GUT MICROIAL ETHANOL METABOLISM CONTRIBUTES AUTO-BREWERY SYNDROME

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ABSTRACT

Auto-Brewery Syndrome (ABS), also known as Gut Fermentation Syndrome, is a rare disorder in which microorganisms in the gastrointestinal tract ferment dietary carbohydrates into ethanol, causing endogenous alcohol intoxication. Gut dysbiosis and the overgrowth of ethanol-producing bacteria and yeasts are the primary causes of the condition. Patients experience symptoms similar to alcohol intoxication despite not consuming alcohol. Diagnosis involves clinical history, carbohydrate challenge testing, blood or breath ethanol measurement, and microbiological analysis. Treatment includes a low-carbohydrate diet, targeted antimicrobial or antifungal therapy, probiotics, and fecal microbiota transplantation (FMT) in selected cases. Recent advances in gut microbiome research have improved the understanding, diagnosis, and management of Auto-Brewery Syndrome.

KEY WORDS: Auto-brewery syndrome, Gut microbiome, Gut dysbiosis, Endogenous ethanol production, carbohydrate fermentation, Fecal Microbiota Transplantation (FMT).

INTRODUCTION

The human gastrointestinal tract contains trillions of microorganisms, including bacteria, fungi, viruses, and archaea, collectively known as the gut microbiome. These microorganisms play a vital role in maintaining human health by aiding digestion, synthesizing vitamins, regulating metabolism, strengthening the intestinal barrier, and supporting immune function. Under normal conditions, the gut microbiota exists in a balanced state that contributes to overall physiological homeostasis[Fig1]. However, disruption of this balance, known as gut dysbiosis, can alter microbial metabolism and contribute to the development of several gastrointestinal,

metabolic, neurological, and liver diseases. One of the rare but clinically significant disorders associated with gut dysbiosis is Auto-Brewery Syndrome (ABS), also called Gut Fermentation Syndrome.

Auto-Brewery Syndrome is a rare medical condition in which microorganisms present in the gastrointestinal tract ferment dietary carbohydrates into ethanol [1]. The ethanol produced is absorbed into the bloodstream, resulting in elevated blood alcohol concentrations and symptoms of alcohol intoxication despite the absence of alcohol consumption. Because the condition is uncommon and its symptoms closely resemble those caused by alcoholic beverages, ABS is frequently misdiagnosed or overlooked in clinical practice. Increasing awareness among healthcare professionals is therefore essential for early diagnosis and appropriate management.

Patients with Auto-Brewery Syndrome may experience repeated episodes of dizziness, confusion, slurred speech, impaired coordination, fatigue, headache, mood changes, memory problems, abdominal discomfort, and nausea. In severe cases, patients may develop blackouts, altered mental status, or loss of consciousness. These symptoms can significantly interfere with daily activities, education, employment, and social relationships, thereby reducing the overall quality of life. Since patients usually deny alcohol consumption, the disorder often creates confusion for both clinicians and family members.

The pathogenesis of Auto-Brewery Syndrome is closely linked to disturbances in the gut microbiome. Under normal physiological conditions, only very small amounts of ethanol are produced during microbial fermentation and are rapidly metabolized by the liver without causing symptoms. However, gut dysbiosis allows excessive growth of ethanol-producing microorganisms, leading to abnormal fermentation of dietary carbohydrates and increased endogenous ethanol production[Fig2]. As a result, ethanol enters the bloodstream and produces intoxication-like symptoms.

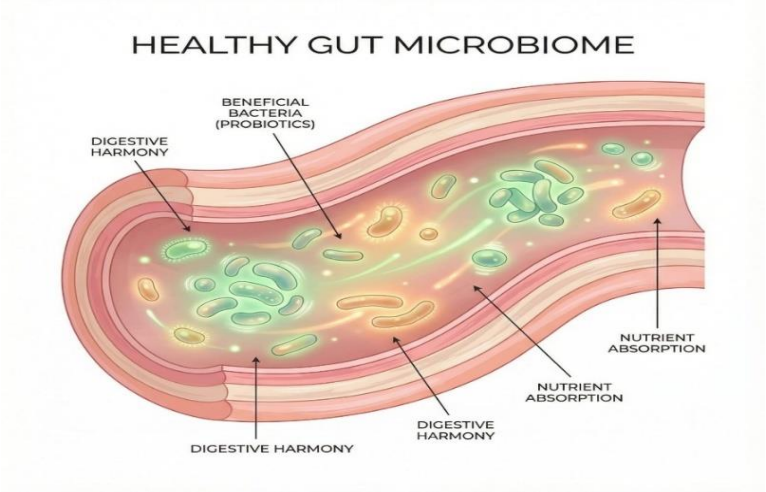

Fig.No.1: Healthy gut microbiome

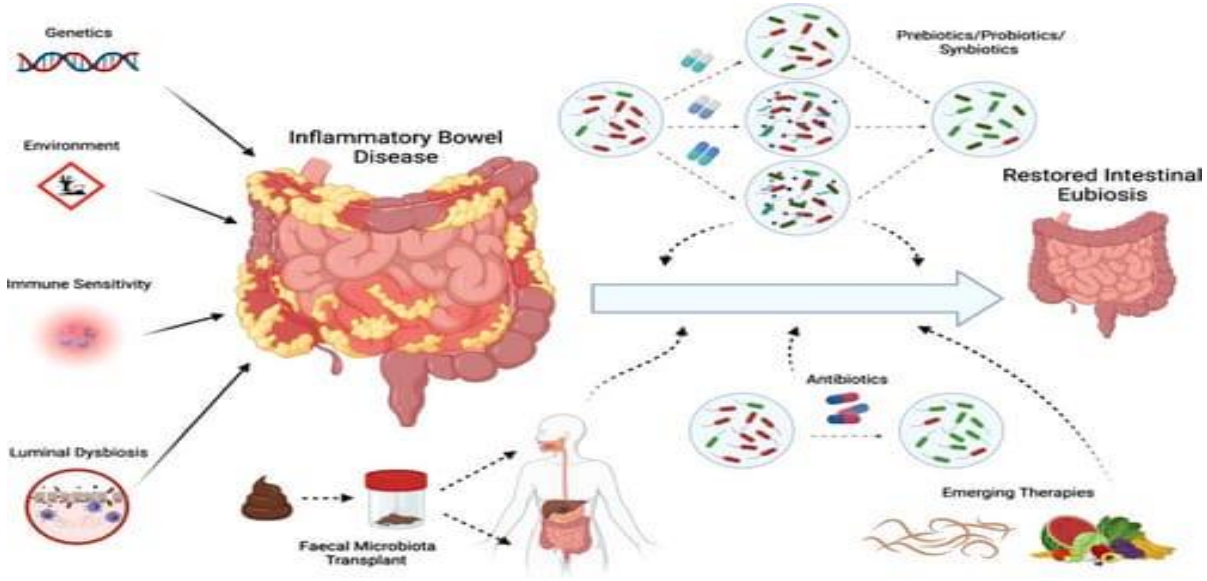

Fig.No.2: Restoration of Gut microbiota Homeostasis

Recent advances in microbiome research have greatly improved the understanding of Auto-Brewery Syndrome. High-throughput sequencing technologies, metagenomic analysis, and metabolomic studies have identified increased numbers of ethanol-producing microorganisms and enhanced microbial fermentation pathways in patients with ABS. Elevated acetate levels and alterations in microbial metabolism have also been associated with increased endogenous ethanol production. These findings suggest that changes in microbial composition and function play a central role in disease development.

Continuous exposure to endogenous ethanol may have harmful effects beyond intoxication. Excessive ethanol production can increase intestinal permeability, promote oxidative stress, trigger inflammatory responses, and facilitate the movement of bacterial endotoxins into the portal circulation. These mechanisms may contribute to liver injury, metabolic disturbances, immune dysregulation, and chronic inflammation, indicating that ABS is a systemic disorder rather than only a gastrointestinal disease [2]. Diagnosing Auto-Brewery Syndrome remains challenging because there are no universally accepted diagnostic guidelines. A detailed medical history, careful evaluation of dietary habits, carbohydrate or glucose challenge tests, serial blood or breath ethanol measurements, stool culture, fungal and bacterial identification, and molecular microbiome analysis are valuable tools for confirming endogenous ethanol production while excluding covert alcohol intake.

Management of Auto-Brewery Syndrome requires a multidisciplinary approach involving gastroenterologists, microbiologists, infectious disease specialists, dietitians, and primary care physicians. Treatment primarily aims to reduce endogenous ethanol production by restricting dietary carbohydrates, eliminating ethanol-producing microorganisms with appropriate antibacterial or antifungal therapy, restoring microbial balance using probiotics, and treating underlying gastrointestinal disorders[3]. In selected refractory cases, fecal microbiota transplantation (FMT) has shown encouraging results by restoring a healthy gut microbial ecosystem and reducing symptom recurrence.

HISTORY OF AUTO-BREWERY SYNDROME

EARLY OBSERVATIONS (1950S)

Auto-Brewery Syndrome (ABS), also known as Gut Fermentation Syndrome, is a rare disorder in which ethanol is produced endogenously within the gastrointestinal tract through microbial fermentation of dietary carbohydrates. Although the syndrome has gained considerable scientific attention in recent years, its history spans more than seven decades. The gradual recognition of ABS has significantly enhanced our understanding of the relationship between the gut microbiome, microbial metabolism, and human health. The earliest observations of endogenous ethanol production were reported during the 1950s, when physicians encountered patients who

exhibited symptoms of alcohol intoxication despite consistently denying alcohol consumption. At that time, the condition was poorly understood, and many affected individuals were mistakenly suspected of hidden alcohol abuse, psychiatric illness, or intentional deception. The absence of reliable microbiological and molecular diagnostic techniques made it difficult to identify the true cause of these unexplained intoxication episodes.

FIRST CLINICAL EVIDENCE (1972)

A major milestone in the history of ABS occurred in 1972, when Japanese researchers published one of the first well-documented clinical cases linking endogenous ethanol production to intestinal yeast overgrowth. This landmark report demonstrated that microorganisms residing in the gastrointestinal tract could ferment dietary carbohydrates into ethanol in quantities sufficient to produce measurable blood alcohol concentrations and clinical symptoms of intoxication[4]. These findings challenged the long-standing belief that alcohol detected in the bloodstream could originate only from external alcoholic beverages.

EXPANSION OF CLINICAL CASES (1970S–1980S)

During the 1970s and 1980s, additional case reports were published from Japan, Europe, and North America. Most patients had a history of prolonged antibiotic therapy, diabetes mellitus, gastrointestinal surgery, inflammatory bowel disease, short bowel syndrome, or other conditions that disrupted the normal intestinal microbiota. Investigators consistently isolated fermentative yeasts, particularly *Saccharomyces cerevisiae* and various *Candida* species, from stool or gastric samples[Fig3]. These microorganisms were shown to convert glucose and other carbohydrates into ethanol through anaerobic fermentation, providing a biological explanation for recurrent episodes of endogenous alcohol intoxication.

UNDERSTANDING THE BIOCHEMICAL MECHANISM

As research progressed, scientists investigated the biochemical mechanisms responsible for microbial ethanol production. They demonstrated that fermentative microorganisms metabolize carbohydrates through glycolysis, producing pyruvate, which is subsequently converted into acetaldehyde by pyruvate decarboxylase and finally into ethanol by alcohol dehydrogenase. This metabolic pathway closely resembles the fermentation process used in brewing and winemaking, leading to the term *Auto-Brewery Syndrome*[5], as alcohol is effectively "brewed" within the patient's gastrointestinal tract.

MOLECULAR ERA (2000S)

The beginning of the 21st century marked a major turning point in ABS research with the introduction of advanced molecular diagnostic technologies. Techniques such as polymerase chain reaction (PCR), 16S ribosomal RNA sequencing, internal transcribed spacer (ITS) sequencing for fungi, metagenomic sequencing, and metabolomic analysis enabled researchers to characterize the intestinal microbiome with unprecedented accuracy. Rather than identifying only individual microorganisms, these approaches allowed comprehensive analysis of entire microbial communities and their metabolic functions.

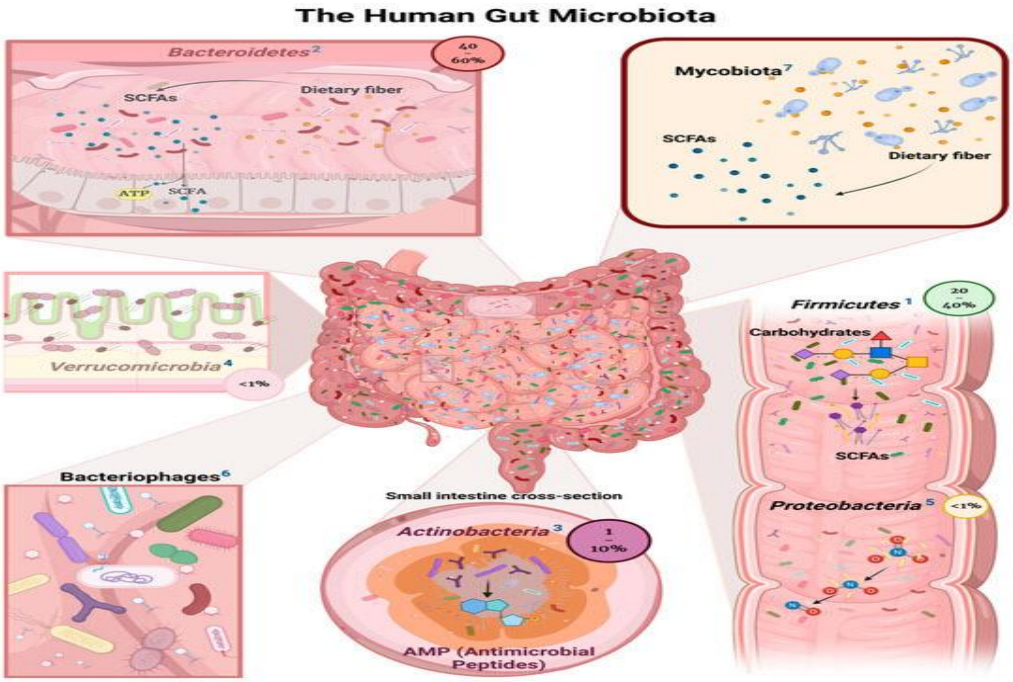

Fig.No.3: Composition and diversity of the human gut microbiota

RECENT ADVANCES (2015–PRESENT)

Recent investigations have further strengthened the association between gut microbial ethanol metabolism and systemic disease. High-alcohol-producing strains of *Klebsiella pneumoniae* have been identified in patients with Auto-Brewery Syndrome and have also been implicated in metabolic-associated liver disease. Experimental studies demonstrated that these bacteria could produce sufficient qualities of ethanol to induce liver injury resembling chronic alcohol exposure, suggesting that endogenous microbial ethanol may contribute to hepatic disease even in individuals who abstain from alcohol.

Modern research has also highlighted the influence of diet on endogenous ethanol production. Diets rich in refined carbohydrates and simple sugars provide abundant substrates for microbial fermentation, thereby increasing ethanol synthesis in susceptible individuals. Conversely, carbohydrate-restricted diets have been shown to reduce microbial fermentation and improve clinical symptoms. These observations emphasize the close relationship between dietary habits, gut microbial composition, and endogenous ethanol production.

Treatment strategies have also evolved considerably over time. Early management primarily focused on antifungal therapy to eliminate intestinal yeast overgrowth. Current therapeutic approaches are more comprehensive and include dietary carbohydrate restriction, targeted antimicrobial or antifungal therapy based on microbiological findings, probiotic supplementation to restore beneficial intestinal microorganisms, management of underlying gastrointestinal disorders, and emerging microbiome-based therapies such as fecal microbiota transplantation (FMT). These interventions aim not only to suppress ethanol-producing microorganisms but also to restore normal gut microbial homeostasis and prevent recurrence.

DEVELOPMENT OF CURATIVE THERAPY FOR AUTO-BREWERY SYNDROME

Current treatment strategies for Auto-Brewery Syndrome (ABS), including dietary modification, antimicrobial or antifungal therapy, and probiotic supplementation, help control symptoms but do not provide a permanent cure. Therefore, current research focuses on developing curative therapies that target the underlying gut microbial dysbiosis by eliminating ethanol-producing microorganisms and restoring a healthy intestinal microbiome. Among the most promising approaches are precision microbiome therapy and fecal microbiota transplantation (FMT)[Fig4], which aim to restore microbial balance, reduce endogenous ethanol production, and prevent disease recurrence. Researchers are also investigating next-generation probiotics, engineered beneficial bacteria, bacteriophage therapy[6], microbiome-modulating drugs, and microbial enzyme inhibitors that selectively suppress ethanol-producing microorganisms while preserving beneficial gut microbes.

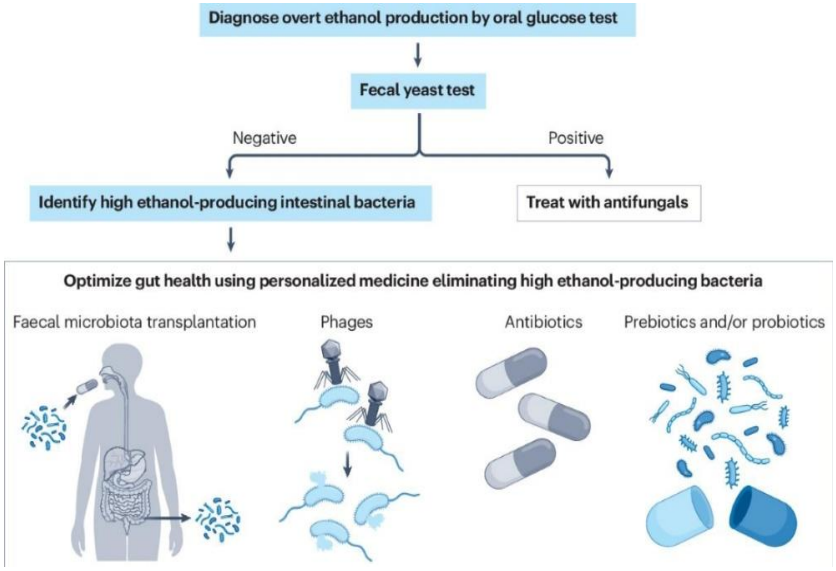

Fig.No.4: Development of therapeutic strategies for ABS

PHARMACOLOGY

✓ **ROLE OF PHARMACOLOGICAL THERAPY:** Pharmacological treatment of Auto-Brewery Syndrome (ABS) aims to eliminate ethanol-producing microorganisms, restore normal gut microbiota, and prevent recurrence. Therapy is usually combined with a low-carbohydrate diet and should be individualized based on the causative microorganism and disease severity.

✓ **ANTIFUNGAL THERAPY:** Antifungal drugs are the first-line treatment when yeasts such as *Candida albicans*, *Candida glabrata*, or *Saccharomyces cerevisiae* are responsible for ethanol production[7]. Common agents include fluconazole, nystatin, and itraconazole. These drugs inhibit fungal cell membrane synthesis, reducing fungal growth, endogenous ethanol production, and clinical symptoms.

✓ **ANTIBIOTIC THERAPY:** When ethanol-producing bacteria such as *Klebsiella pneumoniae*, *Escherichia coli*, or *Enterococcus faecium* are identified, targeted antibiotics are selected based on culture and susceptibility testing[Fig5]. Probiotic supplementation is recommended after antibiotic therapy to restore beneficial gut bacteria. In recurrent or resistant cases, fecal microbiota transplantation (FMT) may be considered.

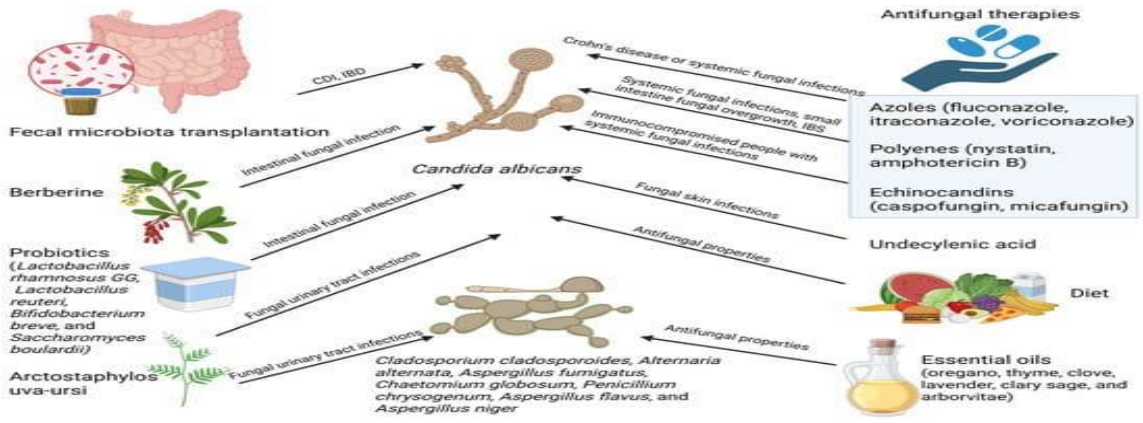

Fig.No.5: Pharmacological and therapeutic approaches for ABS

✓ **PHARMACOKINETIC CONSIDERATION:** Oral antifungal and antibiotic agents should have good gastrointestinal absorption and adequate intestinal concentrations for effective treatment. Drug selection, appropriate dosing, patient adherence, and regular follow-up are essential to achieve successful therapy and prevent relapse.

✓ **ADVERSE EFFECTS AND DRUG SAFETY:** Common adverse effects include nausea, vomiting, diarrhea, abdominal discomfort, and bloating[8]. Long-term or inappropriate antimicrobial use may cause gut dysbiosis and antimicrobial resistance. Therefore, treatment should be guided by microbiological diagnosis and regular clinical monitoring

✓ **MONITORING OF PHARMACOTHERAPY:** Treatment response should be assessed through clinical improvement, stool microbiological analysis, microbial culture, and blood or breath ethanol measurements when required. Regular follow-up helps detect recurrence, monitor adverse effects, and maintain long-term gut microbial balance.

PATHOPHYSIOLOGY

Under normal physiological conditions, small amounts of endogenous ethanol are produced in the gastrointestinal tract through microbial fermentation of dietary carbohydrates. This ethanol is rapidly metabolized by the liver through first-pass metabolism and does not produce symptoms. In Auto-Brewery Syndrome (ABS), intestinal microbial dysbiosis causes excessive growth of ethanol-producing microorganisms, leading to increased fermentation of carbohydrates and excessive endogenous ethanol production. When ethanol production exceeds the liver's metabolic capacity, ethanol enters the systemic circulation[Fig6], producing recurrent intoxication-like symptoms despite the absence of alcohol consumption.

ABS has traditionally been associated with fermentative yeasts such as *Saccharomyces cerevisiae*, *Saccharomyces boulardii*, *Candida albicans*, *Candida glabrata*, and *Candida parapsilosis*[9]. Recent microbiome studies have also identified high-alcohol-producing bacteria, including *Klebsiella pneumoniae*, *Escherichia coli*, *Enterococcus faecium*, and *Citrobacter freundii*, as important contributors to endogenous ethanol production.

Metagenomic and metabolomic studies have shown that patients with ABS possess altered gut microbial communities enriched with carbohydrate fermentation and ethanol biosynthesis pathways. Carbohydrate-rich meals provide substrates for microbial fermentation, resulting in increased blood ethanol levels and recurrent intoxication episodes. Disease severity is influenced by the abundance and metabolic activity of ethanol-producing microorganisms, dietary carbohydrate intake, gut microbial diversity, host gastrointestinal physiology, and previous antibiotic exposure.

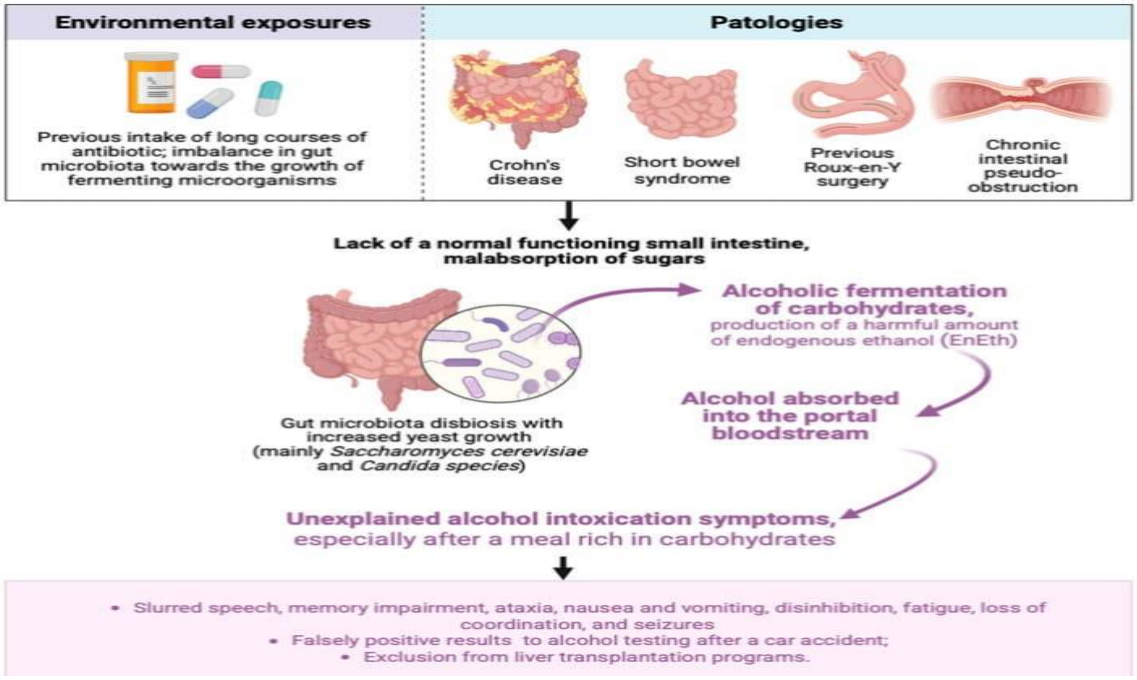

Fig.No.6: Pathophysiological mechanism of ABS

Persistent gut dysbiosis, impaired intestinal barrier function, altered intestinal pH, and reduced microbial diversity create favorable conditions for continued colonization of ethanol-producing microorganisms. This establishes a self-perpetuating cycle of microbial imbalance and excessive ethanol production, contributing to recurrent disease[10]. Rare cases of endogenous ethanol production have also been reported in the oral cavity and urinary tract, although the underlying mechanisms remain poorly understood.

Understanding the pathophysiology of ABS has led to microbiome-directed therapeutic strategies, including dietary carbohydrate restriction, targeted antimicrobial therapy, probiotic supplementation, and fecal microbiota transplantation (FMT). These approaches aim to restore normal gut microbial balance, reduce endogenous ethanol production, and prevent disease recurrence. Ongoing microbiome research is expected to improve diagnostic accuracy and support the development of personalized treatments for Auto-Brewery Syndrome.

ETIOLOGY

Auto-Brewery Syndrome (ABS) is a rare disorder caused by excessive endogenous ethanol production due to abnormal microbial fermentation of dietary carbohydrates in the gastrointestinal tract. The primary etiological factor is gut microbial dysbiosis, in which disruption of the normal intestinal microbiota allows ethanol-producing microorganisms to proliferate[11]. This imbalance alters microbial metabolism, leading to excessive ethanol production and recurrent intoxication-like symptoms despite the absence of alcohol consumption.

GUT MICROBIAL DYSBIOSIS

Gut dysbiosis is the central cause of ABS. Ethanol-producing microorganisms such as *Saccharomyces cerevisiae*, *Candida albicans*, *Candida glabrata*, *Candida tropicalis*, *Klebsiella pneumoniae*, *Escherichia coli*, *Lactobacillus fermentum*, *Weissella confusa*, and *Enterococcus faecium* ferment dietary carbohydrates into ethanol[12]. Repeated or prolonged use of broad-spectrum antibiotics is a major risk factor because it disrupts beneficial gut microbiota and promotes the overgrowth of these microorganisms.

DIETARY FACTORS

A diet rich in refined carbohydrates and simple sugars provides abundant substrates for microbial fermentation, increasing endogenous ethanol production. Poor nutritional status and inadequate dietary fiber further reduce microbial diversity, promoting persistent gut dysbiosis and microbial overgrowth.

GASTROINTESTINAL AND HOST-RELATED FACTORS

Several conditions increase susceptibility to ABS, including impaired intestinal motility, short bowel syndrome, blind-loop syndrome, inflammatory bowel disease, previous gastrointestinal surgery, diabetes mellitus, obesity, prolonged proton pump inhibitor use, and weakened immune function. These factors alter the intestinal environment, allowing ethanol-producing microorganisms to colonize and persist.

MICROBIAL FERMENTATION

During anaerobic metabolism, ethanol-producing microorganisms convert dietary carbohydrates into ethanol through glycolytic and fermentative pathways. Increased activity of these pathways results in excessive endogenous ethanol production and recurrent clinical symptoms.

MICROBIAL INTERACTIONS AND BIOFILM FORMATION

Recent studies suggest that ethanol-producing bacteria and fungi form biofilms, which enhance microbial survival, metabolic cooperation, and resistance to antimicrobial therapy[fig7]. The coexistence of organisms such as *Candida* species, *Saccharomyces cerevisiae*, *Klebsiella pneumoniae*, *Escherichia coli*, and *Enterococcus faecium* can further increase ethanol production[13]. Persistent gut dysbiosis after treatment may lead to recolonization of these microorganisms and disease recurrence.

Overall, the etiology of Auto-Brewery Syndrome is multifactorial, involving interactions among gut microbial dysbiosis, dietary habits, host-related conditions, and microbial metabolism. Restoration of a healthy gut microbiota is essential for long-term disease control and prevention of recurrence.

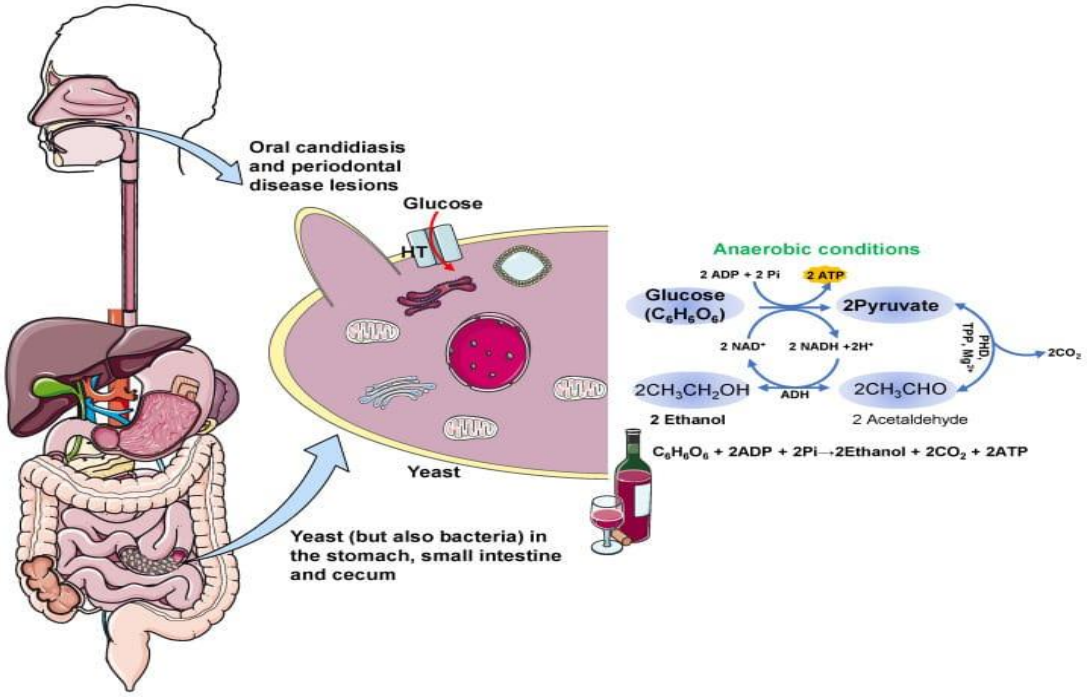

Fig.No.7: Etiological factors contribution to ABS

RISK FACTORS

Auto-Brewery Syndrome (ABS) develops primarily due to factors that disrupt the normal gut microbiota and promote the overgrowth of ethanol-producing microorganisms. Gut microbial dysbiosis is the most significant risk factor, allowing organisms such as *Saccharomyces cerevisiae*, *Candida* species, *Klebsiella pneumoniae*, and high alcohol-producing *Escherichia coli* to ferment dietary carbohydrates into ethanol. Other major risk factors include prolonged or repeated use of broad-spectrum antibiotics, which reduce beneficial gut microorganisms, and diets rich in carbohydrates and refined sugars that enhance microbial fermentation.

Additional risk factors include gastrointestinal disorders such as inflammatory bowel disease (IBD), Crohn's disease, ulcerative colitis, short bowel syndrome, and small intestinal bacterial overgrowth (SIBO). Diabetes mellitus, obesity, previous gastrointestinal surgery, reduced gut microbial diversity, immunocompromised conditions, recurrent antimicrobial exposure, poor nutrition, and genetic variations affecting host–microbiome interactions may also increase susceptibility[14]. Overall, ABS is a multifactorial disorder resulting from interactions among gut dysbiosis, dietary habits, gastrointestinal diseases, and host-related factors.

HIGHER RISK FACTORS

- Gut microbial dysbiosis
- Prolonged or repeated broad-spectrum antibiotic use
- High-carbohydrate and high-sugar diet
- Ethanol-producing microorganisms (*Saccharomyces*, *Candida*, *Klebsiella pneumoniae*, *Escherichia coli*)
- Gastrointestinal disorders (IBD, Crohn's disease, ulcerative colitis, short bowel syndrome, SIBO)

MODERATE AND LOWER RISK FACTORS

- Diabetes mellitus and obesity
- Previous gastrointestinal surgery
- Reduced gut microbial diversity
- Immunocompromised conditions
- Recurrent antimicrobial exposure
- Poor nutritional status
- Genetic factors influencing host–microbiome interactions

EPIDEMIOLOGY

Auto-Brewery Syndrome (ABS) is a rare and likely underdiagnosed disorder in which endogenous ethanol is produced through microbial fermentation of dietary carbohydrates in the gastrointestinal tract. Although the exact prevalence is unknown, cases have been reported worldwide in both adults and children[15]. The condition is associated with gut microbial dysbiosis, particularly the overgrowth of ethanol-producing fungi and bacteria. Individuals with diabetes mellitus, obesity, inflammatory bowel disease (IBD), short bowel syndrome, previous gastrointestinal surgery, prolonged antibiotic, or proton pump inhibitor (PPI) use, and other gastrointestinal disorders are at increased risk because these conditions disrupt the normal intestinal microbiota[16]. Diets rich in refined carbohydrates and sugars further promote microbial fermentation and endogenous ethanol production[Fig8]. Recent studies have identified ethanol-producing bacteria such as *Klebsiella pneumoniae* and *Escherichia coli*, in addition to fermentative yeasts like *Saccharomyces cerevisiae* and *Candida* species, as important contributors to the disease.

ABS affects both sexes and all age groups and has been reported in North America, Europe, and Asia, indicating that it is not restricted to any specific geographical region or ethnic group. However, because its symptoms resemble alcohol intoxication, the disorder is often misdiagnosed as alcohol misuse or psychiatric illness, leading to significant underdiagnosis.

Current epidemiological evidence is based mainly on case reports and small observational studies, making the true prevalence and incidence of ABS difficult to determine[17]. Increasing clinical awareness and advances in microbiome sequencing are improving diagnosis, but large multicenter studies are still needed to define the global burden, identify high-risk populations, and better understand the epidemiology of Auto-Brewery Syndrome.

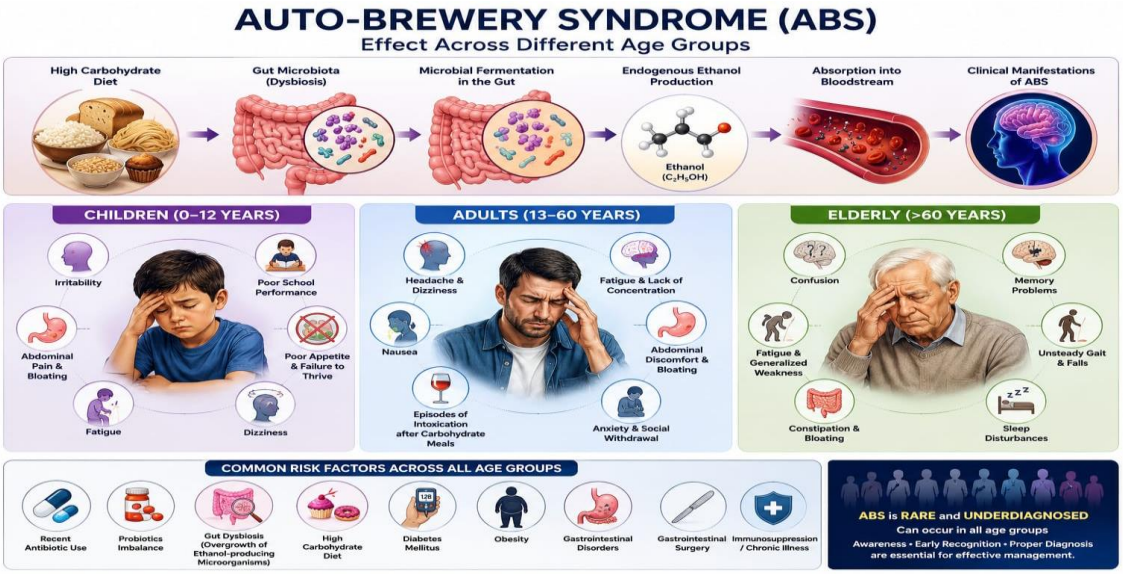

Fig.No.8: Age-wise clinical manifestations of ABS

EVALUATION

The evaluation of Auto-Brewery Syndrome (ABS) aims to confirm excessive endogenous ethanol production caused by ethanol-producing microorganisms in the gastrointestinal tract. Diagnosis requires a combination of clinical assessment, laboratory investigations, microbiological analysis, and molecular diagnostic techniques to distinguish ABS from alcohol consumption and other metabolic disorders.

A detailed medical history is the first step and should include episodes of unexplained intoxication, recent antibiotic use, dietary habits, gastrointestinal diseases, and alcohol intake. Symptoms occurring without alcohol consumption strongly suggest ABS.

Laboratory investigations include blood ethanol concentration and breath alcohol measurements during symptomatic episodes. The oral glucose challenge test is considered one of the most reliable diagnostic methods, in which serial blood and breath ethanol levels are measured after glucose ingestion. A rise in ethanol levels without alcohol intake indicates active microbial fermentation.

Microbiological investigations include stool and fungal cultures, along with molecular techniques such as 16S rRNA sequencing, ITS sequencing, quantitative PCR (qPCR)[18], and shotgun metagenomic sequencing to identify ethanol-producing microorganisms. Common organisms include *Candida albicans*, *Candida glabrata*, *Saccharomyces cerevisiae*, *Klebsiella pneumoniae*, *Escherichia coli*, and *Enterococcus faecium*.

Additional investigations such as stool microbiome profiling, metabolomic analysis, liver function tests, complete blood count, inflammatory markers, and nutritional assessment help evaluate disease severity. In selected patients, endoscopy may be performed to identify underlying gastrointestinal disorders such as small intestinal bacterial overgrowth (SIBO) or inflammatory bowel disease (IBD)[19].

Recent advances in metagenomics, metabolomics, transcriptomics, and artificial intelligence (AI)-assisted microbiome analysis have improved the diagnosis and monitoring of ABS. Repeated microbiome assessment during treatment helps evaluate therapeutic response, detect recurrence, and support personalized treatment strategies. These advances are expected to enhance diagnostic accuracy and promote precision medicine in the management of Auto-Brewery Syndrome.

CLINICAL TRIALS AND RESEARCH EVIDENCE

Auto-Brewery Syndrome (ABS) is a rare disorder; therefore, large-scale randomized clinical trials are limited. Most available evidence comes from case reports, case series, and observational studies, which consistently support excessive endogenous ethanol production by gut microorganisms as the primary cause of the disease.

One of the most important observational studies evaluated 22 patients with ABS and 21 healthy household controls. Fecal samples from patients produced significantly higher ethanol levels than those from controls during laboratory fermentation tests. Metagenomic sequencing identified increased abundance of ethanol-producing microorganisms, particularly Klebsiella pneumoniae, Escherichia coli, and fermentative yeasts. Targeted antimicrobial therapy reduced endogenous ethanol production in most patients, while one treatment-resistant patient achieved long-term remission after Fecal Microbiota Transplantation (FMT) with restoration of a healthy gut microbiota[20].

More than 100 cases of ABS have been reported worldwide in both adults and children. Most patients are 30–60 years old, although pediatric cases have also been documented. Common clinical features include recurrent intoxication-like episodes, dizziness, confusion, impaired coordination, fatigue, slurred speech, and elevated blood alcohol levels despite complete abstinence from alcohol.

Microbiological and metagenomic studies consistently demonstrate increased abundance of ethanol-producing microorganisms, including Klebsiella pneumoniae, Escherichia coli, Candida albicans, Candida glabrata, and Saccharomyces cerevisiae[Fig9]. These organisms' ferment dietary carbohydrates into ethanol[21], contributing directly to endogenous alcohol production and disease development.

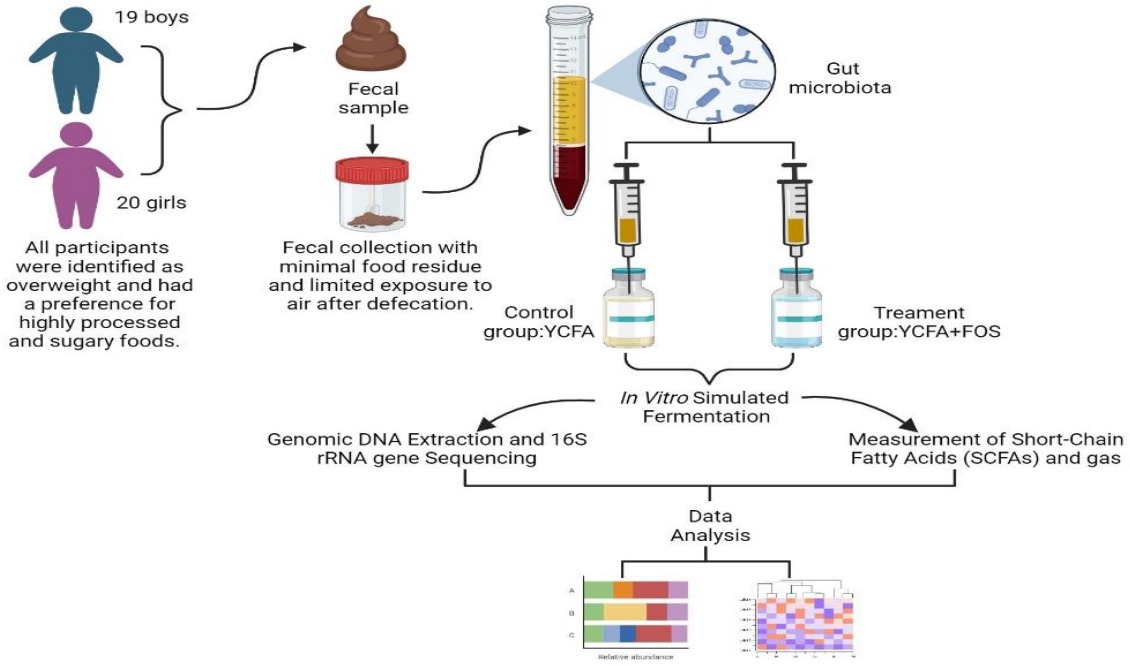

Fig.NO.9: Experimental design for gut microbiota analysis

Clinical evidence also shows that targeted antimicrobial therapy, dietary carbohydrate restriction, and probiotic supplementation significantly reduce endogenous ethanol production and improve symptoms. In treatment-resistant cases, FMT has restored microbial diversity and achieved sustained clinical remission.

TREATMENT AND MANAGEMENT

The primary goal of treating Auto-Brewery Syndrome (ABS) is to reduce endogenous ethanol production by correcting gut microbial dysbiosis, eliminating ethanol-producing microorganisms, relieving symptoms, and preventing recurrence. Management requires a multidisciplinary approach involving dietary modification, antimicrobial therapy, probiotic supplementation, microbiome restoration, treatment of underlying diseases, and long-term follow-up[22].

DIETARY MODIFICATION

Dietary modification is the first-line treatment for ABS. Patients are advised to follow a low-carbohydrate, low-sugar diet and avoid refined sugars, processed foods, sweetened beverages, and excessive starch, as these promote microbial fermentation[23]. A balanced diet rich in protein, dietary fiber, vegetables, healthy fats, and complex carbohydrates helps restore gut microbial balance and reduce recurrence.

ANTIMICROBIAL THERAPY

Targeted antimicrobial therapy is selected based on microbiological findings. Fluconazole, itraconazole, and nystatin are commonly used for yeast-associated ABS, while targeted antibiotics are prescribed for bacterial overgrowth according to culture and susceptibility testing[Fig10]. Appropriate drug selection and treatment duration help eradicate ethanol-producing microorganisms while minimizing antimicrobial resistance and preserving beneficial gut microbiota.

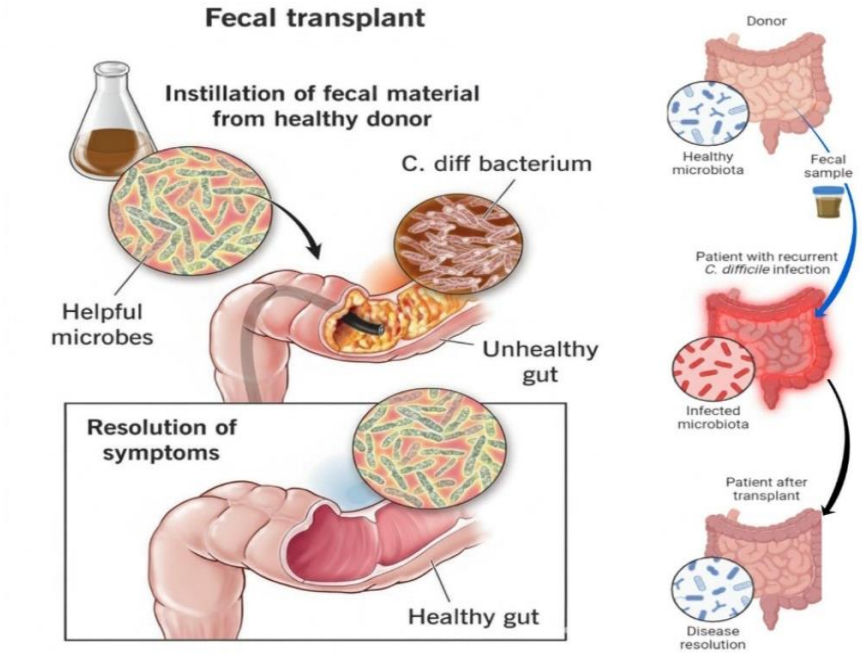

Fig.No.10: Gut microbiota restoration by FMT

FECAL MICROBIOTA TRANSPLANTATION (FMT)

Fecal Microbiota Transplantation (FMT) is a promising option for recurrent or treatment-resistant ABS. By restoring healthy gut microbial diversity[24], FMT has shown successful clinical remission and reduced endogenous ethanol production in reported cases.

MONITORING AND ONG-TERM FOLLOW-UP

Regular follow-up is essential to assess symptom improvement, dietary adherence, medication compliance, and recurrence. Blood and breath ethanol measurements, stool microbiological analysis, and microbiome profiling may be performed when indicated. Patient education regarding diet, medication adherence, and avoidance of unnecessary antibiotic use is important for long-term disease control.

FUTURE PERSPECTIVES

Future research on Auto-Brewery Syndrome (ABS) should focus on understanding gut microbial ethanol metabolism and identifying the microorganisms responsible for excessive endogenous ethanol production. Advanced technologies such as shotgun metagenomic sequencing, meta transcriptomics, metabolomics, proteomics, and microbiome profiling are expected to improve disease diagnosis, identify microbial biomarkers, and support personalized microbiome-based therapies. Promising therapeutic approaches include precision probiotics, prebiotics, symbiotic, engineered beneficial bacteria, bacteriophage therapy, microbial enzyme inhibitors, microbiome-modulating drugs, and Fecal Microbiota Transplantation (FMT)[25]. Future multicenter clinical trials are needed to evaluate their long-term safety, effectiveness, and establish standardized treatment guidelines.

Further studies should investigate the interactions among gut microbiota, dietary carbohydrates, host immunity, and genetic factors to better understand disease susceptibility. Integration of artificial intelligence (AI), precision medicine, and multi-omics technologies is expected to improve early diagnosis, treatment monitoring, and personalized management of Auto-Brewery Syndrome.

CONCLUSION

Auto-Brewery Syndrome (ABS) is a rare but clinically important disorder caused by excessive endogenous ethanol production due to gut microbial dysbiosis. Both ethanol-producing fungi and bacteria contribute to disease development, highlighting the central role of the gut microbiome in its pathogenesis.

Diagnosis requires careful clinical assessment supported by glucose challenge testing, microbiological investigations, molecular diagnostic techniques, and microbiome analysis. Current treatment focuses on dietary carbohydrate restriction, targeted antimicrobial therapy, probiotic supplementation, and restoration of a healthy gut microbiota. Emerging therapies, including precision microbiome modulation, engineered probiotics, bacteriophage therapy, and FMT, offer promising options for long-term disease management.

Future advances in AI, precision medicine, microbiome research, and multi-omics technologies are expected to improve diagnosis, monitoring, and treatment. Large multicenter clinical studies are needed to establish standardized diagnostic criteria and evidence-based treatment guidelines. Continued progress in microbiome science may ultimately lead to safer, more effective, and potentially curative therapies, improving the long-term outcomes and quality of life of patients with Auto-Brewery Syndrome.

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