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ROLE OF PROBIOTICS ON PSYCHIATRIC DISORDERS HOW THEY MODULATE IMMUNE PATHWAY TO IMPROVE BRAIN FUNCTION :THE GUT –BRAIN AXIS

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Abstract

Introduction:- The central and the enteric nervous system, linking emotional and cognitive centers of the brain with peripheral intestinal functions basically its an bidirectional syatem. The interaction between microbiota and GBA appears to be bidirectional, namely through signaling from gut-microbiota to brain and from brain to gut-microbiota by means of neural, endocrine, immune, and humoral links. Studies showed that distension of the gut resulted in activation of key pathways within the brain and that such pathways are exaggerated in disorders such as irritable bowel syndrome (IBS), a functional gastrointestinal (GI) disorder with dysregulated microbiota-gut-brain axis

Material And Methods:-Patients attending OPD clinic in Psychiatry Department with. Depression ,e ither male or female of Age group -more than 10 years to 70 years of age. Around 100 such patients observed followed by Questionnaire based survey from January 2022 to April 2022.

Conclusion:- The deteriorating mental health has become a global health issue and has had a major impact on day to day life of the people. Gut flora is disturbed due to ill food habits of people. Understanding and addressing the mental health issues of patients and general public is important in terms of their efficiency and adaptability towards poor mental health and this is also noteworthy to identify role of probiotics towards promotion of positive mental health.

Keywords : Depression ,Gut flora, mental health, Cognitive function.

Introduction

mental disorder or Illness is a negative phenomenon for the patient, associated with disturbances in daily functioning, especially in fulfilling social roles. This is evident in affective disorders, in the course of psychotic disorders or autism spectrum disorder (ASD), in which emotional, cognitive, and communication disorders are associated with severe limitations in these people's psychophysical and social competencies. Current predictions suggest that the problem of mental illnesses referring to

people worldwide is significant and will only worsen [1]. Therefore, it is essential to understand the functioning of patients on a personal, social, and professional level and apply adequate psychiatric rehabilitation procedures. It seems even more important to look for answers to the question of the etiopathogenesis of these mysterious disorders. Such studies may contribute to changes in the field of prevention and promotion of mental health or the creation of more effective pharmacological agents and other medical interventions that can improve the functioning of people with mental disorders in all spheres of activity. In recent years, scientific attention has been paid to the relationship between neurological and psychiatric disorders and gut microbiota (GM)[2].

The microbiota is a group of microorganisms that colonize the human body, and the composition of this group is not accidental; in turn, the term microbiome covers the genomes of all microorganisms in a particular environment. This complex ecosystem is characterized by a complicated network of positive and negative interrelationships that significantly impact the host's health [3]. Notably, the microbiota currently depends not only on the interdependencies occurring in this specific ecosystem but also on the cells of the macroorganism. Microorganisms inhabit various areas of the human body, ranging from the skin, through the mouth, the upper respiratory tract, the ear canal, and the vagina [4,5]. However, 90% of all microorganisms colonize the initial sections of the small and large intestines [6,7]. Many data indicate that the number of microorganisms that inhabit a macroorganism exceeds ten times the number of its cells.

Recently, the total weight of intestinal microbes was estimated at 1–2 kg [8,9]. According to Daniel's studies [10], the wet weight of intestinal colon content reached approximately 200–250 g of colonic content, in which the bacteria representing the intestinal microbiome constituted about 100 g. It should also be noted that the composition of GM is very diverse.

It is made up not only bacteria but also fungi (a good example is Candida albicans), viruses, and some protists [11]. An essential element of the intestinal microbiota are also microorganisms belonging to a separate kingdom of living organisms, Archaebacteria. These microorganisms occur in a wide variety, often in extreme environments, under strictly anaerobic conditions, obtaining energy from the transformation of simple inorganic or organic compounds (including in the process of methanogenesis, in which energy is obtained during the synthesis of methane from various substrates such as dioxide, carbon, and hydrogen) [12]. Due to variable pH conditions in individual sections of the gastrointestinal (GI) tract, oxygen conditions, access to nutrients, and also variable intestinal peristalsis, various sections of GI are colonized by specific microorganisms [3,13]. Any disturbance in the composition and quality of individual microbial communitiescan have serious health consequences. A characteristic and quite clear example that illustrates such disorders is SIBO(excessive bacteria in the small intestine) [14]. It might result from the impairment of gastric acid secretion, anatomical changes in the gastrointestinal tract as a result of various diseases (disorders of the ileocecal valve, intestinal diverticula, or intestinal tumors), abdominal cavity surgery (e.g., in the case of resection of a fragment of the large intestine in the course of a neoplastic disease), and also reduced intestinal motility in the course of various diseases or disorders (e.g., impairment of the function of the migrating myoelectric complex) [15,16].

The aim of this review is to discuss the microbiota–gut–brain axis relationships. We summarize the knowledge about pathways that are involved in this bidirectional communication.

The importance of the difference factor that affects the gut microbiota is also underlined. In the end we present the results of GM correlation with common psychiatric disorders.

2. Role of Intestinal Microbiota in the Host Organism

In the macroorganism, the intestinal microbiota fulfills many important functions.

First, it maintains the proper functioning of the intestines, ensuring an appropriate pH, proper intestinal peristalsis, and a regular rhythm of bowel movement. Microorganisms colonizing the intestines not only participate in the digestion of food by secreting digestive enzymes or converting complex nutrients into simpler organic compounds and fatmetabolism, but also participate in the absorption of digested food. In addition to the functions mentioned above, the intestinalmicrobiota is

responsible for synthesizing vitamins,mainly those of group B [6,17]. Through anaerobic fermentation of indigestible carbohydrates (mostly dietary fiber),intestinal microorganisms produce short-chain fatty acids (SCFAs), which are the primary source of energy for an epithelial cell of the colon (colonocytes) [18]. Butyric acid plays the most important role in the nourishment of these cells while at the same time being an important factor in stimulating their growth and differentiation [19]. Another important role of the intestinal microbiota is the neutralization of toxins and carcinogenic compounds [20].

Furthermore, intestinal microorganisms create the intestinal barrier, thus protecting the macroorganism against the penetration of pathogenic factors [21]. It should be pointed out hat the intestinal microbiota significantly affects the activity and functioning of the immune system—it has immunomodulatory functions, regulates the levels of cytokines through interaction with the lymphatic tissue of the digestive tract, and it is considered the largest lymphatic organ in the human body [22]. Taking the above into account, there is no doubt that all disturbances in the amount and composition of the intestinal microbiota (intestinal dysbiosis) lead to numerous abnormalities such as disruption of intestinal peristalsis, disturbances in digestion and absorption, disorders in vitamin production or metabolism, and difficulties in digesting fats, but also the destruction of the intestinal barrier and excessive stimulation of the immune system [7,23]. Meta-analysis of GM composition in psychiatric disorders performed by McGuinness et al. [24] revealed that there were no strong differences in the number or distribution (_-diversity) of intestinal bacteria. Still, in the case of major depressive disorder (MDD), schizophrenia (SCZ), and bipolar disorder (BD), after comparing them to controls, there were compositional differences.

Based on work to date, some research models have been used in studies on the impact of intestinal microbiota on brain development and brain function. Such studies include experiments using germ-free mice (GF) that were raised under completely sterile conditions, without any intestinal microbiota [25,26], research with the use of probiotic and antibiotic therapy [27], studies on the use of fecal microbiota transplantation (FMT) [28], and the use of infectious research [29].

Factors Affecting Gut Microbiota

The connection between GM and the central nervous system (CNS) through bidirectional communication begins during intrauterine life and is affected by many intrinsic and extrinsic factors, such as vaginal/caesarean birth, lifestyle habits, living arrangements (urban or rural), dietary and medicament intake, and the host's circadian clock [30–33].

Mode of Delivery

For a long time, it has been assumed that according to the "sterile womb dogma", the human fetus is sterile until delivery and microbes start to colonize the human GI after birth, but some studies indicate the beginning of the infant microbiota colonization in utero [34–36]. This colonization of the infant by Escherichia coli, Enterococcus faecium, and Staphylococcus epidermidis could be associated with its translocation from the mother's gut through the bloodstream and placenta [37]. According to Collado et al. [38], the microbiota observed in the placenta and the amniotic fluid harbor were characterized by low richness and diversity with the predominance of Proteobacteria.The critical factor affecting newborns' colonization of the GI tract is the mode of delivery [39,40]. During recent decades, despite the lack of medical recommendations,the number of cesarean sections (CS) worldwide has increased. In some countries, more than 50% of births occur in this way [41]. Studies have shown that the composition of the intestinal microbiota in vaginally delivered (VD) infants appears to be similar to that of the maternal vaginal microbiota: Lacto bacillus dominates, followed by Senathia spp. and Prevotella, most of which are anaerobic bacteria. CS leads to an imbalance of the infant gut microbiota and decreased diversity. Due to the lack of opportunity to encounter the maternal vaginal microbiota, the hospital environment and the mother's skin constitute their first contact. As a result, pathogens (Enterococcus, Enterobacter, and Klebsiella) from the hospital environment have been found in their intestines [42]. The intestinal microbiota of the infant delivered

by CS contains a lower abundance of Bifidobacteria, Bacteroides, Staphylococcus, Corynebacterium, and a Propionibacterium spp. A higher quantity of Lactobacillus, Prevotella, Sneathia spp., and Clostridium difficile compared to VD children was found [39]. It should be mentioned that a high abundance of C. difficile could cause dysbiosis and an increased risk of developing obesity [43]. Therefore, GM colonization appears to be important for the health and development of the infant due to its proper development of metabolism, immune system function, and the brain in the following stages of life. Interestingly, the method of feeding can also influence the development of specific bacterial strains in the infant's GM,for example, Bifidobacterium longum, by using oligosaccharides in mother's milk, competes with E. coli and Clostridium perfringens.Furthermore, primary studies revealed that Lactobacillus acidophilus LB might reduce necrotizing enterocolitis in preterm infants [44]. Probiotics Currently, the growing number of data indicate probiotics as the form of treatment of mental disorders/neurological and developmental disorders in which increased intestinal permeability has been demonstrated, i.e., depression, anxiety, autism, schizophrenia,or bipolar disorder [50]. The mode of action of probiotic microorganisms includes,among others, regulation of the immune system, production of SCAFs, or support of the gut barrier integrity [51]. Several studies revealed the diversity and specificity of probiotic strains in affecting the brain. According to the meta-analysis of Huang et al. [52],among people with depression, taking probiotics significantly alleviated its symptoms.In the study by Messaoudi et al. [53] involving a group of healthy human volunteers, it was shown that taking probiotics containing Lactobacillus helveticus R0052 and B. longum R0175 for 30 days alleviated symptoms of depression and anxiety, reflected in the reduced rates of the Hospital Anxiety and Depression Scale (HADS), compared to the control group of people taking placebo. Another analysis revealed that certain strains such as B. longum, Bifidobacterium animals lactis, Streptococcus thermophilus, Lactobacillus bulgaricus, L. lactis, and L. helveticus reduce stress levels and alleviate symptoms of depression [54].

Furthermore, the positive effects of taking probiotics were also observed in children with ASD. Critchfield et al. [55] showed that probiotic supplementation in children with ASD can decrease inflammation and alleviate behavioral disorders. There is limited research into the effects of probiotics in SCZ in the human model. Nevertheless, it should be noted that Severance et al. [56] indicated in patients with SCZ an association between gastrointestinal inflammation and food antigen-associated immune activation. Furthermore, in research conducted by Ghaderi et al. [57], it has been revealed that administration of vitamin D to patients with SCZ for 12 weeks in combination with probiotic strains such as Lactobacillus reuteri, L. fermentum, L. acidophilus, and Bifidobacterium bifidum resulted in beneficial effects on the general and total PANSS (Positive and Negative Syndrome Scale) score. Although the influence of prebiotics SCZ does not explain the molecular mechanism of action, and research in this area does not provide crystalline and unambiguous conclusions, there is a temptation to explore the topic of the influence of probiotic strains and prebiotics on the development and course of SCZ. An interesting issue recently raised by scientists is the impact of probiotics on mood improvement during COVID-19. Probiotics, in addition to restoring intestinal balance, reduces risk of colonization of the intestine by opportunistic pathogens [58]. According to Rogers et al. [59], COVID-19 infection could result in posttraumatic stress disorder (PTSD).The dysbiosis of the gut microbiota affected by SARS-CoV-2 infection leads to improper transport of intestinal nutrients [60]. Gu et al. [61] showed the growth of the number of opportunistic pathogens such as Streptococcus, Rothia, Veillonella, and Actinomyces with a simultaneous decline in the number of helpful symbionts in patients with COVID-19 anH1N1 compared to healthy patients.

The Pathways between Gut Microbiota and the Nervous System

As shown in Figure 1, the bidirectional connection between the gut and the brain is based on metabolic, endocrine, neural, and immunological pathways. It includes the vagal nerve, the HPA axis, the production of bacterial metabolites, immune mediators, and entero–endocrine signaling [50].

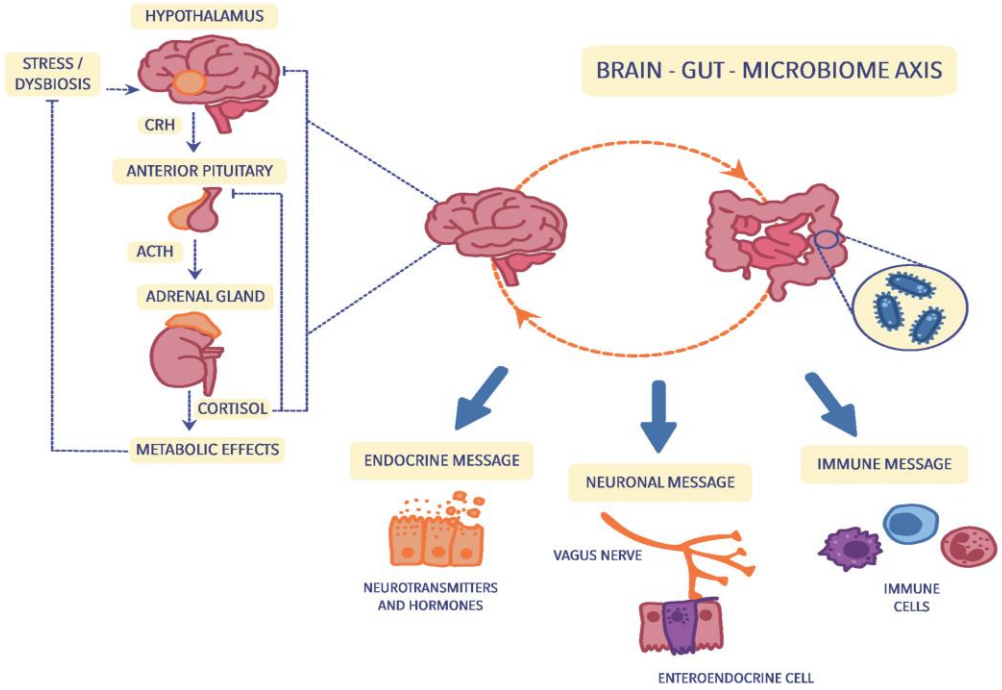

Fig:1 The Hypothalamic–Pituitary–Adrenal (HPA) Axis

The cerebral–intestinal axis is controlled at several levels, and the primary regulatoris the nervous and endocrine (with the primary role of the HPA axis) and the immune pathway. Immune regulation of the HPA axis occurs mainly through the modification of cytokine secretion. In contrast, nervous regulation occurs primarily via the transmission of impulses in the autonomic nervous system, including the vagus nerve, afferent and centrifugal fibers, and the enteric nervous system (ENS). ENS, known as the "gut brain", was first described in 1998 by Michael Gershon of Columbia University Medical Center.

The enteric nervous system is not only responsible for the direct regulation of muscles, mucosa, and vessels in the digestive tract but also for its activity. It comprises a large number of nerve fibers that form an impressive network of connections, and it is worth pointing out that over 30 different neurotransmitters are involved in the functioning of this system. There are about 40 neurons for each intestinal villi.Contrary to the peripheral nervous system, the neuronal elements of the enteric nervous system are not surrounded by collagen and Schwann cells; instead, they are enveloped by glia that resemble CNS astrocytes. The ENS is formed by the Meissner plexus, located in the submucosa of the intestine, and the Auerbach plexus, located between the layer of circular and longitudinal muscles.Due to this location, the ENS, through numerous transmitters and cytokines, remains in close contact with intestinal-associated lymphoid tissue (GALT) and the systemic humoral defense system of mucosa-associated lymphoid tissue (MALT). The neurotransmitters of the intestinal nervous system act, among others, on receptors in Peyer's patches and lymphocytes. Most of GALT consists of lymphocytes of the entire immune system (70%), constituting the first line of defense and playing a particularly important role in the immune response to external antigens.Likewise, microorganisms that inhabit the intestines, certain species of bacteria and fungi, transmit signals to both GALT and ENS through the synthesis and secretion of many different neurotransmitters .Hormonal regulation of cerebral–intestinal communication occurs primarily through the HPA axis, also known as the stress axis, which primarily regulates the course of the stress response. Hypothalamic hormones-corticoliberin, together with vasopressin, start a hormonal cascade along the HPA axis, stimulating the anterior pituitary gland to produce and secrete the corticotropic hormone ACTH, which, along with the bloodstream, goes to the adrenal cortex and stimulates it to secrete glucocorticoids, mainly cortisol .Neuroendocrine Pathways Cortisol plays a key role in the endocrine mechanisms that

regulate the gut–brain axis because it affects the cells of the immune system by modulating the secretion of cytokines that act on the HPA axis, but also significantly affects the functioning and differentiation of the intestinal microbiota.On the other hand, special attention should be paid to the fact that intestinal bacteria produce numerous substances such as –aminobutyric acid (GABA) (Lactobacillus spp., Bifidobacterium spp.), acetylcholine (Lactobacillus spp.),serotonin (Escherichia spp., Candida spp., Enterococcus spp.), dopamine (Bacillus spp.), or noradrenaline (Bacillus spp., Saccharomyces spp.). These substances are involved not only in communication within the intestinal microflora but also in systemic and peripheral effects that affect brain functioning.

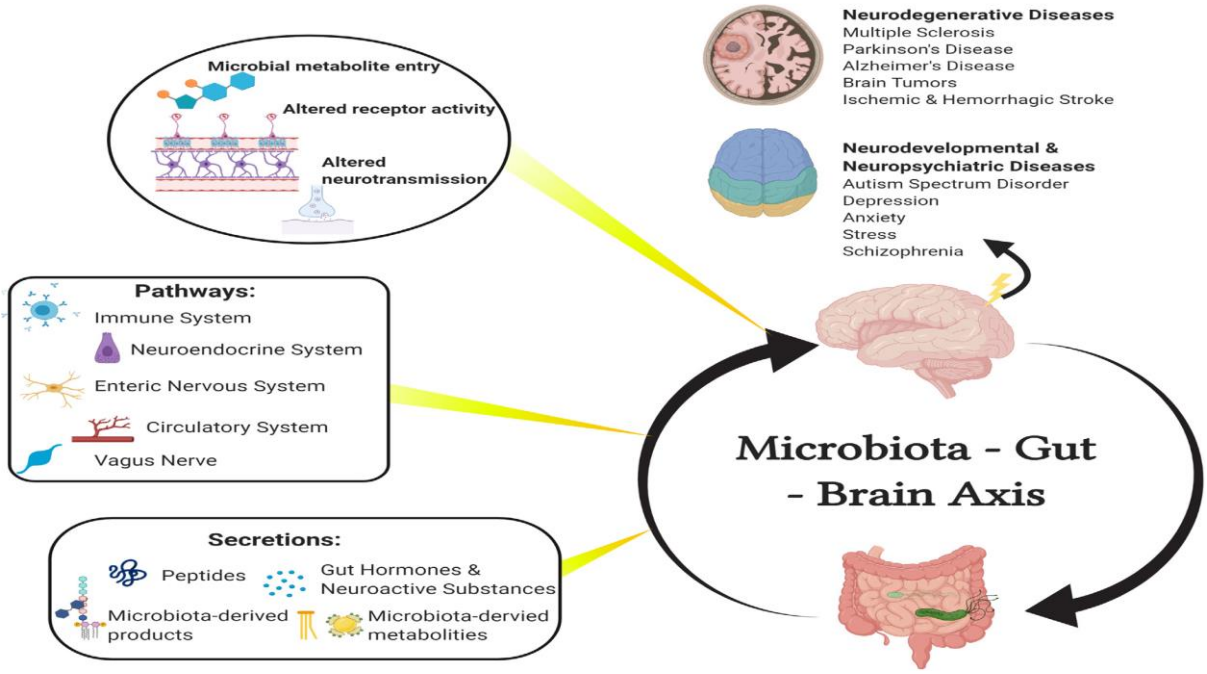

Fig (2)T:he Intestinal Microbiota in Neurological and Psychiatric Disorders

The Intestinal Microbiota in Neurological and Psychiatric Disorders

(a)Depression (Major Depressive Disorder; MDD)

Depression is described as a common mental disorder state, characterized by a continuous feeling of sadness and apathy lasting at least two weeks, as a result of interactions covering social, psychological, and biological factors, for example, significant changes in life, family matters, chronic health problems, or addiction.It is also a common cause of disability and a cause of suicide death. According to WHO, approximately 280 million people worldwide suffer from MDD and every year, and more than 700,000 people die from committing suicide.The data described many factors that link this mental disorder with the components of the intestinal microbiota, which was confirmed by Naseribafrouei et al. [50]. They have shown that the level of the Alistipes genus associated with inflammation and Oscillibacter, which has valeric acid involved in is associated with depression, was elevated in patients with MDD. Zhang et al. [51] showed, using a mouse model, that microbiota dysbiosis was associated with greater intestinal permeability and systemic inflammation. As a result of endogenous melatonin reduction (EMR), the composition of the mice microbiota changed and consisted of a decrease in the relative abundance of Bacteroidetes, an alteration of the Firmicutes/Bacteroidetes ratio, and growth of the relative abundance of Lactobacillus. The study also revealed improved gut permeability (leaky gut) and systemic inflammation in EMR mice. The determination of SCFAs content could be helpful in the analysis of the microbiota composition by patients with MDD. The study concerning the SCAFs profile conducted by Skonieczna-Z˙ ydecka et al. [52] on a group of 116 women aged 52.0 (4.7) years, in which 40.52% of them recognized depression, revealed a lower level of propionic acid and a higher content of isocaproic acid compared to healthy subjects. However, due to the small group size, it cannot be conclusively stated that SCAFs

contribute to the depressive phenotype. Studies on animal models revealed the connection between intestinal microbiota composition and its personalities and behavior, such as anxiety or depression. Gan et al. [53] showed changes in the behavior of shy personalities of Mongolian gerbils (Meriones unguiculates) after transplantation of the gut microbiota of bold individuals. Shy gerbils often exhibited bold behavior after "bold fecal microbiota" transplantation, suggesting the association between the gut microbiota and the host's personality.

(***b). Schizophrenia (SCZ)***

Schizophrenia is a multifactorial disorder involving emotional, occupational, and cognitive impairments [54]. Due to cardiovascular, metabolic, and infectious diseases, adults with SCZ are at risk of early death. For individuals in the United States with SCZ, the average potential life lost is estimated to be 28.5 years. According to Owen et al. [56], SCZ demonstrated three different dimensions determined as positive symptoms (hallucinations and loss of contact with reality), negative symptoms (decrease in motivation and withdrawal), and cognitive weakness (limited efficiency compared to controls). The results of biochemical and neuroimaging studies also try to explain the etiopathogenesis of SCZ. So far, it has been possible to establish some dependencies in the systems of certain neurotransmitters, which, at least to an extent, may explain the development of clinical symptoms of SCZ. The most significant seems to be the participation of dopamine [57], although, in light of recent discoveries, dopamine plays a rather indirect role in this pathophysiology. At the same time, sources of SCZ should be found in the links between other neurotransmitters [58, 59]. Kozłowska et al. pointed to the association of immune/inflammatory processes and the etiology of SCZ, in which host peptides/proteins called alarmins activate signaling pathways, which lead to the development of many infection-induced or sterile inflammatory diseases. There is a growing amount of evidence that points to the significant role of the glutamatergic system. This mainly concerns the neuregulin 1 gene, a substance that activates NMDA receptors, located on the 8p12 chromosome, and the G72 and G30 genes located on chromosome 13q33, the first of which acts as an activator of amino acid oxidase (D-serine amino acid oxidase inhibitor(DAOA) Recognition of these genes supports the neurodevelopmental concept of SCZ and the role of the glutamatergic system in this process.Today, it is known that both the increase in dopaminergic transmission in the mesolimbic part and the inhibition of glutamatergic transmission play an important role in the pathogenesis of positive symptoms of SCZ. Notably, the increasing number of premises proves that kynurenic acid (KYNA) may be a modulator of both these mechanisms.KYNA is a nonselective antagonist of ionotropic receptors for excitatory amino acids: the NMDA receptor and the kainic acid receptor, and it is the AMPA receptor and also an antagonist of the strychnine-independent glycine site in the NMDA receptor complex. Research reveals that the level of KYNA in the CSF of patients with SCZ is elevated. Thanks to KYNA research, more and more is known about its potential role in the physiology and pathology of the CNS. However, the mechanism by which KYNA affects CNS function and, thus, the clinical picture of various diseases has not been directly described. However, significant differences in KYNA concentration in sick and healthy people indicatethe participation of this compound in the pathogenesis of neurological and psychiatric diseases [60]. Because KYNA poorly penetrates the blood–brain barrier and is difficult to determine in the blood, scientists also pay attention to other metabolites of the kynurenine pathway. Recent studies have shown a 3-hydroxykynureine predictable concentration value concerning the reduction of psychopathological symptoms during the treatment of the first episode of SCZ. This offers great hope in finding biological factors that can predict the effectiveness of antipsychotic drugs. Unfortunately, despite advanced research, no effective cure for psychotic disorders, including SCZ, has yet been found, just as it has not been possible to clearly indicate the factors involved in the etiopathogenesis of this mysterious and still incurable disease.

(c). Bipolar Disorder (BD)

Another serious mental illness is bipolar disorder (BD), a chronic and recurrent disease characterized by the return of hypermanic episodes or subsequent depressive episodes, with some symptoms similar to SCZ . Worldwide, it was estimated that in 2017–2019,46 million people suffered from BD, with New Zealanders accounting for the most significant percentage.Although the pathophysiology of BD still requires some elucidation, changes in immune-inflammatory activity, oxidative and nitrosative stress (O&NS), and neuroregulatory tryptophan catabolites (TRYCATs) have been indicated as the etiology and course of BD,With a meta-analysis prepared by Hebbrecht et al. ,TRYCAT levels measured in cerebrospinal fluid (CSF) or serum/plasma in BD patients were lower than in healthy controls. Furthermore, the impact of the gut microbiota should be considered in the development of BD. Modifying the intestinal microbiota composition of patients with BD indicates the association between GM dysbiosis and disease progression. According to studies considering intestinal microbiome diversity, an increased amount of Coriobacteriaceae was associated with a raised cholesterol level and an increased level of Lactobacilli contributes to the development of obesity associated with BD.The low amount of Faecalibacterium, an autochthonous intestinal bacterium, can also be correlated with diseases [63]. In patients diagnosed with BD, the number of Clostridiaceae involved in the fermentation of carbohydrates leading to the production of SCFAs was four times lower than in the control group.

(d). Autism Spectrum Disorder (ASD)

One of the most important and dangerous neurodevelopmental diseases related to the composition of the GI microbiota is autism spectrum disorder (ASD). According to the CDC's Autism and Developmental Disabilities Monitoring Network (ADDM) estimation, approximately 1 in 44 children in the United States has been diagnosed with ASD .ASD is characterized by unconventional behavior, difficulties in communication and building relationships, and hypo- or hypersensitivity responses to environmental sensory signals[28]. Some studies indicated genetic factors, GI abnormalities, inflammation, or other individual and exterior factors (e.g., pre- and postnatal exposure, stress, GI microbiota, or diet), although none of them is capable of absolutely elucidating this disorder.According to Azouz et al. in a group of 40 autistic children aged 3 to 12 years, 82.5% of them showed gastrointestinal symptoms. Furthermore, dysbiosis related to the ratio of Firmicutes and Bacteroides and the phylum number of Firmicutes, Bacteroidetes, Fusobacteria, and Verrucomicrobia was demonstrated in patients diagnosed with ASD.In the same study, the authors revealed that in patients with ASD, the changes also affect the level of SCFAs and volatile organic compounds (VOC), including, among others, indole, whichis a metabolite of tryptophan and the precursor of serotonin and melatonin. However, these data should be carefully interpreted due to the possible influence of antibiotic treatment or personalized diet in patients with ASD [29]. To clearly define the role of the gut microbiota in patients, further research and an entire view to connect dependences between GM andASD are needed.

(e). Attention-Deficit Hyperactivity Disorder (ADHD)

A common neurodevelopmental disorder is attention deficit hyperactivity disorder (ADHD), which affects 6 million children aged 3–17 years . It manifests in difficulties maintaining attention, and sudden, unexpected behaviour. The genes for the dopamine receptors DRD4 and DRD5 and dopamine and serotonin transmitters are considered the main etiological factors of this disease.A growing amount of evidence indicates the connection with themicrobiome–gut–brain axis.In themicrobiome study conducted by Aarts et al. ,96 participants participated, ofwhom19 had been diagnosed with ADHD and 77 were healthy. Results revealed differences in taxa, where in ADHD cases, the phylum Actinobacteria was more abundant (for example, Bifidobacterium), while the abundance of Firmicutes decreased. Interestingly, the same study revealed that the microbiome of cases of ADHD shows a more remarkable ability to produce cyclohexadienyl dehydratase (CDT), which is involved in synthesizing the dopamine precursor (phenylalanine). On the contrary, the meta-

analysis prepared by Wang et al.,which evaluated the intestinal microbiota and ADHD, did not show significant differences at the phylum and family levels beyond the higher level of Blautia in patients with ADHD compared to healthy control. This microorganism plays a regulatory role in metabolic and inflammatory diseases, as well as biotransformation.Future research that specifies the connection between the microbiome–gut–brain axis and ADHD should cover a larger demographically diverse study group [61]. The risk of developing neuropsychiatric disorders could be reduced through probiotic supplementation in early life. Pärtty et al. [62] showed that early administration of Lactobacillus rhamnosus GG might decrease the risk of ADHD. It was shown that L. rhamonsus, through the vagus nerve, regulated emotional behavior and the central GABA receptor expression in a mouse.In addition, the influence of dietary patterns on ADHD patients is important. Since food contains artificial color additives, to decrease the hyperactive behavior of ADHD patients, it is necessary to exclude such products from the diet.Intake of omega-3 PUFAs is also significant, in particular, docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), as both are essential for proper membrane fluidity, neurotransmission, and receptor function.In a study based on animal male models of ADHD, nutrition individuals with a diet enriched in omega-3 PUFAs caused decreased impulsivity and improved concentration.

Material & Methods:-

This is an Observational study was conducted between January 2022 to April 2022 in the Departments of Psychiatry of Government Medical College & Hospitals, Datia, Madhya Pradesh a tertiary care hospital in Central India. Patients attending Psychiatry OPD were segregated with certain criteria which are as follows:

A) Inclusion criteria:Patients attending OPD clinic in Psychiatry Department with Depression .
2.) Either male or female 3.)Agree to give consent.
4.) Age group -more than 10 years to 70 years of age

B)Exclusion criteria:1) Individual with no symptoms,
2.)Children less then 10 year age **a**nd
3.)who did not give informed consent were not included in the study.

C)Sample size -100

Study Design:-

Observational Study, Questionnaire based survey.

Duration:- January 2022 to April 2022.

Aims & Objective: This study is to find out the role of Probiotics on psychiatric disorders how they modulate immune pathwayto improve brain function ;The Gut –Brain Axis".

Secondary objective: To know importance of probiotics in day to day life which is necessary for maintaining good mental Health.

Method: An questionnaire was given to the patients with Sociodemographic data sheet, Beck-Depression Scale. A total of 100 patients participated in the study. Two group of Patients were allotted one with any one antidepressant Escitalopram were given and other with antidepressant and one Probiotic which was given under Hospital supply to reduce the financial burden on patients.

Result & Observation

By analyzing studies on probiotic supplementation, we can observe the relationships between the microbiota and mood disorders and the disease-alleviating effect. Strong evidence suggests that gut microbiota has an important role in bidirectional interactions between the gut and the nervous system.

50 such patients who are on Antidepressant(Escitalopram) along with a Probiotic have better symptoms management and early effect compared with other group 50 patients patints who are on antidepressants only. Micrbiota interacts with CNS by regulating brain chemistry and influencing neuro-endocrine systems associated with stress response, anxiety and memory function. Many of these effects appear to be strain-specific, suggesting a potential role of certain probiotic strains as novel adjuvant strategy for neurologic disorders. In addition, the effects of CNS on microbiota composition are likely mediated by a perturbation of the normal luminal/mucosal habitat that can also be restored by the use of probiotics and possibly by diet.

Summary & Future Perspectives

In summary, the experimental data described in this review confirm that disturbances in the composition of the microbiota lead to the development of mental and psychiatric disorders in the host organism. Knowledge about different communication pathways on the bidirectional gut–brain axis significantly impacts the development of new therapeutic strategies because the gut microbiota undergoes modifications even in utero. Additionally, the dietary composition modulates GM and, thus, the availability of their metabolites in the intestine. This, in turn, enables the design of alternative therapeutic strategies for the treatment of mood disorders. Current scientific reports are based mainly on animal models. Numerous studies are also required on people with mood disorders, showing probiotics' effect.

Conclusions

Our review of the current literature presents bidirectional communication between the gut and the brain through the microbiome–gut–brain axis. In this work, we focus on the pathogenesis of depression, schizophrenia, and bipolar disorder and some factors affecting the formation of gut microbiota. The COVID-19 pandemic has led to an increase in the number of people suffering from mental disorders. Considering the fact that the gut microbiota is altered in people with various mental disorders and bearing in mind that intestinal dysbiosis is associated with the development of inflammation, which is related to the forming and progression of symptoms of these diseases, there is a need to expand knowledge about bacterial species in larger groups of people with mental disorders, including the effects of medications and eating habits. Hence, expanding the knowledge on the association between gut–microbiota–brain, and pathways involved in this communication, is essential to develop protective strategies or create new therapeutic approaches against mental disorders.

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Conflicts of Interest: The authors declare no conflict of interest.

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