Review Article

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Halitosis as a key diagnostic factor to systemic diseases in the primary care

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ABSTRACT

Halitosis might be associated with reduced quality of life for the affected patients as a result of the personal and social embarrassments it might cause. The adequate identification and diagnosis of the underlying condition causing halitosis are important to achieve adequate treatment and prevention of many systemic diseases or even neoplasms. In this literature review study, we have discussed the potential role of halitosis in the diagnosis and identification of systemic diseases. We have discussed many diseases as diseases related to the gastrointestinal tract and liver, others related to metabolic and endocrinal disorders. Furthermore, psychological factors might attribute to pseudo-halitosis, while true halitosis comes secondary to oral and extraoral factors and physiological conditions. Poor oral hygiene might be the only reason for oral malodor, while many oral conditions might also contribute to the development of halitosis. Additionally, some conditions might have a characteristic bad smell, which might significantly enhance the diagnostic value and help clinicians. However, further examination and evaluation should also be conducted to prevent a potential overlap between the different conditions. On the other hand, some extra-oral disorders do not have a characteristic oral smell, which indicates that halitosis alone cannot adequately establish a proper diagnosis. Therefore, raising awareness about seeking medical attention when suffering from halitosis is recommended to achieve better outcomes and help clinicians draw efficacious prevention programs.

Keywords: Halitosis, Family medicine, Systemic diseases, Diagnosis

INTRODUCTION

The definition of halitosis can be summarized as badsmelling oral breath that is attributed to many causes, with an estimated prevalence rate of 31.8-65% globally.¹⁻³ Many synonyms for the disease have been reported, including fetor ex-ore, fetor oris, oral malodor, in addition to bad breath.⁴ It was also demonstrated that bad taste and halitosis are usually accompanied.⁵ Moreover, Systemic, oral, and psychological disorders might attribute to the

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development of halitosis, and accordingly, the condition can be classified into genuine halitosis, pseudohalitosis, or halitophobia. 6-8 Moreover, genuine halitosis has been furtherly classified into pathological and psychological, while pathological might include oral and extraoral conditions.

Furthermore, halitosis might be associated with reduced quality of life for the affected patients as a result of the personal and social embarrassments it might cause. Accordingly, estimates show that halitosis is a primary reason for a dental visit according to many patients. 9,10 Moreover, it should be noted that the rate of halitosis is underreported and is hugely variant among the different populations, and according to the different demographics. Although the condition might not necessarily persist for a long duration, it still has a strong impact on the affected patients. Psychological factors might attribute to pseudohalitosis, while true halitosis comes secondary to oral and extraoral factors and physiological conditions. 11 Poor oral hygiene might be the only reason for oral malodor, while many oral conditions might also contribute to the development of halitosis.

The adequate identification and diagnosis of the underlying condition causing halitosis are important to achieve adequate treatment and prevention of many systemic diseases or even neoplasms. Besides, the severity of malodor and halitosis might be significantly impacted by the psychological status of the affected patient, and the patient's psychological status might be also adversely

impacted by this condition, which indicates the importance of the proper identification and management of the underlying etiology. ^{10,12,13} In this study, we aim to discuss the role of halitosis in the diagnosis and identification of systemic diseases in primary care, according to evidence from the relevant studies in the literature.

METHODS

We performed an extensive literature search of the Medline, Cochrane, and EMBASE databases which was performed in August 2021 using the medical subject headings (MeSH) or a combination of all possible related terms. ^{14,15}

This was followed by the manual search for papers in Google Scholar while the reference lists of the initially included papers. 16,17

Papers discussing the role of halitosis in the diagnosis and identification of systemic diseases were screened for relevant information, with no limitation on date, language, age of participants, or publication type.

DISCUSSION

Clinicians should monitor and adequately evaluate the presence of halitosis, and if psychogenic halitosis was the condition, clinicians should try reassurance and psychiatric evaluation. 18,19

DISEASES	CHARACTERISTIC ODOR
Diabetes mellitus or impending Diabetic coma	Acetone, fruity (not detected in well controlled patients)
Liver failure (terminal stage)	Sweetish musty, feculent "amine" odour resembling a fresh cadaver known as "fetor hepaticus
Portocaval venous anastomoses	Same as fetor hepatic us but characteristically intermittent in nature for long period of time
Lung abscess, tuberculosis, bronchiectasis	Foul, putrefactive
Blood dyscrasias	Resembling decomposed blood of a healing surgical extraction wound
Liver cirrhosis	Resembling decayed blood
Uremia, kidney failure	Ammonia or urine
Toxemia, G.I. disorder, neuro psychiatric	Varies: poor oral hygiene intensifies the odour.
Fever, dehydration, Macroglobulinemia (with salivary gland involvement).	Odor mainly due to Xerostomia with poor oral hygiene and / or toxic waste byproducts accumulated in the body.
Syphilis, exanthematous disease, granuloma venereum	Fetid
Wegeners granulomatosis	Necrotic, putrefactive

Figure 1: Systemic causes and characteristics of halitosis.²⁰

A differential diagnosis would help them establish the underlying condition and etiology of halitosis, and investigating the etiology systematically would aim much

to the diagnostic approaches. Looking for other related signs as gingivitis, coated tongue, periodontal diseases, gingival bleeding, chronic ulcers, xerostomia, and dental caries might also help to establish a proper diagnosis of the cause of halitosis. Personal and medication history is also important because some dietary habits and medications can cause dry mouth and induce halitosis. Referral to specialists as ENT, endocrine and internal medicine specialists, and dentists might also be required in some cases for adequate evaluation. In this section, we will discuss the different systemic diseases that might be associated with halitosis according to the different studies in the literature based on the different systems and organs of the human body. Identifying the specific characteristics of halitosis with each systemic disease might help to establish and properly monitor these diseases. In Figure 1, the systemic causes and characteristics of halitosis are briefly presented.

Blood-borne halitosis

This is a rate cause of halitosis. However, it has been suggested by previously published studies. It has been suggested that the bad odor of the breath can be attributable to the presence of volatiles or exhaled substances within the patient's breath that has been transported to the lungs from the circulating blood secondary to their absorption of development from different diseases and other sources within the body. 21 Furthermore, dimethyl sulfide has been reported to be the main cause of blood-borne halitosis, according to a previous investigation by Tangerman et al²² In the same context, it was also reported that hydrogen sulfide and methyl mercaptan are more frequently associated with the presence of intra-oral causes of halitosis. Besides, the presence of allyl methyl sulfide metabolic products might also be significantly associated with halitosis because these substances are usually present in onions (which is allium derivative) and garlic, and therefore, the frequent administration of these products is associated with the breath odor and status.²³ Many causes of blood-borne halitosis can be explained because the etiology is not confined to a certain disease but to multiple etiologies that can transmit their pathological features to and through the blood.

Therefore, some of the reported diseases might include diabetes mellitus, cirrhosis, kidney diseases, hepatic impairment, and diabetic acidosis. Iatrogenic and food-related causes might also attribute to a temporary status of blood-borne halitosis, however, evidence is not sufficient and further investigations might be needed.

Gastrointestinal and hepatic diseases

Halitosis is a common condition among various gastrointestinal diseases, including gastro-intestinal reflux disease, inflammatory bowel disease, Helicobacter pylori (*H. pylori*) infection, gastritis, and Zenker's diverticulum. However, the prevalence of halitosis among these patients seems to be relatively lower than in the past. However, adequate monitoring and management should still be approached to enhance the outcomes and alleviate the quality of life for the affected patients. Normally, gases

coming up from the gastrointestinal tract (GIT) and the process of digestion do not combine with the exhaled air. Therefore, healthy individuals do not suffer from halitosis. On the other hand, when suffering from GIT-related symptoms like eructation, vomiting, and reflux, it would be easy for these gases to escape from the stomach and mix with the patient's breath. In patients suffering from chronic gastrointestinal reflux disease, halitosis becomes a common condition in these patients as a result of the potentially induced injury to the larynx, pharynx, and tongue root, particularly in patients suffering from a coated tongue. Furthermore, larvngopharvngeal reflux disease was also previously reported to cause halitosis. Accordingly, these conditions should be considered for monitoring these diseases and should be adequately treated with specific approaches. H. pylori is an organism that can cause serious ulcerative and inflammatory conditions to the gastric mucosa, and induce serious damage to the underlying tissues. Despite not being a saprophyte colonizer, H. pylori can still be detected within the oral cavity, which can be a suitable reservoir for these organisms.²⁴ Previous research has also suggested that as a result of such events, recurrence of infection to the gastric mucosa might also develop. Therefore, it has also been suggested that halitosis might develop as a result.²⁵ A previous investigation by Adler et al indicated the association between the presence of halitosis, burning sensations, and hyperplasia of the dorsum root of the tongue and H. pylori infection.²⁶ Therefore, adequate control and management of the oral presentation of these bacteria are essential to achieve better interventions. Another investigation by Serin et al also reported that eradication of H. pylori infection significantly eliminated halitosis in patients that suffered from adequately managed non-ulcer dyspepsia.²⁷ Besides, the authors also estimated that the incidence of halitosis was lower among patients with eradicated *H. pylori* infections than patients suffering from persistence. This indicates the importance of adequately treating *H. pylori*, which plays a significant role in enhancing the patient's breath. This was furtherly indicated by Katsinelos et al that reported that most of their patients suffering from functional dyspepsia-induced halitosis with *H. pylori* infections were adequately treated for these symptoms on a long-term basis.²⁸ These findings were also indicated by previous investigations. 29-33 Accordingly, halitosis is significantly associated with H. pylori infection, and the latter should be adequately diagnosed and managed to enhance the outcomes.

It is well-known that hepatic diseases, particularly liver cirrhosis, are usually associated with fetor hepaticus, which is characterized by a mousy, must, or a slightly fecal odor. Besides, a significant smell of sulfur might also be a characteristic because sulfur-containing malodorant compounds are usually present and accumulated in such diseases. As previously discussed, these compounds are usually transmitted through the bloodstream to the lungs where they are exhaled and excreted through this organ.²¹ In patients suffering from cirrhosis, it has been found that dimethyl sulfide, among other groups of sulfide, is the

major contributor to halitosis in these patients. The abundance of the volatile sulfur compounds might also be attributable to other causes as the potential intraoral breakdown of dietary amino acids by oral anaerobic bacteria leading to increased production of sulfur, a process that might also produce a bad oral smell. However, it has been reported that liver diseases are associated with certain amino acids like butyric acid, organic acids, isovaleric acid, and isobutyric acid.³⁴ In the same context, patients with liver disease might also suffer from other characteristic bad body odors. This has been indicated in a previous investigation by Mitchell et al that reported that patients suffering from different liver diseases have been observed with "fish-odor syndrome". 35 Besides, it has been observed that urinary trimethylamine levels were significantly elevated in these patients.

Metabolic, endocrinal, and otolaryngeology disorders

Many metabolic and endocrinal diseases have been linked with halitosis. For instance, fruity or sweet breath is a common condition among patients with diabetes mellitus, especially when suffering from diabetic ketoacidosis. This happens as a result of the accumulation and transmission of ketone bodies to and through the blood (including βhydroxybutyrate, acetoacetate, and acetone) until they are excreted through the lungs. 36-38 Acetone and acetoacetate, which result from the metabolism of lipids by peroxidation or lipolysis through acetyl-CoA decarboxylation, are the reasons for the fruity breath in these patients and are the most common volatile compounds that are being observed in the breaths of patients with diabetes. Moreover, 2butanone and 2-pentanone can also be detected, despite being less common.³⁹ Fish-odor syndrome is a major characteristic of trimethylaminuria which usually occurs as a result of the increased accumulation of the tertiary aliphatic amines that are derived from dietary products in the patient's expired air, sweat, urine, and other body secretions. The accumulation of trimethylamines has a characteristics pungent ammoniac odor that is close to rotten fish. This odor is usually a characteristic of the affected patients, which might impact the social, personal, and working lives of the corresponding patients. 40-43 Trimethylaminuria might also result secondary to other diseases as hepatic disorders, which might interfere with the proper routes of metabolism of this amino acid (due to the presence of portosystemic shunts or hepatocellular dysfunctions). Accordingly, associated fetor hepaticus might also be present in these patients, who might also suffer from an increased risk of developing coma and hepatic encephalopathy. 35,44,45

Upper GIT and respiratory tract-related inflammation, infections, and malignancies might attribute to the development of halitosis. For instance, previous studies have demonstrated that the accumulation of abnormal debris within the tonsillar crypts, which is called tonsilloliths as a result of these calcified structures, is associated with halitosis, especially when they are found to be crushed and damaged. Furthermore, tonsilitis,

pharyngeal ulcerations, bronchitis, post-tonsillectomy eschar, bronchiectasis, pneumonia, and tuberculosis are also linked with the development of halitosis. 46,49 Nasal and paranasal sinuses-related infections usually interfere with the functions of the respiratory epithelium, leading to stagnation of secretions and bacterial overgrowth. Nocturnal mouth breathing which might result from anatomical variances or inflammation-induced nasal obstruction might be associated with the development of morning halitosis as a result of during of the oral mucosa and bacterial overgrowth at night. 50

CONCLUSION

Some conditions might have a characteristic bad smell, which might significantly enhance the diagnostic value and help clinicians. However, further examination and evaluation should also be conducted to prevent a potential overlap between the different conditions. On the other hand, some extra-oral disorders do not have a characteristic oral smell, which indicates that halitosis alone cannot adequately establish a proper diagnosis. Therefore, raising awareness about seeking medical attention when suffering from halitosis is recommended to achieve better outcomes and help clinicians draw efficacious prevention programs.

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