

**THE EFFECTS OF PREBIOTICS AND PROBIOTICS ON ANXIETY, DEPRESSION AND  
SUICIDAL IDEATION WITH SPECIAL REFERENCE TO ADOLESCENTS  
A REVIEW**

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**Abstract**

*It is long understood that the GI microbiota with their varied microbial communities play important role in various metabolic, protective and immunological processes of the body. Prebiotics and Probiotics take part in the neuro-immune processes that directly influence the mental wellbeing. It is now established that the metabolites produced by the digestion and the consequent fermentation of the nutrients of prebiotics produce anti-inflammatory, antidepressant and anti-anxiety effects on the CNS. Research has indicated that imbalance of the gut bacteria negatively influences mental health. The study of the effects of pathophysiology of mental disorders especially in the perspective of microbiota communications is an emerging and promising field. It is an area of intense research with concepts such as the use of psychobiotics to positively influence the gut. It has been proven that cultures of gut bacteria such as Lactobacillus, Bifidobacterium and Enterococcus are capable of producing neuropeptides and neurotransmitters including GABA, serotonin and BDNF which can be directly discharged in to the brain, thus enhancing their availability. Both human and animal research indicates that adolescence is a sensitive period during with the balance between gut-brain axis is finetuned. Therefore, proper understanding of the methods of influence that probiotics take to influence mind offers a new and a safer pathway for treatment. Depressive disorders and anxiety disorders are commonly found during adolescence along with suicidal ideation. Careful manipulation of the microbiome through psychobiotics in advantage to their cultural prevalence in the form of fermented foods, hopefully leads to more acceptability than the classical drugs which often show low level adherence. It is easy to overlook food habits in relation to prevalence of mental disorders with the influence of globalization and high consumption of processed foods. Even though the complex pathways between gut and brain are not fully understood, it is essential to recognize the importance of food habits along with the presence of prebiotics and probiotics in the diet for overall wellbeing.*

**Keywords:** Prebiotics, Probiotics, Psychobiotics, Gut biome, Depression, Anxiety, Suicide, Adolescence, Food, Nutrition

**Introduction:**

A psychological disorder is a pattern of behavioural or psychological symptoms characterized by a clinically significant disturbance of an individual's cognitive, behavioural and emotional regulation and is usually observed as distress in the social, occupational or other important activities of the individual. [1] It is estimated that nearly 10% of Indian adolescents are likely to suffer from some degree of mental health issues.[2] Though adolescents comprise one fifth of the population of India, there is little research on their mental health.[3]

Adolescents confront a rapidly changing and challenging social environments as well as their rapid physical changes in the body. Their identity, cultural beliefs, support structures, family system, peer relationships and educational opportunities mould their behaviour and personality. The rapidly changing value systems and increasing expectations combined with forces of globalization adversely influence the mental health of the adolescents.

Despite these factors, very little is acknowledged by the parents and adolescents regarding the status of mental health. In India, despite advances in education and awareness, a diagnosis of a psychological problem and consulting the psychiatrist is still seen as a stigma leading to certain discrimination. Parents also often, in fear, wish to deny the condition and associate it with the child's

temperament rather than admitting any possibility of suffering from mental disorder. Oftentimes, medical intervention is avoided from the lack of awareness amongst young people and parents. The prevalence and popularity of unproven alternatives along with religious dogmas in India also poses a threat to the scientific and rational approach to mental health.

Research has indicated high prevalence of anxiety disorder, depressive disorder, ADHD disorders and behavioural disorders amongst adolescents of the country. It has also been indicated that the urban adolescents are more prone to mental disorders when compared to rural adolescents. One factor amongst many is the rapid and extreme changes in diet and nutrition of the urban adolescents with access to highly processed foods.

In these scenarios, the importance of prebiotics and probiotics is garnering prominence as a non-stigmatized yet effective and proven alternative to classical treatment to disorders. The use of psychobiotics through dietary intervention is seen with lesser resistance and more adherence amongst the young. While research in this comparatively new domain of alternative treatment has gained more focus, and young patients seem very optimistic about the prospects of prebiotics and probiotics as these young patients consider it as an innovative, approachable, affordable and a more socially acceptable intervention to mental disorders.[4]

A vast majority of scientist have now accepted that the diverse microfauna present in our intestines may have a strong influence on mood and therefore brain. The gut-brain axis is observed to be a bidirectional balance with the brain's gastrointestinal and immune functions that influence the diversity of the gut's microbiome, and gut microbes in return produce neuroactive compounds, including neurotransmitters that influence the brain. These gut-brain interactions are supposed to occur in various ways: microbial compounds are observed to communicate via the vagus nerve connecting the brain and the digestive tract, and through immune system, which coordinates through its own communication network with brain, by producing metabolites.[5]

This paper attempts to review and compile the various studies that explored the efficacy of prebiotics and probiotics on mental health and their popularity in the youth. The paper also contemplates on the possible pathways of inclusion of psychobiotics into classical treatments to mental disorders in context to Indian society.

#### **Method:**

In order to understand the current research scenario on prebiotics and probiotics as a treatment for psychotic disorders, a total of 15 research papers were studied. Papers that dealt with probiotics as a treatment option for physiological disorders were not considered for the review. Apart from the thus selected papers, articles that dealt with the scope and future of prebiotics were also considered in the study to develop a holistic idea on the current status of the prebiotics and probiotics market.

#### **DISCUSSION:**

The human gut contains more bacterial organisms than total eukaryotic cells in the body. This collection of bacteria referred commonly as gut microbiome or gut flora is said to represent a virtual organ with metabolic activity surpassing that of the liver. The genome of the microbiome of this entire gut flora is more diverse than the entire human genome. Some bacterial species of this gut flora have demonstrated that they can positively influence the health of the host. These species of the gut flora are defined as probiotics and have proven to be beneficial in reducing inflammation and provide protection against gut associated bacterial infections.[7] Apart from positively influencing the physical health, they are also identified to influence the mental health of the host body. Probiotic microorganisms are thought change the CNS biochemistry by affecting the availability of various neurotransmitters including GABA and Dopamine. Some of the species that have been identified to influence mood include *Bifidobacterium*, *Lactobacillus* and *Enterococcus* and are therefore useful in creating anxiolytic and anti-depressant effect.[8]

Prebiotics are defined as indigestible or semi-digestible compounds that can selectively influence the growth, activity and or population of useful bacteria or probiotic organisms in the gut flora. The main

category of prebiotics includes starches such as fructo-oligosaccharides (FOS) and galacto-oligosaccharides (GOS) which are resistant to the digestive enzymes and can therefore reach the colon where they are processed by the prebiotic organisms.<sup>8</sup> Prebiotics such as inulin and pectin have been used to treat intestinal disorders and are claimed to decrease the risks of cardiovascular disease and obesity. [9] Moreover, it has been observed that oligosaccharides present in the milk can reduce symptoms of stress and anxiety like behaviour in mice. Similarly, it has been proven that FOS and GOS mixtures can have an anti-depressant effect on mice. (Better Gut microbiome function)

While the exact pathways that prebiotics and probiotics take to influence mental health are still being studied, it is important to understand the potential that prebiotics and probiotics carry as a way to influence mental health in a positive manner. Probiotics have already been proven useful in various auto-immune inflammatory diseases, however, their use as 'psychotics' has at best been limited to studies. However, the presence of prebiotics compounds and probiotic microorganisms in cultural cuisines of all major cultures. Their presence and utilization are widespread in the cuisines of South East Asia. Probiotics can be found naturally in a assorted variety of food products such as curd, kefir, tempeh, sauerkraut, miso, some cheeses, buttermilk etc.[9] which are widely used in the kitchens of India. With the increasing knowledge of the relationship between diet and health, a lot of food companies have begun to include prebiotic compounds or even produce probiotic supplements. On the other hand, as the usage of antibiotics grows, their harmful effects on the gut flora are also considered during antibiotic treatment, hence many doctors today prescribe probiotics as a way to balance the gut flora after antibiotic use. Therefore, though prebiotics and probiotics are popular as health foods, they are not considered as major treatment options for psychiatric disorders.

#### **Adolescence and Mental Health**

According to some estimated, depression and anxiety affect up to 300 million people worldwide with an increase annually. It is estimated that over 85% of the affected suffer with one or have had experienced the symptoms of the other. They combinedly increase the risk of suicidal ideation and suicide as well as lead to psychological and social impairment.[14] The proportion of the global population with anxiety disorders is estimated to be 3.6%. Depression is ranked by the WHO Report as the single largest contributor to global disability as 7.5% of all people with a disability in 2015, whereas anxiety disorders are ranked 6th (3.4%)[8]

Apart from these life debilitating disorders, suicide thoughts and behaviours are major health problems that can have distressing impact on individuals, families and communities. Suicide accounts for an estimated one million annual deaths which is more than the annual deaths caused by homicide, AIDs and car accidents. It is also estimated that every year 25 million suicide attempts are made worldwide.[15]

In the case of adolescents, there has been an increasing presence of psychiatric disorders. In USA alone, at least one in five youth aged 9–17 years at present has a diagnosable mental health disorder leading to some degree of impairment either in social or academic functions; one in 10 adolescents suffer significant impairment due to these disorders. The most common psychiatric disorders prevalent amongst adolescents are anxiety, mood, attention, and behaviour disorders.[10] Suicide ideation and suicide attempts are the most prevalent health emergencies among adolescents.[11] According to a report by American College of Obstetricians and Gynaecologists, suicide is the second leading cause of death in young people aged 15–24 years.[10]

In Indian adolescents, the situation is far worse. As overserved in the study by Aravind Pillai et al., Young people (aged 10–19 years) make up for a fifth of India's total population with nearly 230 million people. While, the focus on adolescents' health and wellbeing has garnered increased significance in governmental and social policies related to public health, the emphasis has been on more reproductive and sexual health rather than mental wellbeing. While many studies indicate that suicide in young Indians is the leading cause of death, adolescent mental health has never been the prime focus of action plans of neither the government nor social structures. The research in this arena has only recently gained momentum with some published studies dealing with adolescent Indians as

samples have reported prevalence of mental disorders ranging from 2.6% to 35.6% causing a significant discussion in the scientific and health communities.[3]

In a study conducted by Neena Sawant on Indian youth's mental health, she observed the urgency awareness amongst parents and health care providers about the extent of the psychological problems in children. She observed that many common health conditions arise during childhood therefore demand attention from both parents and paediatricians. These ensuing psychosocial problems are the root to various and rather widely prevalent learning and emotional difficulties of Indian children. Parents too are often in denial of their child's psychiatric disorder in fear of social stigma, thus unknowingly causing more stress and trauma to child.[12]

Adolescents face rapid shift in their roles and as well as their perceptions of their social and physical environments. Their belief systems, family and support constructs as well as social relationships and academic expectations influence their behaviour and demand fast rate of adjustment. Globalisation is also considered as a major factor in leading these rapid changes of the otherwise stable sociocultural systems in low and middle income countries, and this sudden changes in expectations from adolescents as well as realization of fluctuating social forces may increase the risk of development of mood and anxiety disorders.[13] Adolescents with mood disorders exhibit more irritability compared to adults with mood disorders. They also tend to frequently engage in self-medication with alcohol and other substances, and are prone to more impulsive behaviours including self-harm and suicide. A majority of these affected individuals are treated with pharmacological treatments and behavioural therapies. However, it has been observed that despite the widespread use of antidepressants, there are an increasing number of studies that question the efficacy of these drugs. There are also growing concerns over the serious and non-serious adverse side effects associated with these drugs. Moreover, the success rate of these treatments is very low (with some studies reporting as low as 50% efficacy) while some treatments yield improved results but it also oftentimes results in the increased risk of development of side effects due to prolonged use of these medications.

#### **Prebiotics and Probiotics as an adjuvant**

In this context, probiotics can be safe and natural adjuvant therapeutic strategy in combination with existing therapies to lessen the burden of depression without the dangers of side effects. Therefore, select strains of commensal and probiotic bacteria can be utilized to gut-microbe-brain axis communication, influencing the behaviour of the host.

Probiotics are proven to be capable of releasing neuroactive substances.[4] As mentioned above, strains of *Bifidobacterium* family can increase the expression of GABA in the brain, while strains of *Streptococcus* and *Enterococcus* are linked with the production of serotonin, the key modulator of sleep. The imbalance of these neurotransmitters is seen as the cause of many mood disorders and are key players in suicidal ideation. A study found that the effect of probiotic interventions to enhance serotonin come apparent in about 4 weeks which is comparable to the common serotonin reuptake inhibitor (SSRIs) drugs used to treat depression. Furthermore, even when they start to affect the mood, the side effects associated cause more than 25% of the patients to discontinue their treatment, when not factoring in the social stigma and fear associated with antidepressants.

The potential of probiotics to be used as a treatment for disorders such as depression and anxiety can have a major impact on both psychiatry and nutrition. While the recent hype of the prebiotics and probiotics has warranted the necessary attention from the public, the clinical effects of prebiotics and the efficacy of these alternatives along with metrics such as strains, dosage and duration of the interventions is necessary. However, it is anticipated that as the significance of these research grows, adolescents' food habits can be monitored and modified towards a better mental health without the need for lifelong prescription to antidepressants and antipsychotics.

#### **Conclusion:**

The way our physiological processes have become aligned, dependent and intertwined with gut microbiota is fascinating. Though, we share a mutual relationship with gut microbiota, it is as if we

are piloted by our gut. Gut microbes play key roles in neural development as well as forming an immunity since early stages of childhood and continue to exert influence on our psychological and immunological states throughout our lives. Thus, probiotics that are known to positively affect neuroendocrine signalling and immunological functions can be utilized as psychobiotics. With new technological advances in our disposal, such as genetic engineering, we can develop these psychoactive bacteria to be more efficient and robust to be used as an option for management or treatment of depressive and neurodegenerative disorders. The research has already established the manipulation of the human microbiota through prebiotics and probiotics can alleviate symptoms of gut related diseases and are being recommended as to prevent the side effects of antibiotics on gut, as evidenced by the presence of growing prebiotic and probiotic market. With more 350 million people worldwide suffering from depression or mood disorders there is an overwhelming urgency to make the treatment safer and affordable than the existing medication and therapy options. This review indicates that treatment with probiotics may improve symptoms associated with depression by enhancing the availability of the neurotransmitter serotonin as well as reducing the inflammatory markers in the brain and body. The potentials of probiotics to be used as a novel treatment for psychiatric disorders will have a positive effect on those that require antidepressant treatment without the burden of social stigma, adherence and side effects associated with typical antidepressants. However, it must be noted that despite extensive preclinical data and animal trails, the clinical properties of probiotics on mental health have yet to be studied comprehensive manner through a sample of depressed individuals with various parameters to establish them as alternatives to conventional drugs. Further research is therefore necessary to determine the efficacy of probiotics and prebiotics in alleviating symptoms in a practically feasible manner as well as the ideal duration of treatment, dosage, and optimum strain of probiotic for achieving the necessary efficacy in comparison to the conventional drugs.

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