

Epidemiological Characteristic of Aphthous Stomatitis and Real Clinical Practice of Management of Patients in Uzbekistan

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Abstract

Introduction: The article provides an epidemiological description for patients with chronic recurrent aphthous stomatitis (RAS) and the frequency of their reversal in the general structure of diseases of the oral mucosa from 2014 to 2018. The structure of clinical forms of RAS in the Republic of Uzbekistan (ICD-10) was taken. The study of the dynamics of frequency and debut of various clinical forms of RAS, the gender characteristics of RAS has led to the need for the introduction of modern standards for examination, treatment, and prevention of the disease. The goal of the research is to study the frequency of occurrence of RAS, as well as the real clinical practice of managing patients in the Republic of Uzbekistan and its compliance with existing recommendations.

Materials and Method: Patients' medical records and records of the patients' consultation journal for five years of work (from 2014 to 2018) were studied.

Results: Taking into account the gender and age characteristics of patients with RAS will determine the real clinical picture and prevalence of this disease, increase the ability of monitoring, medical examination and providing timely specialized care, allowing to prevent the progression and maintain the working capacity of patients with this pathology of OCR.

Conclusion: The frequency of RAS at the general reception for diseases of OCR is $6.22 \pm 0.42\%$; in the general structure of the disease, the fibrinous form prevails 3.46%; the incidence of necrotic periadenitis is 3.15%; herpetiform aphthous stomatitis is recorded in 2.25% of patients and 1.25% - a symptom in Behcet's disease. The debut of RAS falls on the age period of 18-34 years (62.50%), which indicates a negative trend of "rejuvenation" of this pathology. For effective treatment and rehabilitation of patients suffering from RAS, it is necessary to conduct a comprehensive examination attracting internists, an appointment of means of immunomodulating therapy and means effectively correcting the most important homeostatic mechanisms in humans.

Keywords: *The fibrinous form of chronic recurrent aphthous stomatitis, Setton's aphthae, herpetiform aphthous stomatitis, symptom in Behcet's disease.*

Introduction

Chronic recurrent aphthous stomatitis is one of the most common diseases of the oral mucosa, characterized by recurrent rash of aphthae and a prolonged course with periodic manifestations¹². Recurrent aphthous stomatitis (RAS) is a disorder characterized by recurrent ulcers on the oral mucosa in the absence of other symptoms. RAS presents several pathological conditions with similar

clinical manifestations. According to the international classification of diseases (ICD-10), RAS refers to ICD-10: K12.0 ICD-10/K00-K93 CLASS XI Diseases of the digestive system/K00-K14 Diseases of the oral cavity, salivary glands and jaw/K12 Stomatitis and related lesions¹³.

Six clinical forms (fibrinous, necrotic, glandular, scarring, deforming and lichenoid) of ASD have been

distinguished since 1978, based on the analysis of clinical and morphological manifestations. According to foreign authors, ASD is characterized by three main manifestations: small aphthae (Mikulich aphthosis), located mainly on the mucous membrane of the lips, cheeks, the bottom of the oral cavity, large aphthae (necrotic periadenitis of oral mucosa, or Sutton's disease) and herpetiform ulcers – multiple aphthae of round forms¹⁴.

According to various authors, the prevalence of RAS in the overall structure of the pathology of OCR ranges from 1.27 per 1000 population to $8.68 \pm 0.62\%$. Recurrent aphthous stomatitis (RAS) occurred among the population of Sverdlovsk region, in 6.9% cases. Large aphthae, up to 1 cm in diameter, very painful, epithelizing for a long time (up to 5 weeks), the so-called Setton's aphthae, were diagnosed in 12% of patients with RAS⁷. According to the WHO, RAS occurs in 20% of the population, and adults at the age from 20 to 40 suffer from recurrent chronic aphthous stomatitis⁴.

In general, it was determined that the prevalence of RAS had a tendency to increase, which is due to the global aging of the population, an increase in the pathology of OCR, an increase in somatic pathology, and uncontrolled use of immunomodulators and medications with antibacterial properties¹⁰.

In everyday clinical practice, patients, applying for dental care with mucosal diseases present one of the most difficult problems due to difficulties in diagnosis and treatment. The official reports of the dental service of the Republic of Uzbekistan do not include indicators of the incidence of chronic aphthous stomatitis⁴. However, there is an urgent need for studying the prevalence of gender-related morbidity indicators, the age limits for the debut of pathologies belonging to this group of diseases. Information on the epidemiology of aphthous stomatitis in the country should stimulate the development of modern method of diagnosis, therapy and rehabilitation of patients with a similar pathology¹⁰.

Information about the prevalence and characteristics of the clinical course of the disease is necessary for planning the activity of a medical organization and its management; planning of therapeutic and preventive measures; establishing health indicators and the prognosis of morbidity¹². Knowledge of the prevalence and intensity of dental diseases is the basis for developing the need for medical personnel and resources.

The goal of the research is to study the frequency of occurrence of RAS, as well as the real clinical practice of managing patients in the Republic of Uzbekistan and its compliance with existing recommendations.

Materials and Method

We studied the medical records of patients who applied for dental care for the treatment of diseases of the oral mucosa at the dental clinic of Tashkent State Dental Institute TSDI for five years of activity (from 2014 to 2018).

We used the classification of RAS proposed by WHO for identifying the disease: 1. The fibrinous form of RAS (Mikulich aphthosis); 2. Necrotic periadenitis (Setton's aphthae) (recurring scarring deep aphthae, deforming aphthae, creeping aphthae); 3. Herpetiform aphthous stomatitis; 4. Symptom in Behcet's disease.

When studying the history of development of the disease, the emphasis was on identifying the preclinical stage of the disease, the onset of the disease, the duration of the disease, the stage of the disease at the time of diagnosis, the first symptoms, the dynamics of the signs of the disease, previously conducted treatment, its effectiveness, drugs prescribed for treatment, their tolerability, the presence of allergic reactions.

Data about patients were recorded in the Unified Card, designed for this purpose.

The control sample in this series of activity amounted to 40 healthy individuals of the corresponding gender, age and ethnic composition who underwent a complete dental examination.

Results

208 patients applied for treatment of the aphthous stomatitis from 2014 to 2018, thus, the frequency of RAS in the total frequency of RAS treatment complaints was $6.22 \pm 0.42\%$. It should be noted that over the entire sampling period, the frequency of RAS in the overall structure of the RAS diseases did not undergo significant differences and ranged from $5.32 \pm 0.42\%$ (2014) to $7.62 \pm 1.05\%$ (2016) (table 1). Thus, for the diseases that make up the group of aphthous mouth ulcers over the past 5 years, the peak of visits was in 2016-2017, which in general can be described as a negative trend in morbidity increase.

Table 1. Dynamics of the appealing frequency regarding RAS in the general structure of OCR diseases

Diseases	Years					Total
	2014	2015	2016	2017	2018	
RAS	$\frac{32}{5,22 \pm 0,90}$	$\frac{38}{5,32 \pm 0,87}$	$\frac{47}{7,52 \pm 1,05}$	$\frac{49}{7,11 \pm 0,97}$	$\frac{42}{5,97 \pm 0,89}$	$\frac{208}{6,22 \pm 0,42}$
Total with OCR disease	$\frac{612}{100,0}$	$\frac{714}{100,0}$	$\frac{625}{100,0}$	$\frac{689}{100,0}$	$\frac{703}{100,0}$	$\frac{3343}{100,0}$

Note: In the numerator – the number of patients; In the denominator, in % of the total number of patients.

The unit weight of the registered clinical forms (within the framework of ICD-10) within the group of aphthous lesions of the oral cavity is presented in Table 2.

Table 2. The structure of clinical forms of RAS in the Republic of Uzbekistan (ICD-10)

No.	Clinical Form	Abs	%
1.	Fibrinous Form, Mikulich Aphthosis	115	55,29±3,45
2.	Necrotic Peradenitis (Setton's Aphthae) (Recurrent, Deep Aphthae, Deforming Aphthae, Creeping Aphthae)	61	29,33±3,15
3.	Herpetiform Aphthous Stomatitis	25	12,02±2,25
4.	Symptom in Behcet's Disease	7	3,36±1,25
5.	Total	208/100,0	

Table 2 shows that the mainly fibrinous form of the disease (Mikulich aphthosis) is recorded, the proportion of which in the general structure of the diseases was $55.29 \pm 3.45\%$; a significant proportion – $29.33 \pm 3.15\%$ was occupied by severe peradenitis (Setton's aphthae, recurrent, deep aphthae, deforming aphthae, creeping aphthae); $12.02 \pm 2.25\%$ in the total structure of RAS accounted for herpetiform lesions and the proportion

of Behcet's syndrome was the smallest – $3.36 \pm 1.25\%$ (table 2).

It should be noted that the established trend towards a higher incidence of fibrinous disease was recorded throughout the study period. Throughout the entire period of research, a traditionally high unit weight of severe peradenitis was noted (table 3).

Table 3. Dynamics of frequency of various clinical forms of RAS

Clinical course of RAS	Years				
	2014	2015	2016	2017	2018
Fibrinous form	$\frac{20}{62,5 \pm 8,56}$	$\frac{26}{68,21 \pm 7,56}$	$\frac{20}{42,55 \pm 7,21}$	$\frac{23}{46,94 \pm 7,13}$	$\frac{26}{61,90 \pm 7,49}$
Setton's aphthae	$\frac{6}{18,75 \pm 6,90}$	$\frac{10}{26,32 \pm 7,14}$	$\frac{17}{36,17 \pm 7,13}$	$\frac{18}{36,73 \pm 6,88}$	$\frac{10}{23,81 \pm 6,579}$
Herpetiform aphthous stomatitis	$\frac{5}{15,62 \pm 6,42}$	$\frac{1}{2,63 \pm 2,60}$	$\frac{8}{17,02 \pm 5,48}$	$\frac{6}{12,24 \pm 4,64}$	$\frac{5}{11,90 \pm 5,01}$
Symptom in Behcet's disease	$\frac{1}{39,25 \pm 3,08}$	$\frac{1}{2,63 \pm 2,60}$	$\frac{2}{4,26 \pm 2,71}$	$\frac{2}{4,08 \pm 2,80}$	$\frac{1}{2,38 \pm 2,5}$

Clinical course of RAS	Years				
	2014	2015	2016	2017	2018
Total	$\frac{32}{100,0}$	$\frac{38}{100,0}$	$\frac{47}{100,0}$	$\frac{49}{100,0}$	$\frac{42}{100,0}$

Note: In the numerator – the number of patients; In the denominator, in % of the total number of patients.

Clinic development debut among patients with various clinical forms was registered at age from 18 to 24 – $23.08 \pm 2.92\%$; from 25 to 34 – $39.42 \pm 3.39\%$; from 34 to 44 – $23.56 \pm 2.94\%$; from 45 to 54 – $9.61 \pm 2.04\%$. According to archival data, in $4.33\% \pm 1.41$ (9) patients, the disease manifested at the age of more than

55 years, which corresponds to global data. The results obtained indicate a negative trend of “rejuvenation” of this pathology. At the same time, in $62.50 \pm 2.34\%$ of patients, clinical manifestations of the disease formed in the age period of 18 – 34 years (table 4).

Table 4. Debut of various clinical forms of RAS

Age groups, years	Clinical course				Total
	Fibrinous	Setton’s aphthae	Herpetiform aphthous stomatitis	Symptom in Behcet’s disease	
18 -24	$\frac{20}{17,39 \pm 3,53}$	$\frac{15}{24,59 \pm 5,51}$	$\frac{10}{40,0 \pm 9,80}$	$\frac{3}{42,86 \pm 18,70}$	$\frac{48}{23,80 \pm 2,92}$
25-34	$\frac{45}{39,13 \pm 4,54}$	$\frac{21}{34,42 \pm 6,08}$	$\frac{12}{48,0 \pm 9,99}$	$\frac{4}{57,14 \pm 18,70}$	$\frac{82}{39,42 \pm 3,39}$
35-44	$\frac{32}{27,82 \pm}$	$\frac{15}{24,59 \pm 5,51}$	$\frac{2}{8,0 \pm 5,43}$	$\frac{-}{-}$	$\frac{49}{23,56 \pm 2,94}$
45-54	$\frac{12}{10,43 \pm 4,8}$	$\frac{7}{11,47 \pm 4,08}$	$\frac{1}{4,0 \pm 3,92}$	$\frac{-}{-}$	$\frac{20}{9,61 \pm 2,04}$
≥55	$\frac{6}{5,22 \pm 2,03}$	$\frac{3}{4,92 \pm 2,80}$	$\frac{-}{-}$	$\frac{-}{-}$	$\frac{9}{4,33 \pm 1,41}$
Total:	$\frac{115}{100,0}$	$\frac{61}{100,0}$	$\frac{25}{100,0}$	$\frac{7}{100,0}$	$\frac{208}{100,0}$

Note: In the numerator – the number of patients; In the denominator, in % of the total number of patients.

In the analysis of gender differences, it was determined that chronic recurrent aphthous stomatitis is mainly registered among women: over the past 5 years, the frequency of women reporting about RAS was 68.75

$\pm 3.21\%$ against the corresponding frequency among men – $31.21 \pm 3.21\%$. This trend continued throughout the studied period (Table 5).

Table 5. Gender characteristic of RAS

Gender	Clinical course				Total
	Fibrinous	Setton's aphthae	Herpetiform aphthous stomatitis	Symptom in Behcet's disease	
Men	$\frac{33}{28,70 \pm 4,22}$	$\frac{21}{34,43 \pm 6,08}$	$\frac{10}{40,0 \pm 9,80}$	$\frac{1}{14,28 \pm 13,30}$	$\frac{65}{35,25 \pm 3,21}$
Women	$\frac{82}{71,30 \pm 4,22}$	$\frac{40}{65,57 \pm 6,08}$	$\frac{15}{60,0 \pm 9,80}$	$\frac{4}{57,14 \pm 18,70}$	$\frac{143}{68,75 \pm 3,21}$
Total	$\frac{115}{100,0}$	$\frac{61}{100,0}$	$\frac{25}{100,0}$	$\frac{7}{100,0}$	$\frac{208}{100,0}$

Seasonal occurrence of exacerbations was noted, chronic recurrent aphthous stomatitis, as a rule, manifested in spring-autumn period (table 6). Moreover, in $23.08 \pm 2.92\%$ of patients, the onset of the disease

occurred in autumn period of the year; in $36.54 \pm 3.34\%$ in winter; in $25.96 \pm 3.03\%$ in spring, and only in $14.42 \pm 2.43\%$ the onset of the disease occurred in summer season (figure 1).

Table 6. Distribution of patients with RAS by seasons of the year

Clinical course of RAS	Seasons			
	Autumn	Winter	Spring	Summer
Fibrinous form	$\frac{26}{22,61 \pm 6,03}$	$\frac{42}{36,52 \pm 5,52}$	$\frac{31}{26,96 \pm 6,04}$	$\frac{16}{13,91 \pm 6,32}$
Setton's aphthae	$\frac{14}{22,95 \pm 6,07}$	$\frac{20}{32,78 \pm 5,38}$	$\frac{17}{27,87 \pm 6,10}$	$\frac{10}{16,39 \pm 6,76}$
Herpetiform aphthous stomatitis	$\frac{6}{24,0 \pm 6,16}$	$\frac{11}{44,0 \pm 5,69}$	$\frac{5}{20,0 \pm 5,49}$	$\frac{3}{12,0 \pm 5,93}$
Symptom in Behcet's disease	$\frac{2}{28,57 \pm 6,52}$	$\frac{3}{42,86 \pm 5,68}$	$\frac{1}{14,28 \pm 4,76}$	6,39
Total	$\frac{48}{100,0}$	$\frac{76}{100,0}$	$\frac{54}{100,0}$	$\frac{30}{100,0}$

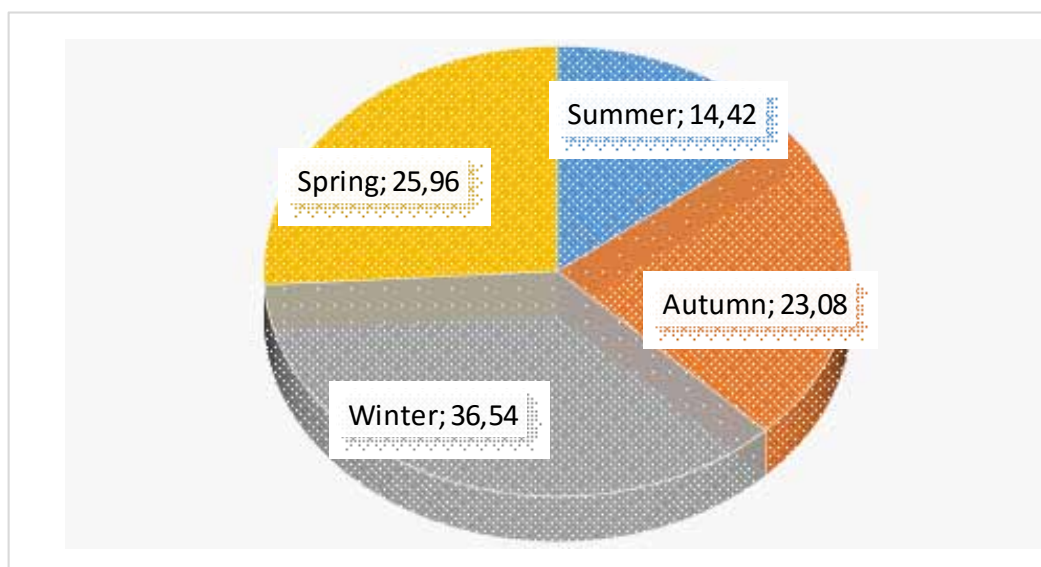


Fig. 1. Distribution of patients with RAS by seasons (in % of the total number of the diseased)

Discussion

Analysis of the duration of the disease at the time of treatment showed that in most patients the disease lasted 3-5 years, the maximum duration at the time of treatment was registered in a more severe form (Setton's aphthae, necrotic periadenitis, deforming aphthae), the average disease duration was 6.88 ± 0.28 year; with a fibrinous form, the disease lasted 3.44 ± 0.17 year and with herpetiform aphthous stomatitis and a symptom in Behcet's disease, 2.84 ± 0.11 and 4.46 ± 0.21 year, respectively.

Analysis of the completeness of the diagnosis, quality of treatment and prevention of RAS revealed the following:

When collecting an anamnesis, as a rule, data on the patient's profession and the presence of occupational hazards and bad habits (smoking, consuming nasvai (a type of non-smoking tobacco product), alcoholism, etc.) were ignored; the nature of nutrition and the use of products that can cause allergic reactions was not taken into account; the history of allergy was not taken into account, the hereditary burden and the presence of RAS among relatives of the first and second lines of kinship were not found out, information about the transferred and concomitant diseases was ignored.

When collecting the anamnesis of only 140 (67.31%) patients, the time of the onset of the first symptoms, the presence of pathology in the past, the nature of the

previous treatment and its results were specified. Data on intolerance to drugs and materials, stress that can trigger this exacerbation, acute condition/disease or exacerbation of a chronic disease that developed less than 6 months before seeking dental care, as well as work involving contact with occupational hazards, were obtained from 122 (58.65%) patients.

Incomplete implementation of diagnostic procedures is noted at the stage of diagnosing the disease. A visual examination with a full description of the elements of the lesion was performed in 108 (51.92%) patients, palpation of the organs of the oral cavity, external examinations of the maxillofacial part, and palpation of the maxillofacial part were not performed in any patient, as well as the degree of opening of the mouth and restriction of mobility of the lower jaw is also not determined.

The oral cavity using additional tools is not examined. Carious cavities are not investigated using a dental probe and periodontal pockets using a periodontal probe. Occlusion and degree of pathological tooth mobility are not determined, as well as the diagnosis of the state of the dentofacial system using method and means of beam imaging. Histological examination of the oral tissue preparation and a biopsy of the oral mucosa was not implemented. Determination of oral hygiene and periodontal indices was carried out only in 54 (25.96%) patients.

At present, the importance of the immune system and disturbances in the microbiocenosis of the most important biotopes of the body in the severity of the clinical course of diseases of OCR is not questioned. In this connection, special attention was paid to the study and prescription of drugs for immunity and intestinal microbiocenosis.

When diagnosing the disease, only 45 (21.63%) patients underwent consultative examination and were prescribed examination and treatment by a general practitioner (gastroenterologist, dermatologist, endocrinologist, occupational therapist, neuropathologist), somewhat more often, consultation with an orthopedic dentist was assigned in 63 (30.29%) patients.

It is obvious that the prognosis of RAS and the relapse rate largely depend on the timeliness and accuracy of the diagnosis. The selected sample based on the results of archival data, the diagnosis of chronic recurrent aphthous stomatitis was carried out on the basis of:

- only anamnesis and objective examination data – in 108 (51.92%) patients;
- anamnesis, objective examination, assessment of dental status data – in 54 (25.96%) patients;
- data of anamnesis, objective examination, assessment of dental status, consultative examination by a physician (gastroenterologist, dermatologist, endocrinologist, occupational therapist, neuropathologist) – in 45 (21.63%) patients;
- data of anamnesis, objective examination, assessment of dental status, assessment of the immune status, study of intestinal microbiocenosis, consultative examination by a physician (gastroenterologist, dermatologist, endocrinologist, occupational therapist, neurologist) – in 30 (14.42%) patients.

In the study of the non-pharmacological assistance provided, it was found that oral sanitation with the implementation of professional oral hygiene was carried out only in 59 (28.36) patients; teaching patients the oral hygiene with carrying out controlled toothbrushing – in 81 (38.94%) patients; removal of odontolith, grinding of sharp edges of teeth, replacement of metal fillings and prostheses from dissimilar metals, orthopedic correction, polishing of dentures and elimination of galvanosis – in 45 (21.63%) patients.

In the overwhelming majority of cases, drug therapy in 200 (96.15%) patients consisted of applying painkillers – 1-2% lidocaine solution, 1-2% trimecaine, cleaning the surface of aphthae from fibrinous or necrotic plaque using proteolytic enzymes: trypsin and chymotrypsin, as well as antiseptic treatment with antiseptic solutions: 0.05% chlorhexidine solution, 1% hydrogen peroxide solution, 0.01% miramistin solution, etc. Subsequently, epithelizing therapy with ointments carotoline, solcoseryl, actovegin and cholisal gel was prescribed.

Prescription of dietary therapy was established in 153 (73.56%) patients. It should be noted that there were no prescriptions in the treatment regimens, including sedative and antihistamines, nonspecific hypersensitizing therapy, metabolic correction drugs (calcium preparations, vitamin therapy), drugs that correct microcirculatory disorders and metabolic trophic processes that normalize the lipoperoxidation process, as well as specific hyposensitizing therapy.

Quite rarely, immunomodulating therapy was registered in 102 (49.04%) patients.

Taking into account the gender and age characteristics of patients with RAS at a dental appointment for OCR diseases allowed to determine the real clinical picture and prevalence of this disease, to increase the possibilities of monitoring, clinical examination and provision of timely specialized care to prevent the progression and preserve the working capacity of patients with this OCR disease.

Conclusion

1. The frequency of RAS at the general reception for diseases of OCR is $6.22 \pm 0.42\%$; in the general structure of the disease, the fibrinous form prevails $55.29 \pm 3.46\%$; the incidence of necrotic periadenitis – $29.33 \pm 3.15\%$; herpetiform aphthous stomatitis is registered among $12.02 \pm 2.25\%$ patients and symptom in Behcet's disease among $3.36 \pm 1.25\%$.
2. The debut of RAS falls on the age period of 18-34 years (62.50%), which indicates a negative trend of "rejuvenation" of this pathology. Women morbidity prevails in the general structure of the disease – $68.75 \pm 3.21\%$.
3. For adequate treatment of RAS, it is necessary to introduce modern standards for the examination, treatment and prevention of the disease.

The results of the study can be used in practical work for predicting the risk of the onset and development of OCR diseases among the population, as well as for improving therapeutic and preventive measures. For the effective treatment and rehabilitation of patients suffering from RAS, it is necessary to conduct a comprehensive examination with participation of internists, the appointment of the immunomodulating therapy and agents that effectively correct the most important homeostatic mechanisms of the body.

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References

1. D.M. A. Improving the effectiveness of treatment of recurrent aphthous stomatitis using ozone. Abstract. 2018;; p. 25-41.
2. Alimova D.M. KKP. Clinical characteristics of recurrent aphthous stomatitis in the Republic of Uzbekistan. Dentistry. 2014; 2: p. 48-64.
3. I.I. D. The prevalence of diseases of the mucous membrane of the mouth and lips among the adult population. 2014 Institute of Dentistry. 2014; 1(62): p. 32-33.
4. Yu.N K. Treatment of aphthous stomatitis. All-Russian Scientific and Practical Internet Conference of Students and Young Scientists of the Scientific and Educational Medical Cluster "Lower Volga" "YSRP-2016" FSBEI of HE Saratov State Medical University named after V.I. Razumovsky of the Ministry. 2017; 1-5(1): p. 11150.
5. Mikhalchenko Ye.V. EDVM. Features of the structure of diseases of the oral mucosa among residents of Volgograd and the Volgograd region. Volgograd Scientific and Medical Journal. 2015; 1: p. 3-8.
6. T.L. R. The dynamics of the incidence of the oral mucosa among the population of the Udmurt Republic. Health, demography, ecology of the Finno-Ugric peoples. 2016; 4: p. 22-24.
7. Kharitonova M.P. KYV, YLI. Features of the structure of the incidence of the mucous membrane of the oral cavity in residents of Sverdlovsk region. Maestro of Dentistry. 2012; 2(46).
8. Khorujaya R.E. TLL, TYS. Local treatment of chronic recurrent aphthous stomatitis with argoderm. Nutrition of experimental and clinical medicin. 2013; 2: p. 313-317.
9. Regezi J. SJ, JR. Oral Pathology: Clinical pathologic correlation. Elsevier. 2012; 97.
10. P. M. Epidemiology of oral diseases. Geneva. 2016;; p. 116.
11. Michalich M. MP, PSea. Role of epidemiology factors in diseases of the buccal mucosa. Arch. Oral. Biol.. 2006; 51: p. 348-353.
12. Mirowski GW JWRC. Aphthous stomatitis treatment and management. 2017.
13. Shruthi H. HK, VA. Prevalence of recurrent aphthous stomayiyis: An institutional study. Cumhuriyet Dental Journal. 2015 18; 2: p. 228-232.
14. Scully C PS. Oral mucosal disease: Recurrent aphthous stomatitis.. Br J Oral Maxillofac Surg. 2008; 46: p. 198-206.