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Review Article

Microbiology Section

Unravelling the Intricacies of Auto Brewery Syndrome and its Microbial Dynamics: A Narrative Review

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ABSTRACT

Auto Brewery Syndrome (ABS), often referred to as Gut Fermentation Syndrome (GFS), is a sporadic disorder characterised by the internal production of alcohol, leading to symptoms that resemble alcohol intoxication, including vertigo, slurred speech and confusion. The article explores uncommon presentations of ABS, such as an oral version and a new variation in which endogenous fermentation within the urinary system results in the production of ethanol. One of the main causes of ABS is thought to be a fungal dysbiosis of the gut, which occurs due to an overabundance of yeast. The pathophysiology of ABS is associated with the mycobiome, a component of the gut microbiota that ferments certain carbohydrates into ethanol, mimicking food allergies or intolerances. Using a comprehensive search strategy that includes the PubMed, Science Direct and Google Scholar databases, this review investigates ABS with a focus on recent research published in the last 10 years. The involvement of gut bacteria is emphasised, particularly the abnormal development that results in endogenous alcohol synthesis. Microbiological strains associated with ABS, including high alcohol-producing variant of *Klebsiella pneumoniae* (HiAlc KPN) and *Candida albicans*, are examined. The article discusses the challenges associated with diagnosing ABS, including the use of breath analysers, clearance rates and variations in endogenous ethanol production among different ethnic groups. Furthermore, medicolegal issues are addressed, such as the use of ABS as a defence in drunk driving cases. In conclusion, ABS illuminates the intricate relationship between the human body and its microbiota, highlighting the potential consequences of microbial imbalance.

Keywords: Alcohol disease, Gut fermentation syndrome, Microbiology disease, Mycobiome

INTRODUCTION

The ABS is a rare condition in which alcohol is produced internally in the body rather than consumed from external sources. Patients with ABS experience symptoms of alcohol intoxication, which can include gastrointestinal distress, slurred speech, confusion and dizziness [1]. To confirm the diagnosis of ABS, medical professionals may use tests such as a glucose tolerance challenge, measurements of elevated blood alcohol levels, oral ethanol levels, or breath tests indicating the presence of alcohol. While the body naturally produces trace amounts of ethanol during digestion, excessive blood alcohol levels can occur when harmful bacteria or yeast ferment food improperly [2,3].

ABS can affect otherwise healthy individuals; however, it is more commonly observed in patients with underlying health conditions such as diabetes, obesity and Crohn's disease. The condition is thought to originate from a fungal dysbiosis in the gastrointestinal tract that ferments certain carbohydrates into ethanol, potentially mimicking a food allergy or intolerance. Patients with chronic gastrointestinal blockages or slow motility, especially after consuming large carbohydrate meals, may present with elevated breath and blood alcohol concentrations and should be evaluated for ABS [4]. Although there have been reports of ABS and the production of ethyl alcohol by gut bacteria, this condition can now also be identified by alcohol formation in the oral cavity [5-7].

The understanding of ABS dates back several decades, with evidence of humans producing alcohol in their digestive systems recorded as early as 1948. One of the first documented cases involved a five-year-old boy whose stomach ruptured due to autonomous alcohol production, potentially triggered by a large meal of sweet potatoes [5]. Some evidence suggests that the pressure from the sweet potato supper caused the stomach to burst, discharging alcohol into the peritoneum [8]. ABS has been noted in numerous studies, particularly in Japanese literature, where it is referred to as Meitei-sho [4].

Treatment for ABS typically involves antifungal medications and dietary changes, especially after ruling out other potential causes. When these microbes convert carbohydrates into ethanol, endogenous alcohol synthesis occurs, resulting in drunkenness without the consumption of alcohol [9,10]. Long-term antibiotic use, microbial fermentation-promoting diets and gastrointestinal disorders are risk factors for ABS [11]. The metabolism of consumed carbohydrates by the intestinal microflora is the most frequent cause of ABS [12]. This phenomenon is limited to certain high-risk individuals and does not occur in the general population. It has been suggested that patients with Diabetes Mellitus (DM) are more likely to develop ABS [11,12].

Alcohol Dehydrogenase (ADH), the Microsomal Ethanol Oxidising System (MEOS) and hepatic catalase are some of the enzymes that allow the liver of a healthy individual to absorb and process the ethanol produced by commensal flora [13,14]. However, ABS is more likely to develop in individuals with conditions where ethanol metabolism is diminished (such as those receiving long-term antibiotics, liver failure and genetic deficiencies of liver enzymes) or where ethanol production is increased (such as in diabetes, obesity, short bowel syndrome and Crohn's disease) [15]. High blood glucose levels are a hallmark of DM, a metabolic disease. Since glucose serves as a beneficial substrate for these bacteria, it has been hypothesised that individuals with diabetes tend to produce measurable amounts of alcohol even when they do not consume alcohol, due to ABS [16].

While earlier studies have described ABS as a condition, this review is unique in its attempt to discuss the microbial aspect of ABS and its relevance to clinical practice. Recognition of certain microorganisms and their metabolic profiles adds valuable information towards the development of accurate diagnostics and treatment.

REVIEW

Search Methodology

A comprehensive review of English-language publications from the PubMed, ScienceDirect and Google Scholar databases was part of the search strategy, emphasising recent studies on ABS. The inclusion criteria prioritised research that clarified the pathophysiology, aetiology, clinical symptoms and treatment modalities of ABS; studies addressing genetic polymorphisms, gut microbiota, and therapeutic approaches were particularly valued.

The keywords used for the search included terms such as ABS, gut microbiota and ABS, ethanol production in humans, ABS pathophysiology, fermentation syndrome, endogenous ethanol production, ABS diagnosis, therapeutic approaches for ABS, genetic polymorphisms and ABS, ABS clinical symptoms, ABS case studies, ABS and gut health, and fungal overgrowth and ABS. These keywords were applied individually and in various Boolean combinations to refine the search results.

For a thorough overview, systematic reviews were taken into consideration and data were combined to provide insights into the symptoms, diagnosis and therapy of ABS. The focus was on research from the previous 10 years, highlighting new developments and robust scientific methods for understanding ABS.

Role of Gut Microbiota, Candidiasis, and Unusual Manifestations in ABS

GBS or ABS is a very rare condition. Endogenous fermentation triggered by ABS leads to the production of excessive levels of alcohol in the digestive tract. This fermentation is caused by the abnormal development of the gut microbiota, which raises the blood alcohol content in non drinkers [17]. The first documented case involved a man in China with severe Non-Alcoholic Steatohepatitis (NASH) and bacterial ABS, where endogenous alcohol production was significantly linked to strains of a HiAlc KPN [18,19]. Presence of *Candida albicans* in the gastric fluids of the ABS patient indicates a diagnosis of mild oesophageal candidiasis. Doctors should exercise extra caution if a patient has received antibiotic treatment in the past and exhibits signs of alcohol intoxication while denying any use of alcohol. This helps differentiate patients with ABS from those who consume large amounts of alcohol [20].

The fungal microbiota, also referred to as the mycobiome, comprises thousands of different microbes in a person's gut, of which less than 0.1% are considered rare [20]. Fungi are part of this unusual biosphere. However, the pathology of ABS is believed to stem from an overgrowth of yeast in the intestines, known as "fungal-type dysbiosis of the gut," which ferments certain carbohydrates into ethanol and may mimic food allergies or intolerances [19,21]. The main fungal species implicated in ABS is *Saccharomyces cerevisiae*, which is more famously recognised for its fermentation capabilities [19]. In some instances, other fungi have also been associated with opportunistic infections, including *Candida albicans*, *Candida glabrata* and *Candida krusei* [11,19]. Most reports of fungal infections in the medical literature focus on yeast and fungal overgrowth in immune-compromised patients, and many medical professionals are sceptical about the possibility of a normally healthy individual developing serious fungemia [22].

Clinical and Diagnostic Considerations in ABS

Patients with diabetes and liver disease may experience ethanol pseudo-toxicity as a sign of ABS [23]. Patients with liver cirrhosis who abstain from alcohol can maintain stable conditions for remarkably long periods; however, their intestinal motility is often irregular [24]. Endogenous ethanol (EnEth), produced by some individuals with liver cirrhosis, may exacerbate liver damage that has already been caused by alcohol or other substances [25].

Ethnic differences in endogenous ethanol production and clearance rates may be attributed to specific genetic polymorphisms that lead to decreased activity of enzymes involved in the hepatic metabolism of ethanol, resulting in minimal first-pass metabolism [26]. An ABS patient should be admitted to an inpatient facility under strict supervision, with no visiting privileges, to restrict alcohol consumption. Periodic blood alcohol testing must be conducted while the patient is in the facility [22]. The blood alcohol content in individuals with ABS is typically elevated. In ABS, neurological examination results are usually normal, while liver function test scores are likewise elevated. Bacteria responsible for periodontal disease and fungi in the oral cavity can contribute to the development of ABS [11,25].

Insights into Hi-Alc *Klebsiella pneumoniae* of ABS

ABS may develop due to the presence of HiAlc KPN in the gastrointestinal tract, which enables the body to produce ethanol from carbohydrates. Research indicates that this specific strain of *Klebsiella pneumoniae* triggers alcohol intoxication symptoms in individuals who abstain from alcohol consumption. The composition of gut microbiota plays a crucial role in the development of ABS, as the presence of multiple strains of *Klebsiella* can lead to severe NASH.

Diagnosing intoxication becomes challenging since the endogenously produced ethanol from HiAlc KPN mimics the consumption levels seen in alcohol drinkers. Given the microbiological complexity of ABS, various gut microbiota strains contribute to the syndrome, necessitating comprehensive diagnostic investigations. Stool cultures aimed at identifying HiAlc KPN may yield valuable insights, particularly in patients who do not respond to standard treatments for ABS [27]. Additionally, fungal stool cultures may help detect other microbial contributors when antifungal treatments show limited efficacy.

As laboratory errors and undisclosed alcohol consumption can complicate accurate diagnosis, repeated laboratory testing during acute episodes becomes essential. Furthermore, using approved breath analysers at home can facilitate the early detection of ethanol production related to ABS, thereby assisting both patients and clinicians in managing the condition [28,29].

Role of *Candida albicans* in ABS

The two main forms of infections caused by *Candida albicans* are systemic candidiasis and superficial infections. Numerous virulence factors and characteristics, including morphological changes and phenotypic switching, enable *Candida albicans* to infect a variety of host environments. To rapidly produce ATP in an aerobic environment, *Candida albicans* employs glycolysis, followed by alcoholic fermentation or mitochondrial respiration. The mRNA expression of several glycolysis-related enzymes is linked to the initial stage of environmental modifications using two strains: NBRC 1385, a type strain, and LSEM 550, a strain from a patient suffering from ABS [30]. In addition to endogenous ethanol, the GFS in NASH is characterised by triglyceride production from gut yeast species, including *Pichia kudriavzevii*, *Candida albicans* and *Candida glabrata* [29].

Antifungal Strategies in ABS Treatment

ABS is caused by yeast and its treatment requires appropriate antifungal medication. To address potential azole-resistant *Candida albicans* in ABS, intravenous micafungin may be employed [28]. Following treatment with micafungin, *Escherichia coli* and *Enterococcus faecalis* tend to proliferate in the gastrointestinal tract instead of *Candida albicans*. The syndrome is primarily managed with medications such as fluconazole and nystatin, alongside a strict diet low in sugar, carbohydrates and alcohol. Micafungin can also be used to treat ABS. If a patient has been diagnosed with ABS, physicians should recommend the most suitable dietary plan. A follow-up appointment is necessary to monitor yeast levels

regularly, even if ABS has been treated and the symptoms have resolved [30].

CONCLUSION(S)

The ABS is a complex medical condition in which the natural fermentation process of the digestive tract produces a significant amount of alcohol. The delicate relationship between the microbiome and human health is underscored by the involvement of gut microbiota, fungal dysbiosis and specific microbial strains such as HiAlc KPN and *Candida albicans*. This review aimed to discuss the microbial aspects of ABS and their relevance to clinical practice. Recognition of certain microorganisms and their metabolic profiles provides valuable information for the development of accurate diagnostics and treatment. Further studies could lead to improved treatment options and offer insights into the intricate relationship between the human body and its microbiota, potentially yielding broader implications for gastrointestinal health.

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