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Case–Control Research Study of Auto-Brewery Syndrome

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Abstract

Background: Auto-brewery syndrome (ABS), also known as Gut Fermentation Syndrome and Endogenous Ethanol Fermentation, is afflicting people worldwide, but little is known about ABS patients' demographics, health history, lifestyle factors, and diet.

Method: We conducted a broad-based case–control survey study on 52 patients known to have a diagnosis of ABS and their household members. The research compares the symptomatic group (N = 28) to the asymptomatic group (N = 18) regarding lifestyle and health, diet, and medical history.

Results: With a response rate of 88% and using rank-sum tests, the data demonstrate that patients with ABS have significant differences compared to people without ABS in lower quality bowel movements ($P = .048$), more frequent bowel movements ($P = .038$), more reports of malodorous breath ($P = .0001$), and self-classify as having poorer health ($P = .009$). Furthermore, participants with ABS consume more water ($P = .038$), consume less tea and coffee ($P = .033$), eat fewer dairy products ($P = .0185$), eat less candy ($P = .032$), eat out less and rely on food prepared at home ($P = .043$), have more aversion to starch ($P = .008$), and have more food sensitivities ($P = .043$) than the group without ABS. The ABS group also reports more diarrhea ($P = .048$), higher amounts of yeast in their gastrointestinal tract ($P = .015$), and using acne medication for a longer time ($P = .037$) than the control group.

Conclusion: Patients with ABS have significant differences in their lifestyle and health, diet, and medical history compared to non-ABS participants and these differences warrant further research.

Keywords

auto-brewery syndrome, gut fermentation, alcohol, yeast overgrowth, research, endogenous ethanol

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Introduction and Review of Literature

Auto-brewery syndrome (ABS), also known as Gut Fermentation Syndrome and Endogenous Ethanol Fermentation, has long been recognized in the literature. The earliest cases were reported in Japan in the 1950s to 1970s[1–3] and continue to be documented, researched, and reported into the current century not only in Japan but also in Great Britain,[4–6] Egypt,[7] and the United States.[8,9] In 2016, authors from the Mayo Clinic stated "… auto-brewery may be considered in a patient with chronic obstruction or hypomotility presenting with elevated serum ethanol levels in the setting of high carbohydrate intake."[10] Despite the many articles describing the syndrome, relatively little is known about the underlying mechanisms, let alone the cause.

We know the microbiome plays a large role in health and illness. When the microbiome is disturbed, for example, through diet, immune dysfunction and disease processes can result such as nonalcoholic fatty liver

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disease and cardiovascular disease.[11] The gut microbiome has been implicated in metabolic disease,[12] inflammatory bowel disease,[13–16] and obesity.[17]

The human microbiome has been studied extensively for many years now, but science is just beginning to understand the fungal microbiota known as the mycobiome.[18] Of the thousands of different microbes in an individual's gut, an estimate of less than 0.1% is considered rare, and fungi belong to this "rare biosphere."[19] Most of the reports of fungal infections in the medical literature focus on yeast and fungal overgrowth when the patient is immune-compromised, and many medical professionals dismiss the idea that an otherwise healthy individual could develop a serious fungemia; however, the pathology of ABS is believed to be an overgrowth of yeast in the intestines known as "fungal-type dysbiosis of the gut" that ferments some carbohydrates into ethanol and may mimic food allergy or intolerance.[20]

ABS certainly seems to be more prevalent in patients with comorbidities such as Crohn disease,[10] short bowel syndrome,[21] and obesity-related liver disease,[22] but there is a growing contingent of patients suffering with otherwise unexplained intoxication. People suffering from ABS universally have a demonstrated overgrowth of intestinal yeast and often have signs of yeast infections in other systems (integumentary, nail beds, etc.), but the actual causes and treatments are poorly understood. Some patients respond to dietary changes alone, while others require antifungal medication, dietary changes, supplements, lifestyle modifications (sufficient sleep, decreasing stress, nonexcessive exercising), and/or probiotics, while a small minority of patients do not seem to respond to any of the mentioned treatments.[9]

The purpose of the current research project is to identify the health history and lifestyle factors of subjects diagnosed and/or experiencing symptoms of ABS and to compare those factors in subjects of 2 control groups without symptoms of ABS. The control group is composed of people without symptoms of ABS who are living with someone who has symptoms of ABS.

Methods

Survey

A 78-item survey titled the *Gut Fermentation Survey* (*GFS*) was developed using questions from the American Gut Project[23] as well as questions from other well-known survey sources which offered validity and reliability for the questions. The American Gut Project is a crowd-funded science project to compare the gut microbiomes of average American citizens with other groups from the United States and around the world. As part of the project, an extensive diet and lifestyle questionnaire related to the gut microbiome is administered. We used their questions except where noted otherwise. Anyone wishing to obtain a complete copy of our questionnaire and methods may contact the corresponding author.

Questions 1 to 8 are demographic questions patterned after the Integrated Postsecondary Education Data System from the National Center for Education Statistics of the Department of Education.[24]

Questions 9 to 11 ask about diagnosis and symptoms of ABS and serve to divide the group of respondents into the ABS group (those with diagnosis and/or symptoms) and the control group (those without symptoms).

Questions 12 to 37 query Lifestyle and Health factors such as living arrangements, dental care, tobacco use, bowel habits, sleep habits, and pets. The tobacco questions come from the World Health Organization,[25] bowel habit questions from the American Gut Project,[23] and the sleep questions from the Mini-Sleep Questionnaire.[26]

Questions 38 to 55 ask about General Diet Information such as type of diet followed, amount and type of liquids consumed, alcohol consumption, and food allergies. The dietary questions were taken from the American Gut Project[23] except for the questions on alcohol use which came from the National Institute on Alcohol Abuse and Alcoholism.[27]

Questions 56 to 72 concern the individual's Health History such as method of birth, whether the subject was breast-fed or given formula and how long, past surgeries, medical conditions past and present, as well as nonfood allergies. The questions on breastfeeding came from the survey methods of breastfeeding from the Centers for Disease Control and Prevention.[28]

Questions 73 to 77 regarded medications and supplements being taken, and question 78 asks if the respondent would be willing to be contacted concerning future research opportunities.

Study Design

A case–control study was chosen as the method to identify factors which individuals with symptoms of ABS might have in higher frequency than those without ABS. Our study was approved by the Institutional Review Board at Panola College in Carthage, TX.

Subjects

We offered the GFS survey to 52 patients known to the authors to have a diagnosis of ABS and their significant others in the household. Potential participants were initially contacted via e-mail and offered a $25 gift card as an incentive to complete the survey. After 30 days, those who had not responded were again contacted by e-mail and encouraged to participate. Forty-six of the people

contacted digitally accepted the informed consent document and completed the survey. Of the 46 respondents, 28 had a history of ABS and the other 18 respondents formed the control group.

Statistical Analysis

The study compared the GFS responses of people that have a history of ABS (N = 28) to the responses of those without diagnosis or symptom history (N = 18). For survey questions that facilitate a comparison between the symptom and control group, *2 by c* contingency tables were created to tabulate question responses and test for row homogeneity using a permutation chi-square test where the data were categorical. All such permutation chi-square tests were calculated using *StatXact* by Cytel in Cambridge, MA. Additional permutation *Kruskal–Wallis* tests reduced to rank-sum tests (also known as *Mann–Whitney Wilcoxon rank-sum tests*) were used to analyze row homogeneity between symptom and control groups in the cases where survey questions generate ordinal responses.

Results

Demographics

The demographics of the 46 participants are detailed in Table 1. Of the 46 participants, 28 were in the ABS group and 18 were in the non-ABS group. All participants were older than 18 years as verified in the informed consent. Of the 28 participants who had ABS, 16 were male and 12 were female. The majority were born in the United States (26), 1 was born in South America, and 1 in Europe. In the group of 18 non-ABS, 14 were female and 4 were male with the majority born in the United States (16), 1 in Ethiopia, and 1 in Europe.

Nearly all the participants have spent most of their lives in the United States with 1 in the ABS group living most of their life in Europe and 1 in the non-ABS group living most of their life in Ethiopia.

One person in the ABS group identified as American Indian or Alaskan Native with the remainder identifying as White; in the non-ABS group, 14 people identified as White, 1 as American Indian or Alaskan Native, 1 as Black or African American, and 2 as Asian.

Of the 28 ABS participants, 3 identified as Hispanic or Latino, 1 did not answer, and the remaining 24 selected Not Hispanic or Latino. In the non-ABS group, 1 did not answer, and the remaining 17 selected Not Hispanic or Latino.

Lifestyle and Health

The differences found in this section of the survey pertain uniquely to bowel movement frequency and quality. The P values for these 2 questions are each .04 with patients in the ABS group reporting a higher frequency and lower quality of bowel movements than the control group. Also, those with ABS history are frequently told their breath is odorous ($P = .0001$) and self-classify as having poorer overall health than their peers in the control group ($P = .009$).

General Diet Information

Here, the ABS patients consume more water ($P = .038$) and less tea and coffee ($P = .033$) than the control group and eat dairy products and candy at a lesser rate than the control group ($P = .018$ and .032, respectively). Those with a history of ABS tend to eat out less and rely more on food prepared at home ($P = .043$) and have an aversion to starch ($P = .0008$).

Table 1. Demographics of Respondents.

Group	ABS (N = 28)	Non-ABS (N = 18)
Sex	F = 12; M = 16	F = 14; M = 4
Continent where born	1 = South America	1 = Ethiopia
	1 = Europe	1 = Europe
	26 = United States	16 = United States
Continent where lived most of life	1 = Europe	1 = Ethiopia
	27 = United States	17 = United States
Race	1 = American Indian or Alaskan Native	1 = American Indian or Alaskan Native
	27 = White	1 = Black or African American
		2 = Asian
		14 = White
Ethnicity	3 = Hispanic or Latino	1 = Did not answer
	1 = Did not answer	17 = Not Hispanic or Latino
	24 = Not Hispanic or Latino	

Abbreviation: ABS, auto-brewery syndrome.

Health History

Finally, the "Health History" section of the survey revealed those with ABS symptoms experience food sensitivities at a higher rate than those in the control group ($P = .043$), diarrhea at a higher rate ($P = .016$), and yeast in their gastrointestinal (GI) tract at a higher rate ($P = .015$). Regarding medications, patients experiencing symptoms of ABS who need acne medication use it for a longer period than control group peers needing such medication ($P = .03$).

The results of the questions showing differences between the ABS group and the control group, for lifestyle and health, general diet information, and health history are detailed in Table 2.

Discussion

Our study group (N = 28) consisted predominantly of white, non-Hispanic males born in the United States. This is similar to other recent case studies of people with ABS[8–10,21] with the exception of the older case studies written in Japan[1–3] where the subjects were presumably of Japanese descent even though it was not specified. In 1998, a survey of 25 patients with fungal-type dysbiosis of the gut was conducted in London, England, that included 19 females and 6 males but did not identify race or ethnicity[20] and only looked at yeast infections, not fermentation. Although most of the people with ABS who have contacted us are males, it may be that female caregivers are more willing to reach out for help and information.

We discovered that people with symptoms of ABS have lower quality and more frequent bowel movements described as diarrhea than the control group. No other research studies of people with ABS were found that looked at bowel function although several case studies of ABS described accompanying GI symptoms such as diarrhea, bloating, abdominal discomfort, nausea, and vomiting.[3,9,10,20]

The strongest finding in our study is that the breath of ABS sufferers is reported as malodorous more often than the control group. A previous study that compared ethanol producers and nonproducers demonstrated no significant differences in lactulose breath hydrogen;[29] however, at least 1 case study of ABS reports odor of alcohol on the breath.[3] Other ABS case studies report negative breath tests during a GI workup,[8,9] but the workups were not conducted while the patients were actively fermenting.

Anecdotally, family members report the smell, not as alcohol, but as somewhat fruity and foul. Others relate a smell more like a "hangover breath" than intoxication and several describe the smell as being similar to but different from diabetic ketoacidosis breath. Several breath studies have been conducted for irritable bowel syndrome and small intestinal bacterial overgrowth

Table 2. Lifestyle, Diet, and Health History Survey Questions With Significant Differences in Data.

Question No.	Shortened Question	*P*	Interpretation
31	Bowel movement per day	.0378	Those with GFS symptoms have more frequent bowel movements.
32	Bowel quality	.0477	Those with GFS symptoms have more frequent diarrhea.
34	Breath odor	<.0001	Those with GFS symptoms have people state they have breath odor at a far greater rate than those without symptoms.
37	Rate your health	.0090	Those with GFS symptoms rate themselves in worse health at a greater rate than those without symptoms.
39	Water consumption	.0380	Those with GFS symptoms consume 64+ ounces of water per day at a higher rate.
45	Tea/Coffee	.0334	Those with GFS symptoms consume tea/coffee at a less rate.
50	Dairy	.0185	Those with GFS symptoms tend to eat dairy products at a less rate than those without symptoms.
52	Starch	.0008	Those with GFS symptoms tend to eat starch at much less rate than those without symptoms.
53	Eat out	.0432	Those with GFS symptoms eat food prepared away from home at a less rate.
54	Eat candy	.0321	Those with GFS symptoms eat chocolate and candy at a less rate.
69	Food sensitivity	.0433	Those with GFS symptoms have been tested and removed offending foods at a higher rate.
70a	Yeast in GI tract	.0153	Those with GFS symptoms have had intestinal fungal overgrowth at a higher rate than those without symptoms.
74	How long medications for acne	.0373	Those with GFS symptoms who need medication for acne have taken it longer.

Abbreviations: GFS, Gut Fermentation Survey; GI, gastrointestinal.

(SIBO) that agree there are changes in breath for lactose, lactulose, fructose, and so on.[30,31]

The data revealed the overall health of sufferers is poorer than the control group ($P = .009$). This is similar to Eaton's study of 30 patients with ABS who were found to have poorer health as measured by deficiency of B vitamins, zinc, and magnesium.[5] Additional research points to concomitant health issues to ABS such as chronic fatigue syndrome, eczema, and chronic vaginal yeast infection.[2,5] Other studies support that gut dysbiosis, which may be an underlying cause of ABS, is implicated in inflammatory bowel disorders such as Irritable Bowel Syndrome (IBS) and Crohn's disease.[13,14,32] Case studies point to ABS as a development from an underlying disorder such as short bowel syndrome or Crohn's disease.[10,21,33]

Another related question on the research GFS asked the respondents to check all GI illnesses they had from a list of 18 illnesses, such as Celiac disease, Diverticular disease, SIBO, and Acid Reflux, and 24 of the 28 symptomatic respondents checked at least 1 illness while only 11 of the 18 in the control group checked at least 1. Although not statistically significant, this borderline significance warrants a closer look. Even more interesting, is the information that of the 24 symptomatic respondents who checked at least 1 GI illness, 16 checked 2, 10 checked 3, 8 checked 4, 6 checked 5, and 3 checked 6. These data taken together with the "overall health" question beg for additional research with a larger group of patients and a longer list of illnesses. There may be strong connections between GI, other illnesses and ABS that have not yet been identified.

The significant differences demonstrated in the General Diet Information section are interesting in that we found people with ABS consume more water, less tea and coffee, and fewer dairy products and candy than the control group. Other studies have shown that people with ABS tend to crave sugar and carbohydrates and have reported "binging" on sugary foods.[4,5] These same studies in addition to the case studies of ABS all recommend low carbohydrate or low glycemic index diets during treatment. Our data may reflect the attempt to control symptoms of ABS once becoming aware of dietary triggers. In conversations with ABS patients, many of them report a history of high-carbohydrate, high-sugar diets but then drastically changing their diets to low-carb once they became aware their symptoms are diet-related.

The same could be said of our findings that those with a history of ABS tend to eat out less and rely more on food prepared at home and avoid eating starchy foods than the control group. Other studies of ABS, gut dysbiosis, and IBS support the importance of diet in controlling symptoms.[8,9,34,35]

The most interesting section of the survey data is the Health History section that reveals those with ABS experience food sensitivities at a higher rate than the control group. Our data correlate with other studies demonstrating links between ABS and food sensitivities, IBS with food sensitivities, and intestinal permeability with food sensitivities and depression.[4,36,37]

This section also found that patients with ABS were diagnosed with higher than normal yeast in their GI tract. This correlates with many other research studies that verify patients with ABS have yeast overgrowth in various parts of their GI system.[2,3,8–10,21]

Lastly, we found the ABS group had a longer use of antibiotics for acne than those in the control group ($P = .03$). The theory of a gut dysbiosis severe enough to cause intoxication has long rested on the fact that antibiotics are known to disturb the gut microbiota. Although other research has not specifically reported on long-term antibiotic use for acne, numerous other reports support the fact that antibiotic use disturbs the GI system and can lead to yeast overgrowth.[38,39]

Limitations

There are several limitations to our study. First, we used a convenience sample of patients that the coauthors knew had ABS and their family members. Second, many of the survey questions are subjective and are thus at risk of being answered inaccurately. Third, it was a seemingly small sample size but considering how rare ABS is, we felt fortunate to have as many participants as we did. However, because our analysis contained patients from 4 continents and our response rate was 88%, our results can be generalized to the growing field of ABS.

Conclusion and Recommendations

ABS is affecting people worldwide. Very little is known about the lifestyle, health, diet, and medical history of ABS patients. Using a nationwide survey of ABS and non-ABS patients, our research showed statistically significant differences in 14 questions between ABS and non-ABS patients, which we believe are important elements for future research in ABS. The findings in this case–control study give insights into common factors experienced by people with ABS.

Declaration of Conflicting Interests

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