Probiotics works at different level of gastro-intestinal tract. Where probiotics choose to reside is governed predominantly by the conditions in different areas of the gut including pH, oxygen levels and the type of bacteria in the microbiome. Small intestine contains more oxygen and acidic pH compared to large intestine. These conditions support distinct

microbial communities adapted to their respective environments. Probiotics produce certain acids which discourage pathogen growth and increases level of beneficial bacteria, so it improves digestion and wellbeing and helps in growth of good bacteria [9].

In our case studies, in the first case, patient started to improve after she had maintained proper compliance of medication prescribed by physician, in the second case, patient got improvement in both somatic and gastrointestinal symptoms simultaneously. In the third case, patient showed improvement even without psychiatric treatment and responded well with probiotics.

Antidepressants may alter composition of intestinal microbiota, which are closely related to the treatment outcomes of depression and sometimes this alteration may result in possible side effects. The SSRIs- fluoxetine and escitalopram were found to reduce the abundance of intestinal microbiota, especially that of *Ruminococcus*, *Adlercreutzia*, and an undefined *Alphaproteobacteria* that lead to side effects [10].

Similarly, some antibiotics, such as minocycline has antidepressant actions, especially in impacting microglia [11]. Microglia are involved in the secretion of cytokines and chemokines as well as other proinflammatory mediators after infection or brain damage, which have been linked to major depressive disorder (MDD). Studies also suggests that anti-inflammatory drugs have antidepressant activities [12]. Other evidences suggest that penicillin and quinolones, can cause an increase in the risk of depression and anxiety [11].

CONCLUSION

We have observed the significance of gut microbiota having role in several psychiatric disorders. This work covers important links of the pathophysiology of depression and anxiety with the immune system and the microbiota-gut-brain axis. Therefore, probiotic, and prebiotic supplements deserve some attention when it comes to treating psychiatric conditions. Furthermore, some promising approaches considering the antimicrobial effects of psychotropic drugs may aid in resolving the dynamics of psychosis and depression, and provide some helpful remedies. Timely diagnosis and prompt treatment of functional gastro-intestinal disorders are of utmost importance to prevent adverse mental health consequences such as depression and anxiety. In the case studies presented hereby are highlighting the presence and overlap of psychiatric symptoms along with GI symptoms. These have its own causal correlation and management approach as many of such cases may not have very specific psychiatric diagnosis.

Thus, further research may fill in the existing gaps regarding treatment for psychiatric disorders, as it is imperative to mitigate their influence and promote the overall health.

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