International Journal of Otorhinolaryngology and Head and Neck Surgery
Al-Nuaimi DSA et al. Int J Otorhinolaryngol Head Neck Surg. 2019 Mar;5(2):262-268
http://www.ijorl.com
pISSN 2454-5929 | eISSN 2454-5937

Original Research Article

DOI: http://dx.doi.org/10.18203/issn.2454-5929.ijohns20190757

Acute xerostomia in head and neck radiotherapy

Dalya S. A. Al-Nuaimi[1]*, Khudair J. Al-Rawaq[2], Ali G. M. Noori[3], Marwa A. N. Fattah[3]

[1]Baghdad Radiation Oncology and Nuclear Medicine Center, Baghdad Medical City Complex, Ministry of Health/ Environment, Baghdad, Iraq
[2]Department of Surgery, College of Medicine, Baghdad, University, Baghdad, Iraq
[3]Al-Amal National Hospital, Baghdad Medical City Complex, Ministry of Health/ Environment, Baghdad, Iraq

Received: 23 November 2018
Revised: 04 January 2019
Accepted: 07 January 2019

***Correspondence:**
Dr. Dalya S. A. Al-Nuaimi,
E-mail: ahmeds201258@yahoo.com

ABSTRACT

Background: Xerostomia is a common complaint experienced with radiotherapy to the head and neck and it is caused by salivary glands dysfunction.
Methods: Xerostomia is a common complaint experienced with radiotherapy to the head and neck and it is caused by salivary glands dysfunction.
Results: The mean age was 51.69±13.7 years; 67% were men and 33% were women. Nasopharyngeal tumor and larynx cancer were the common tumors diagnosed (29% and 28% respectively), 78% of the tumors were squamous cell carcinoma and 53% of them in stage III. Most patients didn't take chemotherapy during radiotherapy (90%), while 68% of them have previously received chemotherapy. The mean dose of radiotherapy used was 63.2±9.65 Gray. Post radiotherapy, the highest proportion diagnosed with xerostomia grade I (37%), while 21% of them were free of xerostomia. Female, negative past medical history, site, stage and dose of radiation were associated factors that increased prevalence of xerostomia.
Conclusions: After radiotherapy, there is a high chance for developing xerostomia. Females, negative past medical history, advanced stage of tumor, high dose of radiation and site of tumor (oral, nasopharyngeal, and parotid) were significantly associated factors. Tumor site was a significant factor associated with the grade of xerostomia.

Keywords: Xerostomia, Radiotherapy, Salivary gland dysfunction, Head and neck cancer

INTRODUCTION

Head and neck cancer is the eighth common cancer in Western countries. The incidence of head and neck tumors in Iraq is <2% of all cancers, which are mostly squamous cell carcinomas arising from the mucosa of the upper aero digestive tract.[1,2] Radiation has securely part of head and neck treatment since the 1960s because of lead to cure when used alone or in combination with surgery. The development of concurrent chemotherapy and radiation schedules be one of the greatest advances in oncology.[3] During a course of H and N radiation therapy, there are many side effects including fatigue, loss of taste acuity, radiation dermatitis, and xerostomia.[4] Xerostomia, is caused by salivary gland dysfunction as a result of damage in the field of radiation.[5] There are three major paired salivary glands (parotid, submandibular, and sublingual) producing the majority of the saliva. The remaining saliva is produced from more than 600 minor simple encapsulated tubule-alveolar glands, located throughout the upper aero digestive tract mucosa.[6] Decreased salivation can lead to dental caries, periodontal diseases, a shift of oral flora, poor tolerability to dental prosthesis and inflammation, atrophy and ulceration of mucosa. As a result, radiation-induced xerostomia has a debilitating impact on health and overall quality of life.[5]

Table 1: Grades of xerostomia.[7]

	Mild	Moderate	Severe
Dry mouth	Symptomatic (e.g., dry or thick saliva) without significant dietary alteration; un-stimulated saliva flow >0.2 ml/min	Oral intake alterations (e.g., copious water, other lubricants, diet limited to purees and/or soft, moist foods); un-stimulated saliva 0.1 to 0.2 ml/min	Inability to adequately aliment orally; tube feeding or TPN indicated; un-stimulated saliva <0.1 ml/min

METHODS

Study design, setting and data collection

A prospective observational study conducted in the Oncology Teaching Center/Radiation Therapy Department at the Medical City Complex, Baghdad, Iraq. In a period of six months from November 2017 to April 2018.

Study patients and sample size

Total number of 100, all of them diagnosed with HNC as proofed by clinical and histopathological examination and treated by External Beam Radiotherapy (EBRT). All patients subjected to complete evaluation for proper staging with full history, physical examination, and radiological investigations. The HNC was primary in all the patients. The data collection done through daily visits and selected randomly.

Procedure

The dose of external beam radiotherapy used for the treatment of different patients was (30-70 Gray), with a standard fractionation. Each fraction is two GY and five fractions per week. Some patients treated with radiation only, while some others treated with chemotherapy, prior to or concurrent with the Radiotherapy. Radiation delivered for all patients with 3D conformal technique, using Elekta infinity, and Elekta synergy machines.

Partitions

The patients assessed for symptoms and signs of xerostomia according to subjective experience of dry mouth and patients classified by xerostomia grades into the following:

1. Mild symptomatic (dry or thick saliva) without significant dietary alteration.
2. Moderate symptomatic and significant oral intake alteration (eg, copious water, other lubricants, diet limited to purees and/or soft moist foods).
3. Severe symptoms leading to inability to adequately aliment orally; IV fluids, tube feedings, or parenteral nutrition indicate.

Statistical analysis

The data analysed using Statistical Package for Social Sciences (SPSS) version 25. The data presented as mean, standard deviation and ranges. Categorical data presented by frequencies and percentages. Pearson's Chi–square test used to assess statistical association between certain variables and outcome. A level of p–value less than 0.05 considered significant.

Ethical approval

All patients verbally informed about the study and they asked the permission to be a part of the study. All personal information kept anonymous. Data exclusively used for the sake of this study.

RESULTS

Age and gender

Study patient's age ranging from 13-78 years with a mean 51.69±13.7 years. The highest proportion found in age group 40-59 years (52%), Figure 1. Figure 2 shown the distribution of gender, males higher than females (67% versus 33%) with male to female ratio of 2:1.

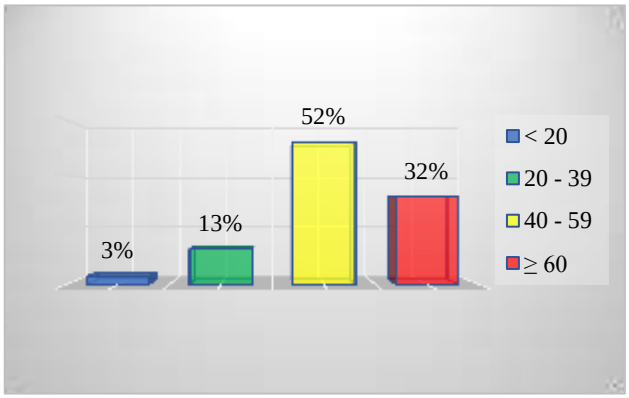

Figure 1: Distribution of study patients by age.

Tumors details

Table 2 shown the distribution of the tumor details. We noticed that nasopharyngeal tumor and larynx cancer were the common tumors diagnosed (29% and 28% respectively). Regarding types of the tumor, more than

three quarters diagnosed with squamous cell carcinoma (78%), and 53% of patients were in stage III.

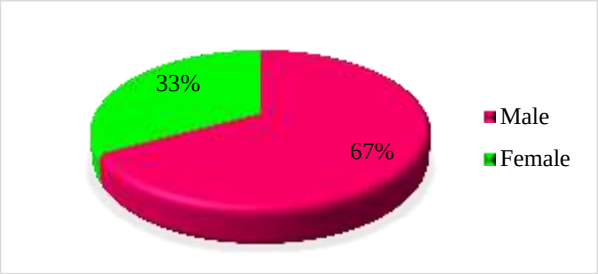

Figure 2: Distribution of study patients by gender.

Table 2: Distribution of tumor details (n=100).

Variables	N	%
Alcohol drinking		
Yes	9	9.0
No	91	91.0
Smoking		
Former	54	54.0
Non-smoker	45	45.0
Current	1	1.0
Past medical history		
No history	80	80.0
HTN and/or DM	20	20.0
Diagnosis		
Ca larynx	28	28.0
Ca tongue	10	10.0
Maxillary sinus tumor	6	6.0
Nasopharyngeal tumor	29	29.0
Oral cavity tumor	5	5.0
Oral floor of mouth tumor	1	1.0
Parotid tumor	16	16.0
Post cricoid tumor	2	2.0
Cervical tumor	3	3.0
Type		
SCC	78	78.0
Hodgkin lymphoma	3	3.0
MPNST	1	1.0
Adenoid cystic	6	6.0
Mucoepidemoid	6	6.0
Mixed adenoma	4	4.0
Undifferentiated	1	1.0
Esthinineuroblastoma	1	1.0
Stage		
II	15	15.0
III	53	53.0
IV	32	32.0
Radiotherapy dose (GY)		
<50	4	4.0
50–59	18	18.0
60–69	29	29.0
≥70	49	49.0

Past medical history and social habits

Most of patients were non-drinker and had no past medical history (91% and 80% respectively). Concerning smoking, the highest proportion of study patients were former smokers (54%) (Table 2).

Dose of radiotherapy

Study patient's dose of radiotherapy was ranging from 30 to 70 GY with a mean of 63.2 GY and SD of ±9.65 GY. About half of patients (49%) received dose of radiotherapy ≥70 GY (Table 2).

Prior and concurrent chemotherapy

Figure 3 shown the distribution by prior and concurrent chemotherapy. Most of the patients didn't take chemotherapy during radiotherapy (90%), while 68% of them were previously received chemotherapy.

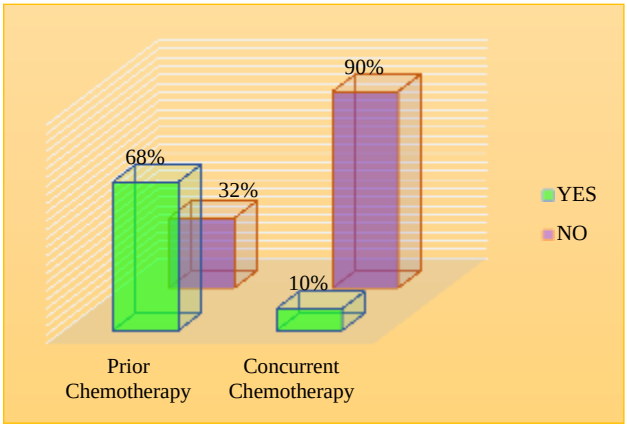

Figure 3: Distribution of study patients by prior and concurrent chemotherapy.

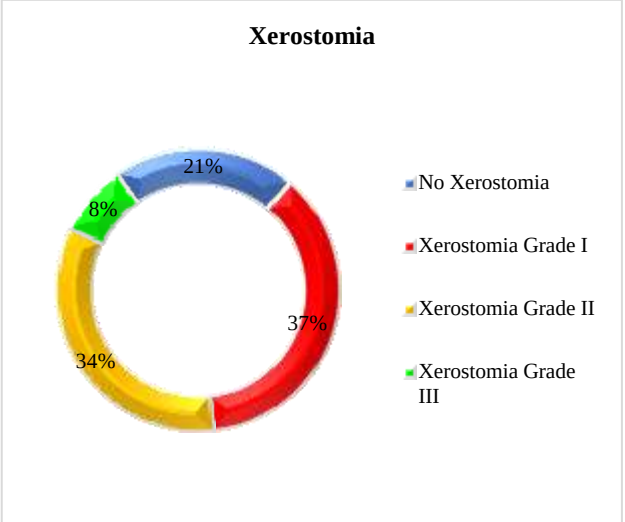

Figure 4: Distribution of study patients by diagnosis of xerostomia.

Table 3: Association between xerostomia, demographic characteristics, and tumors details.

Demographic characteristics	Xerostomia			P value
	n=79	n=21	n=100	
	Yes (%)	No (%)	Total (%)	
Age group (years)				
<20	3 (100.0)	0 (0)	3 (3.0)	0.65
20-39	11 (84.6)	2 (15.4)	13 (13.0)	
40-59	39 (75.0)	13 (25.0)	52 (52.0)	
≥60	26 (81.3)	6 (18.8)	32 (32.0)	
Gender				
Male	48 (71.6)	19 (28.4)	67 (67)	0.01
Female	31 (93.9)	2 (6.1)	33 (33)	
Smoking				
Former	44 (81.5)	10 (18.5)	54 (54.0)	0.674
Non-smoker	34 (75.6)	11 (24.4)	45 (45.0)	
Current	1 (100.0)	0 (0)	1 (1.0)	
Alcohol drinking				
Yes	6 (66.7)	3 (33.3)	9 (9)	0.34
No	73 (80.2)	18 (19.8)	91 (91)	
Past medical history				
No	68 (85.0)	12 (15.0)	80 (80.0)	0.003
HTN and/or DM	11 (55.0)	9 (45.0)	20 (20.0)	
Tumor details				
Diagnosis				
Neck tumor	14 (42.4)	19 (57.6)	31 (31.0)	0.001
Oral tumor	16 (100.0)	0 (0)	16 (16.0)	
Maxillary sinus tumor	4 (66.7)	2 (33.3)	6 (6.0)	
Nasopharyngeal tumor	29 (100.0)	0 (0)	29 (29.0)	
Parotid tumor	16 (100.0)	0 (0)	16 (16.0)	
Stage				
II	8 (53.3)	7 (46.7)	15 (15)	0.005
III	41 (77.4)	12 (22.6)	53 (53)	
IV	30 (93.8)	2 (6.3)	32 (32)	
Chemotherapy				
Prior chemotherapy				
Yes	57 (83.8)	11 (16.2)	68 (68.0)	0.084
No	22 (68.8)	10 (31.3)	32 (32.0)	
Concurrent chemotherapy				
Yes	9 (90.0)	1 (10.0)	10 (10.0)	0.368
No	70 (77.8)	20 (22.2)	90 (90.0)	
Radiotherapy dose (GY)				
<50	1 (25.0)	3 (75.0)	4 (4.0)	0.047
50–59	14 (77.8)	4 (22.2)	18 (18.0)	
60–69	25 (86.2)	4 (13.6)	29 (29.0)	
≥70	39 (79.6)	10 (20.4)	49 (49.0)	

Xerostomia

The distribution by diagnosis of xerostomia is shown in Figure 4. We noticed that the highest proportion diagnosed with grade I (37%), while 21% of them free. The association between xerostomia and general characteristics shown in (Table 3), the highest prevalence of xerostomia seen in females (93.9%) with a significant association (p=0.01). Regarding past medical history, the highest prevalence seen in patients who didn't have past medical history (85%) with a significant association (p=0.003). No statistical significant association (p≥0.05) between prevalence of xerostomia and all other variables. Table 3 shown the association between xerostomia and tumor details. All patients diagnosed with oral, nasopharyngeal, and parotid tumor developed xerostomia (100%) with a significant association (p=0.001). It was

obvious that there was no significant association (p≥0.05) between prevalence of xerostomia and prior or concurrent chemotherapy. The prevalence of xerostomia increasing as the dose of radiotherapy increased until dose of 70 GY, when it remained about the same level, so the highest prevalence of xerostomia seen radiotherapy dose between 60–69 GY (86.2%), with a significant association (p=0.047). The highest prevalence of xerostomia grade III seen in patients diagnosed with parotid tumor (37.5%) with a significant association (p=0.001). No significant association (p≥0.05) between xerostomia grade and both of tumor stage and radiation dose (Table 4).

Table 4: Association between xerostomia grades and tumor diagnosis, tumor stage and radiotherapy dose.

Variable	Xerostomia grade				P value
	n=37	n=34	n=8	N=79	
	I (%)	II (%)	III (%)	Total (%)	
Tumor diagnosis					
Neck tumor	13 (92.9)	1 (7.1)	0 (0)	14 (17.7)	0.001
Oral tumor	8 (50.0)	8 (50.0)	0 (0)	16 (20.3)	
Maxillary sinus tumor	1 (25.0)	3 (75.0)	0 (0)	4 (5.1)	
Nasopharyngeal tumor	15 (51.7)	12 (41.4)	2 (6.9)	29 (36.7)	
Parotid tumor	0 (0)	10 (62.5)	6 (37.5)	16 (20.3)	
Tumor stage					
II	4 (50.0)	3 (37.5)	1 (12.5)	8 (10.1)	0.633
III	17 (41.5)	21 (51.2)	3 (7.3)	41 (51.9)	
IV	16 (53.3)	10 (33.3)	4 (13.3)	30 (38.0)	
Radiotherapy dose					
<50	1 (100.0)	0 (0)	0 (0)	1 (1.3)	0.722
50–59	6 (42.9)	6 (42.9)	2 (14.3)	14 (17.7)	
60–69	10 (40.0)	11 (44.0)	4 (16.0)	25 (31.6)	
≥70	20 (51.3)	17 (43.6)	2 (5.1)	39 (49.4)	

DISCUSSION

Radiation-induced xerostomia is a side effect after treatment for oral and oropharyngeal cancers. This may induce swallowing difficulties, compromised oral well-being, reduced nutrition intake, or speech deficiencies. The quality of life is often impaired for these patients.[8] In the present study, nasopharyngeal and larynx cancer were the commonest tumors (29% and 28% respectively), and 78% of patients diagnosed with squamous cell carcinoma when 53% of them were in stage III. When compared to results of Iranian study conducted on 63 head and neck cancer in 2012, laryngeal and oropharyngeal tumor had the highest prevalence constituted 31.7% and 26.9% respectively.[9] Another different results observed in USA study conducted in 2006, as the primary tumor sites was in the oropharynx as (68%).[10] An agreement observed in study conducted in Greece (2017) included 60 patients, where half of them had laryngeal/hypopharyngeal cancer (28% and 2% respectively).[11] About half of patients (49%) received radiotherapy ≥70 GY, and concerning the chemotherapy (90%) of the patients didn't take chemotherapy, only 68% previously received chemotherapy. In Iran (2012), 63 head and neck cancer patients, give different results observed when chemo-radiation used in 55 patients (87.3%), while RT alone used in 8 patients (12.7%) at doses of at least 25–30 GY with average received radiation doses was 53.9 GY.[10] In Greece (2017), 78.3% of patients with head and neck cancer had undergone chemotherapy in addition to radiotherapy.[11] which disagreed with our study. In 37% of patients had xerostomia grade I and 21% of them free of xerostomia and significantly associated with gender (p=0.01), as xerostomia seen in females in (93.9%), it also significantly associated with past medical history (p=0.003), and in patients who didn't have past medical history (85%). Significant association (p=0.001) found with tumor, as all patients with oral, nasopharyngeal, and parotid tumor had xerostomia. Radiotherapy dose significantly associated with xerostomia (p=0.047), since the highest prevalence found in patients who received radiotherapy dose between 60–69 GY (86.2%), while no significant association found with concurrent chemotherapy (p≥0.05).

Finally, xerostomia grade III found in parotid tumor (37.5%), which is significantly associated with xerostomia (p=0.001). In Iran (2012) the follow up visits conducted two, four, and six weeks later, they found that a significant difference in xerostomia score throughout follow-up period and xerostomia was significantly lower in period prior to the start of radiotherapy, which represented 11% in pre-treatment and reached to 14% and 25% in the following radiotherapy session which was not significantly associated (p=0.13).[9] Another studies showed much higher results, as in Belgium (2008), 75 head and neck cancer patients enrolled in a study yielded results showed that majority of patients (93%) suffered

from xerostomia and 65% had moderate to severe xerostomia (grade II to III).[12] Another German study in 2011 included 95 patients who underwent radiotherapy for head and neck cancer and recorded information regarding xerostomia development, they noticed that incidence of xerostomia was significantly higher in patients who received higher radiotherapy doses to the parotid glands (p=0.0195) in comparison to other region with small doses.[13] All these studies, although differed in the percentages and association, but agreed in facts that serious xerostomia easily occurred after a larger exposure dose to the neck, and furthermore, differences in results observed might be attributed to several factors as sample size, dose and type of radiotherapy used, site and grade of tumor for which radiotherapy was used and location of radiotherapy applied. Males were more prevalent than females (67% versus 33%) with male to female ratio of 2:1. Age was ranging from 13 to 78 years with a mean 51.69±13.7 years and the highest proportion was found in age group 40-59 years (52%). Out of 63 Iranian patients participated in a study conducted in 2012, 43 patients (77.8%) were male with male: female ratio was 3.5:1.[10] Finally, higher results observed in Greece in a study conducted on 60 patients with head and neck cancer, as male represented 80% of them (48 patients) with male: female ratio was 4:1.[11]

CONCLUSION

Females, negative past medical history, advanced stage of tumor, high dose of radiotherapy and site of tumor (oral, nasopharyngeal, and parotid) were significantly associated factors with incidence of xerostomia. Tumor site was significant factor associated with the grade of xerostomia.

Recommendations

- Delivering the radiation therapy for head and neck cancers with sparing the salivary gland tissue by the use of new radiotherapy techniques, IMRT may help to decrease the intensity of xerostomia.
- Maintaining good oral health by educating the patients about dental care before and during radiotherapy in the form of frequent brushing, flossing and use of flouride treatment.
- Dietary management by advising patients to drink plenty of fluids to maintain hydration and avoid hot drinks, spicy food, smoking and alcohol.
- The use of amifostine during radiation treatment in order to prevent xerostomia and educate patients about the use of artificial saliva, chewing gum and pilocarpine to manage xerostomia.
- Further researches and studies about this disturbing side effect are needed to confirm the results of this study and to know more illustrate causes and ways of management.

ACKNOWLEDGEMENTS

Great thankful for Dr. Rasha K. Al-Saad, Ph D candidate, Baghdad University and Dr. Ahmed S. Al-Shewered, Baghdad Radiation Oncology Centre/Medical city complex for their helping.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Elizabeth C, Corina J. Head and Neck Cancer: Treatment, Rehabilitation, and Outcomes. 2nd ed. Plural Publishing, Inc. US; 2014.
2. Iraqi Cancer Registry. Ministry Of Health, Iraqi Cancer Board, Baghdad, 2011. Available at: https://moh.gov.iq/upload/upfile/ar/273.pdf. Accessed on 11 October 2018.
3. Brizel DM, Adelstein DJ. Perez & Brady's Principles and Practice of Radiation Oncology. In: Halperin EC, Wazer DE, Perez CA, et al eds. Locally Advanced Squamous Carcinoma of the Head and Neck. 6th ed. Wolters Kluwer Health / Lippincott Williams & Wilkins, China: 2013.
4. Mendenhall WM, Werning JW, Pfister DG. Devita, Hellman, Rosenberg. Cancer: principles & practice of oncology: Cancers of head and neck. In: Devita VT. Lawrence TS, Rosenberg SA. 10th ed. USA: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2014.
5. Common Terminology Criteria for Adverse Events (CTCAE) v5.0. Available at: https://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm#ctc_50. Accessed on 23 October 2018.
6. Dirix P, Nuyts S, Vander Poorten V, Delaere P, Van den Bogaert W. The influence of xerostomia after radiotherapy on quality of life. Supportive Care Cancer. 2008;16(2):171-9.
7. Kaae JK, Stenfeldt L, Eriksen JG. Xerostomia after Radiotherapy for Oral and Oropharyngeal Cancer: Increasing Salivary Flow with Tasteless Sugar-free Chewing Gum. Frontiers Oncol. 2016;6(111):1-6.
8. Kakoei S, Haghdoost AA, Rad M, Mohammadalizadeh S, Pourdamghan N, Nakhaei M, et al. Xerostomia after Radiotherapy and its Effect on Quality of Life in Head and Neck Cancer Patients. Arch Iran Med. 2012;15(4):214–8.
9. Meirovitz A, Murdoch-Kinch CA, Schipper M, Pan C, Eisbruch A. Grading xerostomia by physicians or by patients after intensity-modulated radiotherapy of head-and-neck cancer. Int J Radiat Oncol Biol Phys. 2006;66(2):445-53.
10. Memtsa PT, Tolia M, Tzitzikas I, Bizakis J, Pistevou Gombaki K, Charalambidou M, et al. Assessment of xerostomia and its impact on quality of life in head and neck cancer patients undergoing radiation therapy. Mol Clin Oncol. 2017;6(5):789-93.

11. Pow EH, Kwong DL, McMillan AS, Wong MC, Sham JS, Leung LH, et al. Xerostomia and quality of life after intensity-modulated radiotherapy vs. conventional radiotherapy for early-stage nasopharyngeal carcinoma: initial report on a randomized controlled clinical trial. Int J Radiat Oncol Biol Phys. 2006;66(4):981-91.
12. Tribius S, Prosch C, Tennstedt P, Bajrovic A, Kruell A, Petersen C, et al. Xerostomia After Radiotherapy: What Matters-Mean Total Dose or Dose to Each Parotid? Initial Results. Int J Radiat Oncol Biol Phys. 2011;81(2):496-7.
13. Jellema AP, Doornaert P, Slotman BJ, Leemans CR, Langendijk JA. Does radiation dose to the salivary glands and oral cavity predict patient-rated xerostomia and sticky saliva in head and neck cancer patients treated with curative radiotherapy? Radiother Oncol. 2005;77(2):164-71.

Cite this article as: Al-Nuaimi DSA, Al-Rawaq KJ, Noori AGM, Fattah MAN. Acute xerostomia in head and neck radiotherapy. Int J Otorhinolaryngol Head Neck Surg 2019;5:262-8.