ORIGINAL ARTICLE

RELIABILITY AND VALIDITY OF LIGHT-BASED SCREENING TECHNIQUES IN DETECTION OF ORAL PREMALIGNANT LESIONS

[1]**Sultan Mohammed Kaleem, MDS;** [1]**Shaik Mohammed Asif**, MDS; [2]**Mohammad Zahir Kota**, MDS; [3]**Abdul Kareem**, BDS; [3]**Ali Othman**, BDS; [3]**Mohammed Alhusin**, BDS; [3]**Ali Hudian**, BDS

ABSTRACT

Objective: To assess and create awareness towards risk factors like Kath chewing and other tobacco related habits and prevalence of premalignant lesions and early detection through light based Screening tool. ***Methodology:*** First stage comprised of an interview to get demographic and preliminary data for the study. In the second stage, the entire recruited participants underwent an oral examination, and suspected lesions were further seen by specialist dental surgeon. Exclusion is done by a specialist dentist to group them into clinical types based on clinical provisional diagnosis and are referred for histopathologic examination for further management. Third stage all suspected red and white lesions, inconspicuous lesions are screened by Acetic acid and VElscope to identify & confirm visible changes which required histopathological examination for further definitive treatment options. ***Result:*** 75% study subjects showed Aceto-whitening, 9.3% subjects showed negative result and 11.4% subjects showed false positive results and 2.8% projected as No Abnormality Detected in acetic acid test. In VElscope examination, 65.6% Showed Positive Dark areas, followed by 34.3 % False Positive results. There were no negative finding. Positive Predictive Value stands more with age old Acetic acid test (75%) when compared with advance methods like VELscope (65.6%). ***Conclusion:*** The oral cavity should be carefully examined in tobacco users. Any changes in color or texture of oral mucosa should arouse suspicion of the presence pre malignant lesions and/or oral cancer. Devices like VELscope can be used as a diagnostic aid for identification of these lesions. However, we have to realize that still the histopathological examination is the most accurate method to confirm the diagnosis.

Key words: Oral Pre malignant Lesion, VELscope, Khat

---

[1]Assistant Professor, Dept. of DDS, College of Dentistry, King Khalid University, Abha, Kingdom of Saudi Arabia
[2]Assistant Professor, Dept. of OMFS, College of Dentistry, King Khalid University, Abha, Kingdom of Saudi Arabia
[3]Intern, College of Dentistry King Khalid University, Abha, Kingdom of Saudi Arabia

Correspondence should be addressed to:
Dr. Sultan Mohammed Kaleem, MDS
Assistant professor,
Dept. of DDS, College of Dentistry
King Khalid University
Abha - KSA
Email: skalem@kku.edu.sa
Mobile: 0568322600

INTRODUCTION

The population in southern region of Aseer province in kingdom of Saudi Arabia comprises mostly mixed sects of tribes, expats and intellectuals. Most of the people who are in farming hail from Jazan, Fifa, Najaran in Southern Aseer Region who are habituated to "Khat" chewing (a kind of shrub leaves) which is available on the mountain terrains of this province. Khat is a natural stimulant from the Catha Edulis plant that is cultivated in the Republic of Yemen and most of the countries of East Africa. Its young buds and tender leaves are chewed to attain a state of euphoria and stimulation. The Khat chewers experience a sense of increased energy levels, increased alertness and ability to concentrate, improvement in self-esteem and an increase in libido.[1, 2]

The overall prevalence of "Khat" chewing in all the studied population was 21.4% (colleges 15.2% versus schools 21.5%). There were 3.8% female Khat chewers and 37.70% male Khat chewers.[1,2] Significant differences were found between Khat chewers according to age, gender and residence ($p < 0.05$). The prevalence was different in different colleges and in different provinces of Jazan region.[1, 2]

In Saudi Arabia; smoking tobacco is also among the major public health problems and it is prevalent in the Saudi population at different age groups. The overall prevalence of current smoking in Saudi Arabia ranges from 2.4- 52.3%. in which 12-29.8% among school students, and 2.4- 37% among university students[3]. Prevalence among adult population, ranges from 11.6-52.3%with13-38% among men and 1-16% in women.[3] These deleterious habits are a potential risk factors for pre malignant change in the oral cavity. Oral cancer is the eighth most common cancer globally and its incidence levels among men range from one to 10 cases per 100,000 which is twice as high in developing countries as they are in developed countries.[4] Countries that once rarely experienced high levels of oral cancer are likely to see a considerable increase of this disease.[4, 5] Studies have shown that between less than 1 and up to 18% of oral pre-malignant lesions will develop into oral cancer. Early detection of premalignant lesions can improve the prognosis and is well proved as an effective aid in disease prevention.[6]

This study will assess the prevalence of risk factors and occurrence of oral precancerous lesions in a general population hailing from the terrains of Aseer province in Saudi Arabia with advance light based screening tool such as VElscope.

Early detection of oral cancer is believed to reduce the morbidity and increase the survival of patients, histopathological analysis of suspected lesions is the gold standard for oral cancer diagnosis. However, it can only be provided for patients with highly suspicious lesions to confirm the clinical diagnosis. On the other hand, screening tests, which include conventional visual examination, diagnostic adjuncts such as Toluidine Blue, and light-based screening methods, are provided for asymptomatic individuals to ameliorate the early detection of malignant or premalignant lesions.[7]

There is evidence that screening for oral cancer with conventional visual examination can reduce mortality in high-risk individuals. Visualization adjuncts may be used in combination with conventional examination or alone. The light-based screening methods include applying acetic acid mouth rinse to produce aceto-whitening which can be visualized by inspection or with the use of a LED hand-held device which emits visible light (VElscope) or (Vizilite).[5,6,8]

The oral tissues can retain fluorescent characteristics after excitation with ultra-violet light or applied chemicals and the malignant lesion shows up as bright white or dark, depending on the device used.[6,8] Visually Enhanced Lesion Scope (VELscope) is a reusable light source that emits a blue light in 400-460nm wavelength which is used to examine the oral cavity.[9, 10] The oral mucosa can be visualized directly through a narrow band filter embedded within the viewing hand piece, providing direct fluorescent visualization. According to the manufacturer the oral mucosal tissues suspected of epithelial dysplasia or squamous cell carcinoma show loss of fluorescence and appear dark, whereas normal healthy mucosal tissue shows apple green fluorescence.[5,9,10]

A number of reviews have been published and reported a lack of evidence to support the use of auto fluorescence as a diagnostic tool for detection of pre malignant lesions. However, since the last review

several more studies have been published requiring reanalysis of the diagnostic value of auto fluorescence.

Therefore, the aim of the present study is to evaluate the reliability and validity of VELscope as an adjunct tool for visual examination in oral cancer screening, and to systematically review the clinical usefulness and efficacy of VELscope device in identifying Oral premalignant lesions detection.

MATERIAL AND METHODS

Research Design:
In the present study, two examination methods like Acetic Acid test and auto fluorescence visualization by VELscope, is used to examine patients with suspected, unidentified suspicious areas of pre-malignant lesions and referring those for histopathologic examination for confirmation. Population hailing from the terrains of Aseer province in Saudi Arabia who have habit of chewing Khat, Smokeless tobacco and Smoking tobacco were included in the study. This population-based cross-sectional study was conducted on patients visiting for dental checkup in dental college outpatient department.
Ethical clearance: SRC ethical approval (SRC/REG/2016-2017/115) is taken from the scientific committee of college of dentistry King Khalid University for undertaking this research project.
Informed Consent: subjects' consent is taken on a separate consent form before application of any diagnostic procedures in the patient's mouth.
Inclusion and Exclusion criteria: Population above 18 years who have habits of Smoking tobacco, Khat and smokeless tobacco chewing as mentioned in their personal history were randomly selected from outpatient department in college of dentistry on daily basis were included and thus organized for first two months of study during April 2017 till June 2017. Subjects below 18 years, with known history of oral malignancy, and in whom lesions were obviously visible on inspection are excluded from the study.
Sampling method: Initially a pilot study was carried out to determine the sample size, using the formula $n = z^2*P (1-P)/d^2$ t. to check the feasibility of the study and note any difficulties encountered during examination. Based on this a Simple Random sampling is used to accommodate the subjects of interests based on their personal history. the sample size estimated to be 100. The pilot study subjects are not included in the main study.
Data Collection Instruments: Questionnaire pertaining to Demographics, and personal history in detail are used as data collection instruments along with Basic Diagnostic Instruments (mouth mirror, Explorer, Tweezer), gloves, Masks, Cheek retractors, Gauze cloths, Cotton swabs, Disposable glasses, Basic dental Chair with Illumination, specialized instruments like VElscope Vx system 4200 series (H-12-08276) which is class A digital apparatus compiles with Canadian ICES-003, Pre prepared 5% acetic acid, photographic SLR camera.

Methodology: Participants are screened initially in the dental OPD and were interviewed to get demographic and preliminary data for the study by two trained members involved in the research with providing a close-ended questionnaire which contain questions relating to risk factors of oral cancer and socio-demographic situation.

All the investigators were trained prior to the study about questions to be asked in a predetermined questionnaire to prevent any interpersonal bias. This questionnaire is tailored for the study by modifying the WHO oral health assessment form like in the layout of form and inclusion of custom made questions about the personal habits. Participants who are having positive personal history like smoking, tobacco chewing and Khat chewing are taken to a venue equipped with screening facilities in the clinics and they were explained about the purpose of the study and then a written informed consent is taken from each of them before screening.

The participants are given the options not to participate in the study if they wanted while waiting for medical assessment. In the second stage, the entire recruited participants underwent an oral examination by one researcher and suspected lesions are further screened by specialist dental surgeon (principal investigator). All lesions not pertaining to any disease, not a normal variant, detected by the specialist is considered as suspected lesions. Further exclusion is done by a specialist dentist to group them into clinical types based on clinical provisional diagnosis like leukoplakia, Errythroplakia, Pouch keratosis and linea-alba. Oral sub-mucous fibrosis is grouped into any one

of these groups according to the clinical presentation. Any ulcerative or mixed lesions are grouped into red and white category.
Lesions which were obvious on visual inspection such as leucoplakia, oral sub mucous fibrosis, pouch keratosis are referred for histopathologic examination for confirmation and management.

All suspected red and white lesions, inconspicuous lesions are screened by Acetic acid and VElscope to identify & confirm visible changes which required histopathological examination for further definitive treatment options. Pre-prepared 5% acetic acid is applied to the lesion in suspicion with a cotton swab for one minute and the patient is asked to rinse thoroughly with plain water, to look for the Aceto-whitening of the lesion and the same area is projected for VElscope screening to look for the change in fluorescence. The lesion thus identified is photographed for recording purpose and patients are referred for further evaluation & conformation by histopathology. In our study 21 subjects who showed positive dark areas under VELscope were referred to undergo histopathological examination. The positive cases diagnosed are referred to oral medicine and oral pathology departments for counselling and for further treatment needs.
Statistical Analysis: Data thus obtained and collected is evaluated in excel sheet 2010 and subjected to required statistics (Student t test and Chi square test)

RESULTS

The research team has Examined 100 patients from Dental out Patient Department in a period of 6 months at college of dentistry King Khalid University- Abha, Kingdom of Saudi Arabia. Out of these 44 patients has positive personal history like smoking, tobacco chewing and Khat chewing and hence formed the Study group for our study (Table 1)

According to the frequency Distribution of intake of Tobacco (Table 2) it is inferred from our study that, 65.9% of Study Group smokes more than 5 cigarettes per day since more than one year followed by 52.27% chew tobacco less than 5 times per day since more than one year. 61.3 % of Subjects are habituated for chewing Khat more than 10 times in a day since less than one-year duration. 60.4% subjects sustains Khat in their mouth for less than one hour (Table 3).

Table 1: Prevalence of risk factors in Southern Aseer region in KSA

Total no of pts	100	No of pts with smoking, tobacco chewing and Khat chewing habits	12%
		No of pts with any 2 habits	31%
		Pts with any one habit	1%
		Total no with Habits	44%
% Study Group			44%

Table 2: Frequency Distribution of intake of Tobacco and Khat

Mode Of Tobacco	Less than 5/day	More than 5/day	More than 10/day	Total	Less than 1 month	Less than 1 year	More than 1 year	Total
Cigarettes	4 (10%)	29 (65.9%)	11 (25%)	44	11 (25%)	4 (10%)	29 (65.9%)	44
Tobacco chewing	23 (52.27%)	10 (22.72%)	11 (25%)	44	11 (25%)	10 (22.72%)	23 (52.27%)	44
Khat chewing	12 (27.27%)	5 (11.36%)	27 (61.3%)	44	12 (27.27%)	27 (61.3%)	5 (11.36%)	44

Tale 3: Sustainability period of Khat (Type of Leaf) in mouth

Type	< ½ hour	< 1hour	>1Hour
Khat	14	26 (60.4%)	5

According to our study it was observed that Cigarette smoking and smoke-less tobacco chewing are the most prevalent habits in our study group with more than one year's duration as compared with Khat chewing having highest frequency of intake more than 10 per day. 49% of subjects has all the three habits more than 10 per day as compared with 57% take these forms since more than 1-year duration (Table 4).

Out of 44 Study subjects, specificity for lesions on visual inspection stand's out to the highest frequency were inconspicuous whiteness and Clinically not diagnosable (No Abnormality Detected) which was observed in 29 subjects, 2 pouch keratosis and 1 ulcer. These 32 subjects (72.7%) are subjected to further evaluation by Acetic acid test and VElscope.

12 Subjects (27.2%) which are distinct with visual inspection like leukoplakia and linea Alba, are excluded from other examinations as they stand conspicuous through inspection (Table 5).

Table 4: Frequency & Duration of Mode of tobacco intake in Study group

Mode of tobacco	>10/day	>1 year
Cigarette smoking	11 (25%)	29 (65.9%)
Khat chewing	27 (61.3%)	5 (11.36%)
Smoke less Tobacco chewing	11 (25%)	23 (52.27%)
Total	49%	57%

Table 5: Lesion with Highest Frequency in Visual Inspection (specificity)

Type of Lesion	No of Study Group	Percentage
Inconspicuous	18	40.9%
Linea alba	6	13.9%
Leucoplakia	6	13.9%
ulcer	1	2.3%
Pouch keratosis	2	4.6%
NAD	11	25.5%
Total	44	

Specificity of Acetic Acid and VElscope Test in Study group (Table 6). After Exclusion of leukoplakia, linea-alba and oral sub mucous fibrosis in visual inspection, the study subjects for other diagnostic methods is 32(72.7%).75% (24 subjects from 32) showed Aceto-whitening, 9.3% (3 subjects) showed negative result and 11.4% (4 subjects) showed False positive result followed by 2.8% (1 subject) NAD. 65.6% (21 Subjects) Showed Positive Dark areas under VElscope examination followed by 34.3% (11 Subjects) with False Positive results. There were no negative finding through VElscope.

Table 6: Acetic Acid and VElscope Test in Study Group (Specificity)

Diagnostic Methods	Positive (Aceto-whitening and Dark Areas)	Negative	False positive	NAD
Acetic Acid Test	24(75%)	3 (9.3%)	4 (11.4%)	1 (2.8%)
VELscope	21(65.6%)	0	11 (34.3%)	0

The false positivity stands more with VElscope examination (34.3%) when compared with Acetic acid testing (11.4%) hence Negative predictive value is also more with VELscope (34.3%) when compared to acetic acid testing (25%)

True negative result is evident with acetic acid (9.3%) when compared with VELscope (0%) hence forth false negative result is seen with acetic acid test (3.1%) when compared to VELscope (0%), hence in our study Positive Predictive Value stands more with age old Acetic acid test (75%) when compared with advance methods like VELscope (65.6%), negative predictive value is more with VELscope (34.3%) and hence more specific in detecting pre malignant lesions with specificity 34.3%. (Table 7).

Table 7: Validity of Acetic acid Test versus VELscope in diagnosis of suspicious lesions

Diagnostic method	True +iv Sensitivity	True -iv	False +iv Specificity	False -iv	PPv %	NPv %
Acetic acid	24(75%)	3(9.3%)	4 (11.4%)	1 (3.1%)	75%	25%
VELscope	21(65.6%)	0(0%)	11(34.3%)	0 (0%)	65.6%	34.3%

DISCUSSION

It has been well documented that the habitual use of tobacco either smoked or non-smoked is responsible for increased rate of oral cancer. Early detection and evaluation of oral pre-malignant lesions can decrease the mortality rate of this serious disease.[10, 11] Periodic clinical oral examination is the main stay for early detection of oral cancer. It was shown to decrease mortality from oral cancer by 32% in high-risk patients.[11] However because of the various clinical pictures of oral pre-malignant lesions, it is necessary to biopsy these lesions for obtaining a histopathological diagnosis. Additionally, using adjunctive aids such as, VELscope, and Toluidine Blue stain, has been widely accepted to improve the effectiveness of diagnosis in large-scale screening for oral cancer. [4, 10,]
The present study was conducted in College of Dentistry King Khalid University- Abha, Saudi Arabia aiming for assessing the reliability of two visual diagnostic procedures like Acetic Acid Test and VEL scope in Screening of premalignant lesions.

To our knowledge, these 2 procedures are used for the first time to detect early oral mucosal changes related to tobacco use among an adult sample selected from population clusters in Abha, Saudi Arabia.

Results of the current Study showed that out of 100 subjects examined, the Study Group consists of 44 subjects who have Smoking, Tobacco Chewing, and Kath chewing habits.

According to our study it is inferred that 65.9% of Study Group smokes more than 5 cigarettes per day since more than one year followed by 52.27% chew tobacco less than 5 times per day since more than one year. 61.3 % of Subjects are habituated for chewing Khat more than 10 times in a day since less than one year duration. 60.4% subjects sustains Khat in their mouth for less than one hour. Out of 44 Study

subjects, Inconspicuous whiteness and Lesion undiagnosed (NAD) was observed in 29 subjects and together with 2 pouch keratosis and 1 ulcerated lesion form 32 subjects (72.7%) which were subjected to further evaluation by Acetic acid test and VElscope. 12 Subjects (27.2%) which were distinct with visual inspection like Linea Alba, leukoplakia and OSMF, are excluded from other Visual examinations. Therefore, conspicuous change has seen in (27%) of subjects by visual inspection. After Exclusion of lesions obvious with visual Inspection, other 32 subjects (72.7%) are subjected to Acetic acid test and VElscope for further evaluation.

Acetic Acid Test Inference: 75 % showed Aceto-whitening, 9.3% showed negative result and 11.4% showed false positive result followed by 3.1% false negative. The positive predictive value and negative predictive value for Acetic acid test is 75% & 25% respectively.

VELscope Inference: 65.6% Showed Positive Dark areas under VELscope examination followed by 34.3 % with False Positive results. There were no negative and false negative finding through VEL-scope. The PPV for VELscope is 65.6% and NPV is 34.3%. Since the NPV for VELscope is more than Acetic acid test (25%) hence more specific in detecting pre-malignant lesions. The auto fluorescence examination of these lesions by VEL-scope showed sensitivity of 65.6% and specificity of 34.3 % respectively. We concluded that VEL-scope can be useful in detecting oral pre-malignant lesions but is unable to distinguish between high-risk and low-risk ones.
The lesions which have positivity through VELscope are hence-forth, suggested for histopathological examination for confirmation.

In a study done by Lane-et al,[12] they investigated 44 precancerous or cancer lesions. Following clinical oral examination, screening of the oral cavity of all patients was done by VELscope and areas of loss of auto fluorescence were biopsied. The sensitivity and specificity of VELscope as a screening device demonstrated 98% and 100%, respectively, when compared to the histopathological method. The strength of this study is because it was directly compared to the Acetic acid Test done by Huber et al.[13] and the presence of high degree of sensitivity which were similar to our findings. The high percentage of specificity in Lane et al. study was also encouraging us to conclude that this device might be considered as a suitable tool for screening of precancer and cancer of the oral cavity.

However, our study had a number of weaknesses such as a small sample size (n = 44) and the presence of lesions like leukoplakia, pouch keratosis and oral sub mucous fibrosis in patients which accounted for the high specificity of Acetic acid test with VEL-scope examination. In contrast to our results, Scheer et al.[11, 13] used VEL-scope to examine 64 patients at risk for oral cancer. After VELscope examination, biopsies were taken from all patients. A loss of auto fluorescence was observed in 22 patients (34.4%) revealing intra-epithelial or invasive carcinoma. The VELscope identified the precancerous and cancerous areas with a sensitivity of 100% and a specificity of 80.8% compared with acetic acid test and histopathology as gold standard[13]. Again, this high percentage of specificity of VELscope examination which was much higher than ours made us support the concept of using VELscope in the early detection and distinguishing of OPL and malignant lesions from normal oral mucosa. However, the same device is not able to distinguish non-malignant from malignant or pre-malignant oral lesions.[14,15] The accuracy of the VELscope was evaluated by Rana-et al.[10] and they concluded that the additional use of the VELscope increased sensitivity of examination from 17 to 100% compared to clinical oral examination alone in detecting oral pre-malignant lesions. Supporting the role of VELscope as a diagnostic tool, we concluded that VEL-scope device can help in prevention or reducing the rate of occurrence of oral cancer.

Based upon the results, VELscope use leads to a sensitivity of 65.6%, and specificity of 34.3% when compared with Acetic acid test with a higher sensitivity rate compared to VELscope 75% and specificity less than VELscope 11.4%. Since the specificity of VELscope is higher than acetic acid test, it was concluded that the VELscope device can help the experienced clinician to find oral precancerous lesions at an early stage thereby facilitating the patient for early management.

CONCLUSION

The oral cavity should be carefully examined in tobacco users. Any changes in colour or texture of oral mucosa should arouse suspicion of the presence OPL and/or oral cancer. Devices like VELscope can be used as a diagnostic aid for identification of these lesions. However, we have to realize that still the histopathological examination is the most accurate method to confirm the diagnosis and the comparison of histopathology and VELscope avails better opportunity for further study.

Conflict of Interest: None

ACKNOWLEDGMENTS

I would like to thank the interns who voluntarily participated in this study. I acknowledge Dr. Hussain Mubarak (Clinical director), Dr. Ibrahim Al Shahrani (Dean) for allowing us to perform this research by using VELscope. This work was done in King Khalid University, College of Dentistry - Abha as an Intern Research for Batch 17.

REFERENCES

1. Ageely H.M. Prevalence of Khat chewing in college and secondary (high) school students of Jazan region, Saudi Arabia Harm Reduction Journal 2009; 6(11) 1-7.
2. Lqman W, Donaldson T. The use of Khat (Catha edulis) in Yemen. Social and Medical Observations. Ann Intern Med. 1976; 85(2):246–249
3. Ibrahim I.A.E, Abdelkhalig M, AlSherin A, Alzahrani T, Alghamdi M, Alzahrani A. et.al. Smoking Prevalence, Its Motives and Association with Academic Performance among the Students of Medicine and Science Colleges at AL Baha University, Al-Baha, Saudi Arabia Merit Research Journal of Medicine and Medical Sciences 2016; 4(4) 183-189.
4. Ram S, Siar CH. Chemiluminescence as a diagnostic aid in the detection of oral cancer and potentially malignant epithelial lesions, Int J Oral Maxillofacial Surg, 2005; 34:521-527.
5. Farah CS, McCullough MJ.A pilot case control study on the efficacy of acetic acid wash and chemiluminescent illumination (ViziLite) in the visualization of oral mucosal white lesions. Oral Oncol. 2007; 43(8):820-4.
6. Awan KH, Patil S. Efficacy of Autofluorence imaging as an adjunctive technique for examination and detection of oral potentially malignant disorders: A systematic review. Journal of Contemporary dental practice, 2015; 16(9): 744-749.
7. Vinuth DP, Agarwal P, Kale A.D, Hallikeramath S, Deepika S. Acetic acid as an adjunct vital stain in diagnosis of tobacco-associated oral lesions: A pilot study J Oral Maxillofacial Pathol. 2015 May-Aug; 19(2): 134–138.
8. Awan KH, Patil S, Islam S A, Jafer M. Early Detection of Oral Cancer – Guidelines for Dental Practitioners Journal of International Oral Health 2016; 8(3):399-403.
9. Patton L.L, Epstein J B, Kerr A.R. Adjunctive techniques for oral cancer examination and lesion diagnosis A systematic review of the literature JADA, 2008;139:896-905.
10. Ranaa M, Zapf A, Kuehlea M, et al., Clinical evaluation of an auto fluorescence diagnostic device for oral cancer detection: a prospective randomized diagnostic study, European Journal of Cancer Prevention; 2012.21:460-466.
11. Scheer M, Neugebauer J, Derman A, Fuss J, Drebber U etal. Auto fluorescence imaging of potentially malignant mucosa lesions. Oral Surg Oral Med Oral Pathol Oral Radio Endod, 2011.111:568-77.
12. Lane PM, Gilhuly T, Whitehead P, *et al.* Simple device for the direct visualization of oral cavity tissue fluorescence, J Biomed Opt; 2006. 11(2): 0240061-7.
13. Huber MA, b.Soul SA, Terezhalmy GT. Acetic acid wash and chemiluminescent illumination as an adjunct to conventional oral soft tissue examination for the detection of dysplasia: a pilot study, Quintessence Int. 2004; 35:378-384.
14. Sankaranarayanan R, Ramadas K, Thomas G, Muwage R, Thara S, Mathew B. *etal.*Effect of screening on oral cancer mortality in Kerala, India: a cluster-randomized controlled trial, Lancet; 2005. 365:1927-33.
15. Kavarodi A.M, Thomas M, Kannampilly J. Prevalence of Pre-malignant Lesions and Risk Factors in an Indian Low Income Migrant Group in Qatar Asian Pacific Journal of Cancer Prevention, Asian Pac J Cancer Prev. 2014; 15 (10): 4325-4329.