



Burning Mouth Syndrome in an Iraqi Sample of Patients: a preliminary study of 52 Cases

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Abstract

Evaluation of the clinical characteristics of burning mouth syndrome in a sample of Iraqi patients referred to a large teaching dental clinic in Baghdad.

Fifty two patients with burning mouth syndrome were followed up through a prospective study ,investigating the clinical characteristics of using pre- established criteria's and tests for each feature .

Forty four women and 8 men with burning mouth syndrome ranging in age from 46 – 72 years. Their cause of attendance was disturbed sleep (46.1%), fear of serious disease (44.2%) and anxiety (36.5%). The pain duration since it started ranged from 3 – 48 months (Mean 18.17 ± 12.78) months.

Twenty six patients (50%) reported precipitating event and 32 (61.9%) reported a change in taste sensation of which (56.25%) had a bitter taste. VAS pain levels were (6.13 ± 0.02 for females and 6 ± 0.91 for males). 25% of the patients had medical comorbidities that were under control.

The location of pain was mostly on the tongue (76.9%) and mainly on its margins (57.7%) unilaterally. And only 25% of the patients had subjective xerostomia with stimulated parotid salivary flow rate less than 0.5 ml/ min.

Estradiol levels among females were (68.18%) below 15 pg/ml and (31.72%) above that in spite of 75% of them were post-menopause. And these patients were subject to stress ranging from 35-146 (L. c. u's) with a mean of 2.73 ± 1.28 events per patient and about 7.69% of them had one severe stress accident .

The classification of psychiatric comorbidities occurring among the patients sample were (17.3% = free), (40.38% = Depressive neurosis) and (20.08% = Anxiety neurosis) and none of the patients reached the level of psychosis.

Burning mouth syndrome is possibly of high prevalence and with high range of etiologies that should be more investigated including its relation with psychological stress and neurosis.

Key words: BMS = burning mouth syndrome, Lcu = Life change unit, HIV = human immunodeficiency virus, VAS = visual analogue scale, PBI = protein bound iodine, T₃=Triiodothyronine, MRI = magnetic resonance imaging.

Introduction

Since the development of the concept of evidence – based dentistry and the specialty of dental prevention have been centered in the middle of the dental and oral treatment philosophy to

include evaluating treatments in different branches such as periodontology, oral surgery, oral medicine and endodontics in addition to dental and maxillo – facial trauma.

This evidence that a particular treatment is an improvement to previously accepted treatments was best shown by systematic reviews, prospective clinical studies and randomized controlled trials.

As a result efforts are made to identify best practice, avoid unnecessary treatments, provide the most appropriate care and reduce the need for further intervention.⁽¹⁾

Historically B.M.S. was evolved as a distinct clinical entity^(2,3,4,5,6) and has been reported worldwide and also named as glossopyrosis⁽⁷⁾, glossodynia⁽³⁾ and oral dysaesthesia⁽⁴⁾.

The increased incidence of B.M.S. in women after menopause and due to high female / male ratio has led the investigators to suspect a relationship between the two conditions^(8, 5, 6). But lately some researchers claim little evidence that women having the condition have more hormonal abnormalities than matched controls who are free of the condition^(9,10,11,12) but others still believe that this relation exists^(13,17,15,16,14,18).

So burning mouth syndrome can be defined as a distinctive nosological entity characterized by unremitting oral burning or similar pain in the absence of detectable mucosal changes⁽¹⁹⁾.

It is also referred as a burning, painful intraoral condition with no observable mucosal lesions⁽²⁰⁾.

The epidemiology of burning mouth syndrome reaches up to five persons per 100000 populations⁽¹²⁾ and according to recent studies, it affect 3.7% of the population^(21, 22). And its prevalence has been published in epidemiological studies in different countries and cultures, for example in the United States 0.7% of the population is estimated to suffer this illness while it's prevalence in Europe is higher reaching to 7% of the population⁽²³⁾.

Around 1-3% of the adult populations in the developed countries are affected⁽²⁴⁾.

It comprised 4.5% of all patients with orofacial pain attending oro-facial pain clinic in Brazil⁽¹⁶⁾. But some epidemiological studies have estimated it's prevalence to be between 2.6% - 5.1% and its rate of occurrence in men is less by 20% than women i.e. 1:5 ratio^(5, 25, 26) while in some studies this ratio reached 1:7⁽²⁷⁾.

Recently, there has been a tendency to separate B.M.S. into two groups: primary, or essential / Idiopathic or secondary, where the symptoms result from local / systemic pathological conditions⁽²⁸⁾, but despite this there is no consensus on the most appropriate criteria for classifying B.M.S., nor there is an acceptable definition of the condition, especially it is considered as a form of neuropathic pain⁽¹⁶⁾.

There is no precipitating cause in over 50% of the patients while others local and systemic factors are identified⁽¹²⁾ including:

- a) Foods and additives – like chestnuts, cinnamon, instant coffee, nicotinic acid, pea nuts, sorbic acid, benzoic acid and aldehyde.
- b) Metals – like mercury, nickel, cobalt chloride, cadmium and palladium.
- c) Plastics – like epoxy resins, methyl methacrylate, propylene, glycol, benzoyl peroxide and bisphenol A.
- d) Clinical conditions:
 - 1) Local – like allergies, bruxism, tongue thrusting, restricted tongue space due to poor denture, candidiasis, dermatosis (e.g. lichen planus), dry mouth, erythema migrans (Geographic tongue), fissured tongue and glossitis.
 - 2) Systemic – like, anemia's (pernicious, iron deficiency,

vitamin B deficiency especially B₁₂ and folate).

Drugs – like cytotoxics, (ACE) angiotensin converting enzyme inhibitor such as enalapril or guinapril, protease inhibitors such as atazavir (Reyataz) and RTV (Norvir).

Hormonal –prior to post menopausal females, diabetes mellitus, hypothyroidism, hyposalivation, hiatus hernia and HIV.

Psychogenic – Lately there is increasing evidence that B.M.S. is psychogenic as discovered by several studies^(29, 9, 30). Anxiety, depression and cancer phobia were found in 20% of the cases^(12, 31), also it was found that they were reaching up to 50% in a study on 180 patients in the university of Turin, Italy⁽³²⁾ and 50.4% in a study on 140 patients on Catalan population in the university of Barcelona, Spain⁽³³⁾.

However, there is not yet clear evidence whether psychological distress is the cause of oral symptoms or whether these factors are the result of chronic pain experienced by these patients themselves⁽³⁴⁾.

Many recent studies attempting to relate B.M.S to resent life events suffered by the patient^(35, 36) in the last six months before the occurrence of the symptoms, but no significant difference was found between the patients and the control group, however many of these patients reported psychiatric treatment or hospitalization compared to the control group⁽³⁴⁾.

Also some studied related B.M.S patients to their personality profile by comparing their pain experience with the controls⁽²⁰⁾.

From the neurological point of view, changes of taste occurred in over 60% of the patients particularly with abnormal bitter taste⁽³⁷⁾ which suggested a defect in the sensory peripheral neural mechanism⁽³⁸⁾, but

MRI of the brain in these patients demonstrated a brain activity pattern similar to other neuropathic disorders, suggesting that brain hypo activity play a role⁽³⁹⁾.

Many studies which looked at estradiol levels for menopause women considered a low level (<15 pg/ml) as an indicator for menopause^(40,16) while normal levels may reach up to 30 pg/ml.

The aim of this study was to evaluate the clinical characteristics of consecutive patients with spontaneous complaints of burning mouth in the absence of mucosal lesions referred to a large teaching clinic in order to better understand possible etiologies of B.M.S. Then a further step was to exclude any possible local or systemic causes in addition to possible organic brain syndrome or neurological disease or medical disease. Then the referral of the remaining patients to a psychiatric department related to the College of Medicine in Baghdad University for the psychiatric evaluation.

Materials and Methods

In this prospective study patient referred to the outpatient clinic of the Consolatory Dental Clinic at the Institute of Medical Technology at the period from January 2002 to January 2006 suffering from B.M.S.

Patients with thrush, recent dentures, tongue thrusting, bruxism, allergy, dermatitis (lichen plannus), geographic or fissured tongue, glossitis, were excluded from the study.

The sample left were 52 patients (44 females and 8 males, female /male = 5.5/1) with average age range (46–72 years for females, median = 53.5 years) and (50–67 years for males, median = 58.5 years).

A case sheet of questionnaire investigated the followings:

- 1) Cause of attendance – Anxiety, disturbed sleep, fear of a serious disease.
- 2) Duration of pain since it started.
- 3) Time course of pain.
- 4) Precipitating factors.
- 5) Change of taste and its types.
- 6) Intensity of pain – by using VAS (Visual Analogue Scale) score which consists of 10 cm line where 0 cm = no pain and 10 cm = pain as bad as it could be. Patient mark a point along the line that best represent his or her pain and pain is measured in either numeric scale (1-10) or descriptive rating (e.g. : no pain , mild , moderate and severe pain) ^(41,42) .
- 7) Location of pain.
- 8) Presence of medical comorbidities.
- 9) Laboratory Investigations: each patient was sent for investigations including:
 - a) Hematological investigations – comprised full blood count, mean corpuscular volume, mean corpuscular hemoglobin, serum ferritin, and vitamin B₁₂ and folate concentration.
 - b) Biochemical investigations – include fasting blood sugar and if it was abnormal then glucose tolerance test was performed.
 - c) Salivary gland Investigations – stimulated parotid salivary gland flow rate was investigated with Carlsson– Crittenden cup after stimulation with 1ml of 10% citric acid. When the volume of saliva in one minute time was less than 0.5 ml/minute, it was considered abnormal ^(43, 9, 44) .
 - d) Hormonal Investigations – Estrogen levels were measured for females regardless of her menstrual or menopausal condition, according to Yen and Taffe (1986) ⁽⁴⁰⁾ . Estradiol levels less than 15 pg / ml were considered low.
- Thyroid function tests (PBI and T₃) were done for both females and males to exclude hypothyroidism (PBI < 50 nmol/L and T₃ < 2 nmol /L) ⁽⁴⁵⁾ .
- e) Microbiological Investigations – oral swab for detection of *Candida albicans* on smear and culture ⁽¹⁰⁾ .
- 10) Stress Analysis : The questionnaire included recent life changes adopted by Holmes and Rahe (1967) ⁽⁴⁶⁾ which include a list of possible life events like , death of spouse ,divorce, separation ,jail term, death of close family member, marriage , fired at work , retirement , pregnancy , sex difficulties , change in number of arguments with spouse , changes in responsibilities at work or residence , changes in home habits and other stressful events that the patient feel note worthy . The life change units (LCU) for each event are recorded and then a stress scale for each patient is calculated.
- 11) Psychological classification : The B.M.S. patients were sent for psychological examination by a specialist physician in psychiatry related to the college of medicine at Baghdad university and apply the classification of neurosis and psychosis adopted by Adams (1980) and Scully and Cawson (1982) ^(47,48) which include the following states :
 - A) Neurosis; include, Depressive neurosis, Anxiety neurosis, phobic neurosis, obsessional neurosis, Hysterical neurosis, Hypochondriacal neurosis.
 - B) Psychosis; include, Manic depressive psychosis, schizophrenia, Korsakoffs psychosis.

Results

The age distribution of the sample was as follows:-

- 46 – 55 years (28 patients = 53.8%)
- 56 – 65 years (17 patients = 32.7%)
- 65+ years (7 patients = 13.5%)

1) Cause of attendance:

The chief complaint that made patients attend to doctors was as follows (fig.1).

- a) Disturbed sleep (24 patients, F = 20, M = 4) (46.1%)
- b) Fear of serious disease (23 patients, F = 20, M = 3) (44.2%)
- c) Anxiety (19 patients, F = 16, M = 3) (36.5%)

2) Duration of pain since it started:

The mean duration of pain reported by the patients was 18.17 ± 12.78 months ranging between 3 – 48 months.

3) Time course of pain:

28 patients (53.6%) complained of burning on waking which persist throughout the day and 24 patients (46.4%) complained of pain developing during the day and worsen as the day goes on.

4) Precipitating factors of pain:

Twenty six patients (50%) did not report any precipitating event before the occurrence of B.M.S , but 8 patients (30.77%) reported local mechanical trauma , 6 patients (23.07%) reported facial trauma after road traffic accident, 4 patients (15.34%) reported dental surgery treatment and 5 patients (19.2%) reported periodontal treatment and 3 patients (11.5%) reported antibiotic therapy particularly tetracycline .

5) Change of taste:

Phantom taste was reported by 32 patients (61.9%), with 18 patients (56.25%) reporting bitter taste and 6 patients (18.75%) reporting sour taste and 4 patients (12.5%) reporting salty taste and 4 patients (12.5%) reported sweet taste.

6) VAS pain levels:

VAS pain levels showed an overall mean of 6.15 with 6.13 ± 0.02 in women and 6 ± 0.91 in men.

7) Location of pain: (Table no.1)

The tongue was involved in 76.9% of the patients, distributed accordingly as 13.4% on tip, 57.7% on margins (unilaterally) and whole tongue (5.8%).

The palate and lips were each 3.8% of the cases and both affected bilaterally the dental ridge 5.8% of the cases and usually unilaterally, and the buccal mucosa in 9.6% of the cases and usually bilaterally.

8) Presence of Medical Comorbidities:

Out of 52 B.M.S patients of the study sample 13 patients (25%) were free from any illness while 39 patients (75%) (32 females and 7 males) suffered the following chronic diseases: Controlled diabetes mellitus 8 patients (20.5%), controlled hypertension 8 patients (20.5%) cardiopathies 5 patients (12.8%), rheumatoid arthritis 16 patients (41%) and respiratory disease 3 patients (7.7%).

Any patient whose medical comorbidities were not under control or their medicines were from those that initiate B.M.S were excluded.

9) Results of Laboratory Investigations:

a) None of the patients have shown any type of anemia or vitamins B or folate deficiency.

b) Fasting blood sugar was done to all patients including diabetic patients and all their results were within the normal values.

c) Twenty six patients thought they had xerostomia and suffered from oral dryness. Stimulated parotid flow rates below 0.5 ml / min were present in 13 patients (50% of these patients i.e. 25% of the whole B.M.S sample).

d) Hormonal Investigations:

Thyroid function tests have shown PBI and T₃ concentrations in the B.M.S patients sample were within normal.

But with regards to women who had menopause among our sample, 33 women (75%) of our women sample had passed the menopause and the rest (25%) were ranging between normal menstrual cycles to premenopausal symptoms.

And concerning the estradiol levels among the women sample, 30 women (68.18%) were below 15 pg / ml and 14 patients (31.72%) were above 15 pg/ml as it can be seen in Table no. (2).

T-test = 0.01 > P so there is a significant difference between low estradiol and high estradiol level in the incidence of B.M.S in the females sample.

Chai square test= 0.5 > P > 0.1 proving that there is no significant difference among the distribution of estradiol levels in relation to different age groups of the females sample .

10) Stress Analysis:

The results of the role of stressful life events that happened in the last 6 months for the B.M.S patients were as follows:

- a) They had a range of 1-5 life changing events.
- b) The mean of life changing events were 2.73 ± 1.28 events per patient.
- c) The range of life change units (L.c.u.) among the B.M.S sample were between 35-145 L.c.u with a mean of 73.56 L.c.u.
- d) At least 4 patients (7.69%) had at least one severe event.

But these results were not significant.

11) Psychological classification:

36 females (81.81%) had some form of neurosis in relation to their burning mouth sensation while 8

females (18.19%) were free of any psychiatric comorbidity.

7 males (87.5%) had some form of neurosis in relation to their burning mouth sensation while 1 male (12.5%) was free of any psychiatric comorbidity. (Table 3)

None of the patients in the sample reached to level of psychosis as it was introduced in the methodology.

Chai Square value= $p > 0.5$ level proving a significant difference in the distribution of neurosis among both sexes.

None of the patients were diagnosed as hysterical or hypochondriacal neurosis.

Discussions

The patients sample range between 46 – 72 with a median age of 53.5 years for females and 58.5 years for males is generally younger than many studies in Europe^(32, 49, 50, 33, 9) while it was nearer to the age of studies in South America^(16, 50) and in Israel⁽³⁴⁾ and that is probably due to the small sample size and the absence of a referral system in Iraq and also due to shorter life expectancy , since the study is on old age .

The female to male ratio of 5.5/1 in this study is smaller than Glasgow Britain^(9,27) and than that in Basque , Spain⁽⁴⁹⁾ while it was close to Barcelona , Spain (33) and higher than Brazil and Chile^(16,50) and than that in Israel⁽³⁴⁾ .

The main attendance cause was disturbed sleep (46.1%), followed by fear of serious disease (cancer phobia) (44.2%) and lastly anxiety (36.5%). Sleep disturbance reported in other studies was higher than this study^(9, 16, 49, 33) , while fear of serious disease was less reported than those in other studies^(32, 9, 34) .

The mean duration of pain reported by patients was longer than many other studies in Britain and Brazil^(9, 16) but shorter than Israel⁽³⁴⁾ and this is probably due to the difference in the follow up of patients and the referral system, because although there are a lot of doctors and dentist in Iraq, still people who suffer a disease like B.M.S do not know where to go and even the medical profession might be confused of his referral.

The course of pain , although the majority complained of burning on waking and its persistence during the day (53.6%) but the complaint was reported in lower levels than other studies^(34,32) , while it was higher than those reported in the Basque in Spain⁽⁴⁹⁾ .

In this study 60% of the B.M.S patients had a change of taste with a similar ratio to other studies^(16, 34, 49) , but the bitter taste was reported lower than those studies.

Almost half the patients did not report any precipitating factor and about 54% of them reported trauma either local or after a traffic accident, similar results were reported in the studies in Brazil^(16, 51) .

The visual analogue scale (VAS) showed a mean of 6.15 (6.13 ± 0.02 for women and 6 ± 0.91 for men), which was higher than the Brazilian study⁽¹⁶⁾ and the British study⁽⁹⁾ as well as the Israel study⁽³⁴⁾ .

On the location of pain, the tongue was involved in much higher percentage than all the studies (76.9%) (Table 1) but the significant difference within this involvement was in the site of pain in the tongue which was on the margins of the tongue (unilaterally) (57.7%) while the rest of the studies , the tip of the tongue is the most common site^(9,16,32,49) .

The number of patients free of medical comorbidities in this study is higher than those reported in other

studies^(9, 16) and this is probably due to the methodology by which we selected our sample towards the target of psychological evaluation, using similar principles like the study in Turin, Italy⁽³²⁾ .

To many scientists B.M.S was considered as a manifestations of xerostomia or salivary gland hypofunction^(52,16,49,9,53,25,54,20,55,56) which found that more than 50% - 60% of the B.M.S patients suffer xerostomia , but in this study only 25% of the sample (13 patients) had parotid flow rates below 0.5 ml/minute . And also it should be noted that salivary secretion is affected in old age but this is usually the result of medications or disease rather than age per se^(12, 57, 10) , while the stimulated salivary flow rate is not affected. This was evidenced by a study by Becks and Wainwright back in 1943⁽⁵⁸⁾ which was done on 650 subjects ranging in age from 5 – 95 years ,but the age affects the mucous glands of the hard palate thus decreasing the un stimulated whole salivary flow rate⁽⁵⁹⁾ and even this occurs in healthy old non – medicated subjects⁽¹⁰⁾ .

The results of the effect of female sex hormone estradiol were controversial , although a 25% of our women sample were not in the stage of menopause , there were 31.72% with estradiol level over 15 pg/ml and 68.18% below 15 pg/ml and all of them were B.M.S sufferers (Table 2) and on the same table chai square test was $0.5 > P > 0.1$ proving no significant difference among the distribution of estradiol levels in relation to different age groups also t-test was $0.01 > P$ proving a significant difference between low and high estradiol levels in the incidence of B.M.S among the females . Thus these results confirm the relationship between estradiol level and B.M.S and

this support many studies^(13, 17, 15, 16, 14, 18).

The results of stress analysis of life changing events of the last 6 months before the onset of the symptoms, the range LCU scores between 35 – 145 and the number of events was 2.73 ± 1.28 events per patient and 7.69% of the patients had at least one severe event which was lower than that reported in the Italian study⁽³²⁾. Trying to correlate the life changing events with B.M.S proved to be non significant thus supporting the conclusions of the above study which found the crucial difference lies in the severity of events rather than their number⁽³²⁾.

The results of the psychological classification proved that over 82.6% of the patients were suffering from some form of neurosis but none reached the level of psychosis according to Adams (1980) and Scully and Cawson (1982)^(47,48). These results were much higher than noted by Scully and Hegarty (2003)⁽³¹⁾.

Depressive and anxiety neurosis comprised about 63.5% of the whole patients these results were similar to other studies^(32, 34, 33, 50, 49, 9) when combining these two psychological comorbidities. But in this study depressive neurosis (40.38%) was higher than anxiety neurosis (23.08%) these results come in agreement with results of other studies^(9,32,33,34,60,61,62) and in disagreement with other studies^(50,63), phobic neurosis and obsessional neurosis comprised (19.24%) of the patients and these are listed for the first time in the B.M.S studies.

The problem behind such studies in Iraq or other Middle Eastern countries is that patients are not ready to cooperate neither a control group is ready to be followed up particularly when the study include psychiatric or mental diagnosis and treatment due to the social stigma of mental illness.

Conclusions

- 1) B.M.S is not a minor syndrome but epidemiological surveys proved that its prevalence may reach as high as 7% of the population in Europe and female to male ratio was 5.5:1.
- 2) Disturbed sleep, fear of serious disease and anxiety are the major causes of patient's attendance for medical care.
- 3) Local Mechanical and facial trauma after road traffic accidents are the major precipitating factors.
- 4) Taste changes were reported in 61.9% of patients are particularly bitter tastes followed by sour then salty and sweet.
- 5) There is no specific site for B.M.S pain where different to all other studies the major site of pain was the margins of the tongue unilaterally.
- 6) There is a direct linkage between the estradiol level and B.M.S particularly in menopausal women.
- 7) The assessment of stress analysis could not prove a relation to B.M.S but single severe event was more crucial in the etiology of B.M.S.
- 8) The psychological classification of the B.M.S patient have shown that most of them lie in the level of neurosis and none of them reached to the level of psychosis. And depression and anxiety are the major a etiological factors for B.M.S, followed by phobic and obsessive neurosis.
- 9) Further studies are needed on this disease in order to understand its etiology and natural history.

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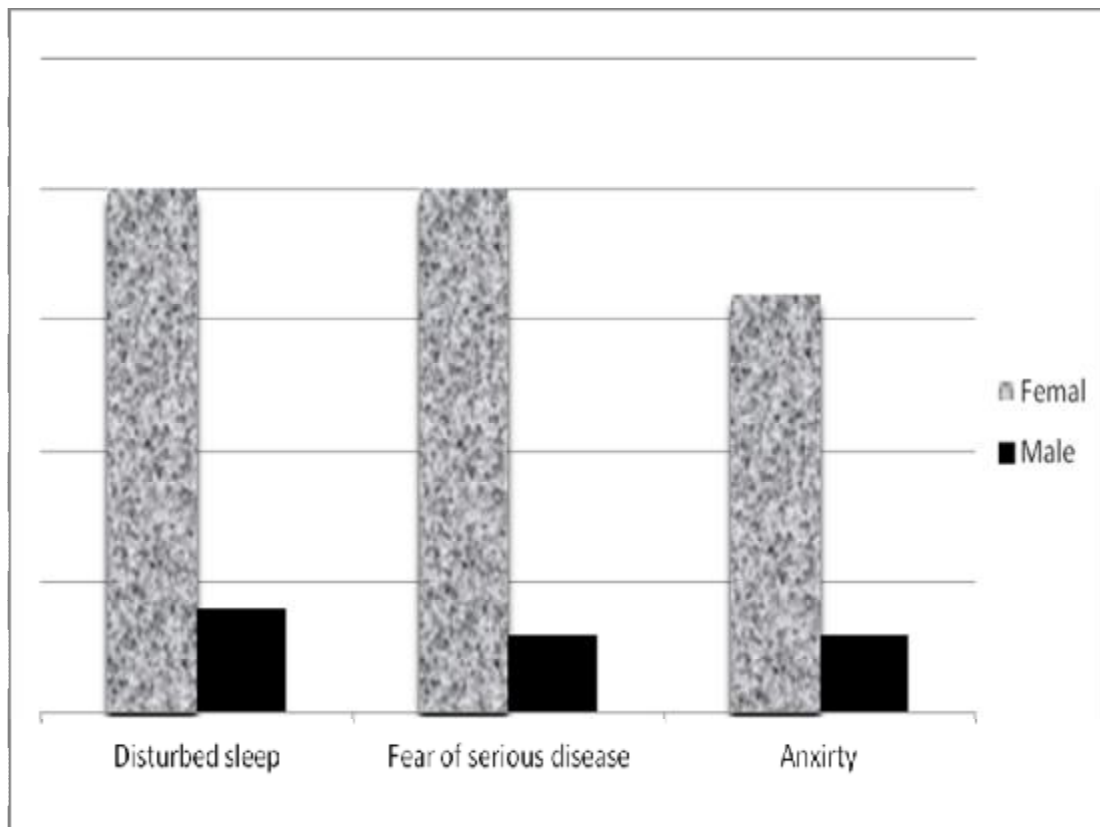


Figure (1) B.M.S. patient's reasons for attendance

Table (1) B.M.S pain location

Location	N.	%
<u>Tongue</u>	40	76.9%
Tip	7	13.4%
Margins (unilateral)	30	57.7%
Whole tongue	3	5.8%
<u>Dental Ridge (unilateral)</u>	3	5.8%
<u>Buccal mucosa (Bilateral)</u>	5	9.6%
<u>Palate (Bilateral)</u>	2	3.8%
<u>Lips (Bilateral)</u>	2	3.8%

Table (2) Distribution of estradiol levels among different age group of the B.M.S female sample

Age (years)	<15 pg/ml	>15 pg/ml	Total
46 – 50	7 (15.9%)	5 (11.3%)	12 (27.3%)
51 -56	11 (25%)	2 (4.5%)	13 (29.5%)
56 – 60	3 (6.82%)	3 (6.82%)	6 (13.6%)
61 – 65	4 (9.1%)	4 (9.1%)	8 (18.2%)
66+	5 (11.3%)	-	5 (11.4%)
Total	30 (68.18%)	14 (31.72%)	44 (100%)

Table no. (3) Classification of psychiatric comorbidities among the B.M.S sample

Type of psychiatric neurosis	Male (No + %)	Female (No+ %)	Total (No+ %)
Depressive neurosis	4 (50%)	17 (38.63%)	21 (40.38%)
Anxiety neurosis	2 (25%)	10 (22.73%)	12 (23.08%)
Phobic neurosis	1 (12.5%)	4 (9.09%)	5 (9.62%)
Obsessional neurosis	0 -	5 (11.36%)	5 (9.62%)
Free	1 (12.5%)	8 (18.19%)	9 (17.30%)
Total	8 (100%)	44 (100%)	52 (100%)