Detection of Cytopathological Changes Among Cigarette Smokers in Faculty of Applied Medical Science – Taif University

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Dr. Magdi M Salih (Corresponding author)

Abstract

There is a wide need for early detection methods of lung cancer. Sputum cytology examination can lead to detection of abnormal changes in the lung at early stages of cancer development. This is the first cytopathological study for detection of cytopathological changes among active and passive smokers in the Kingdom of Saudi Arabia. This study aimed to detect cytopathological changes among smokers in the Faculty of Applied Medical Sciences at Taif University using a sputum cytology method.

A sputum cytology screening was performed for 175 participants according to the sputum pooling method, and Papanicolaou stain was used to detect abnormal cells. The mean age of study subjects was 23.8 years. The cytopathological findings were as follows: 17 (9.7%) exhibited mild dyskerosis while six (3.4 %) and three (1.7) exhibited moderate and severe dyskerosis, respectively, and four (2.3%) presented metaplastic changes. There were significant associations between smoking duration and passive smoking as well as abnormal cytopathological changes. Individuals exposed to passive smoking have high risks of abnormal cytopathological changes that are detectable through sputum cytology.

The initiation of a screening program for early detection of lung precancerous changes using sputum cytology is recommended. Also, further studies are needed with larger sample sizes.

Keywords: Cytopathology, Kingdom of Saudi Arabia, Sputum
1. Introduction

Cytology is the study of cells exfoliated from epithelial surfaces. Saccomanno defined the cytological changes that occur during the development of lung cancer, and there currently exist many cytopathological techniques for the rapid and early diagnosis of malignancy (1, 2).

Cancer of the lung is considered a smoker’s disease. However nearly 10-15% of lung cancers occur in non-smokers (3, 4). There are signaling mechanisms triggered by smoke in lung cells that could lead to the activation of a growth factor signaling pathway, thereby promoting hyper proliferation of lung epithelial cells (5). Furthermore the exposure to environmental tobacco smoke can give rise to pro-mutagenic lesions in the lower airway, and this can be best investigated in a sputum sample (6). Tobacco smoking in Saudi Arabia is prevalent at different age groups (7). In King Saud University the consumption patterns of tobacco use among university students was investigated including different risk factors which may contribute to tobacco smoking (8). These studies only used epidemiological surveys and differ from our study in which we focused on demonstrating the cytopathological changes. Lung cancer in non-smokers is the seventh most common cause of cancer death (9, 10). Risk factors, including passive smoke and genetic susceptibility (11), have been associated with lung cancer in non-smokers (12). The prevalence of oral mucosal malignancy was assessed in Saudi Arabia with a clinical and questionnaire study. They determined that smoking was associated with a wide range of oral mucosal lesions, and that those suspicious for malignancy were linked with chewable forms of tobacco (13). Kuzu and his colleague studied the value of treatment for non-small cell lung cancer with positive sputum cytology (14). Sputum cytology examination is useful for early detection in populations at high risk for lung cancer (15). This study aimed to detect cytopathological changes using a sputum cytology method among smokers in the Faculty of Applied Medical Sciences at Taif University.

1.2 Materials and methods

1.2.1 Study design

We used a prospective screening study to determine the cytological changes among active and passive smokers.
1.2.2 Study area

This study was conducted at the Faculty of Applied Medical Sciences, at Taif University, during the period between March 2013 and January 2014.

1.2.3 Study population and selection criteria

Participants included students, workers and staff members. Participants were aged 20 years or older, and included non-smokers, active cigarette smokers for a minimum duration of five years, and individuals subjected to passive smoking. Excluded were those who had a diagnosis of acute respiratory infection or failed to provide an adequate sputum sample.

1.2.4 Ethical consideration

The proposal of this study was approved by the research board ethical committee of the Faculty of Applied Medical Science at Taif University. All participant agreed to participate in this study with verbal consent.

1.2.5 Methods for sputum collection and preparation.

Participants’ information, smoking history, and clinical findings were obtained by interview and examination at the time of enrollment. Each participant was instructed to give sputum by coughing vigorously. Sputum was collected in wide-mouthed, disposable plastic containers. The sputum was decanted into a Petri dish and examined against a black background. When present, blood-tinged, discolored or solid particles were selected for examination. The sputum samples were spread evenly over two clean glass slides. One slide was fixed immediately in 95% ethyl alcohol for 30 minutes, then stained with Papanicolaou's procedure (Hughes and Dodds, 1968) \(^{(16)}\). The other smear was allowed to air dry, then post-fixed in methanol and stained with May-Grunwald Giemsa stain \(^{(17)}\). Both smears were screened for detection of abnormal cells, and categorized by well-trained cytologists. Final diagnosis was determined and confirmed by a cytopathologist, and smears were classified as not adequate, negative, squamous metaplasia, mild dyskerosis, moderate dyskerosis, or severe dyskerosis.
1.2.6 Statistical Methods

The methods employed were descriptive relative to the demographic and cytological reports. Univariate and multivariate logistic regression modeling was performed and checked for statistical significance, $P < 0.05$ (chi square test).

1.3 Results

Sputum samples from 175 participants were collected and examined for cytological changes. In Table 1, demographic characteristics presented that the majority (83.4%) of the participants were students at Taif University. The mean age was 23.8 years. A large portion (155, 88.6%) of the study group were between 15 to 25 years of age. The presence of participants with 35 years of age or older was attributed to the entrance employees and worker participants. This group had smoking histories of more than 10 years. Distribution of individuals according to residence or geographical area was heavily skewed to the Taif province (86.9%) followed by Al baha and Mecca area. Data collected on clinical status, passive smoking exposure and smoking history included smoking status. All of these were described in Table 2 in which six (3.4%) provided sputum samples unsuitable for cytodiagnosis. There were 169 adequate samples. A total of 17 (9.7%) had cytopathological diagnoses of mild dyskerosis, six (3.4 %) and three (1.7) had moderate and severe dyskerosis, respectively, and four (2.3%) presented metaplastic changes (see Figure 1).

Univariate and multivariate logistic regression modeling was used to determine whether age, clinical status, smoking duration and passive smoking variables could be identified as statistically significant predictors of the specific expected cytological outcome (mild dyskerosis, moderate dyskerosis, metaplasia, and severe dyskerosis). The only apparent significant associations found from both univariate and multivariate analyses (Table 3) were between smoking duration and passive smoking history from one side and abnormal cytopathological changes from the other side. There were increases in mild and moderate dyskerosis that were more reported among participants with smoking durations of more than five years.
Table 1. Study groups demographical characteristics

<table>
<thead>
<tr>
<th>Age groups in years</th>
<th>Occupation</th>
<th>Residence area</th>
<th>Number of cigarettes/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td>N (%)</td>
<td>N (%)</td>
<td>N (%)</td>
</tr>
<tr>
<td>15-25</td>
<td>Student</td>
<td>Taif province</td>
<td>None smoker</td>
</tr>
<tr>
<td>155 (88.6%)</td>
<td>146 (83.4%)</td>
<td>152 (86.9%)</td>
<td>50 (28.6)</td>
</tr>
<tr>
<td>26-35</td>
<td>Workers</td>
<td>Al baha</td>
<td>1-10</td>
</tr>
<tr>
<td>13 (7.4%)</td>
<td>15 (8.6%)</td>
<td>18 (10.3%)</td>
<td>38 (21.7%)</td>
</tr>
<tr>
<td>36-45</td>
<td>Employs</td>
<td>Mecca area</td>
<td>11-20</td>
</tr>
<tr>
<td>3 (1.7%)</td>
<td>10 (5.7%)</td>
<td>5 (10.3%)</td>
<td>44 (25%)</td>
</tr>
<tr>
<td>46-55</td>
<td>Teaching staff</td>
<td></td>
<td>21-40</td>
</tr>
<tr>
<td>4 (2.3%)</td>
<td></td>
<td></td>
<td>43 (24.6)</td>
</tr>
<tr>
<td>Total</td>
<td>175 (100%)</td>
<td>175 (100%)</td>
<td>175 (100%)</td>
</tr>
</tbody>
</table>

Table 2. Cytopathological diagnosis and smoking habit among study group

<table>
<thead>
<tr>
<th>Cytopathological changes</th>
<th>Smoking</th>
<th>Duration of smoking / years</th>
<th>Passive smoking exposure</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Smoker N (%)</td>
<td>None N (%)</td>
<td>&lt;5 years N (%)</td>
<td>&lt;5 years N (%)</td>
</tr>
<tr>
<td>Negative</td>
<td>32(42.6)</td>
<td>38(22.3)</td>
<td>36(21.2)</td>
<td>47 (27.7)</td>
</tr>
<tr>
<td>Inflammation</td>
<td>19(11.2)</td>
<td>7(4.1)</td>
<td>6(3.5%)</td>
<td>14(8.2)</td>
</tr>
<tr>
<td>Mild dyskerosis</td>
<td>16 (9.4)</td>
<td>2 (1.2)</td>
<td>2 (1.2)</td>
<td>5 (3.0)</td>
</tr>
<tr>
<td>Metaplastic changes</td>
<td>3 (1.8)</td>
<td>1 (0.6)</td>
<td>10 (6.0)</td>
<td>2 (1.1)</td>
</tr>
<tr>
<td>Moderate dyskerosis</td>
<td>8 (4.8)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Severe Dyskerosis</td>
<td>2 (1.2)</td>
<td>1 (0.6)</td>
<td>10 (6.0)</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>Total</td>
<td>120 (71.1)</td>
<td>49 (28.9)</td>
<td>46 (27.1)</td>
<td>69 (40.7)</td>
</tr>
</tbody>
</table>

P value=0.024 P value=0.0001 P value=0.000
Inadequate sample= 6 (3.4%)

Table 3: Data analysis

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable form</td>
<td>OR 95% CI P</td>
<td>OR 95% CI P</td>
</tr>
<tr>
<td>Age</td>
<td>1.0</td>
<td>0.9b 1.0</td>
</tr>
<tr>
<td>Smoking</td>
<td>4.1</td>
<td>4.1b 14.2</td>
</tr>
<tr>
<td>Duration of the smoking</td>
<td>3.1</td>
<td>3.6b 5.8</td>
</tr>
<tr>
<td>Passive smoking</td>
<td>2.9</td>
<td>1.7b 5.1</td>
</tr>
<tr>
<td>Occupation</td>
<td>1.4</td>
<td>0.7b 2.5</td>
</tr>
</tbody>
</table>
Figure 1: showed Frequency of Cytopathological changes

Papanicolaou stain of inflammatory cell sputum (original magnification X400)

Alveolar macrophage in the sputum (original magnification X400)

Papanicolaou stain of squamous metaplastic in the sputum (original magnification X400)

Papanicolaou stain of severe dyskerosis in the sputum (original magnification X400)
1.4.1 Discussion

This is the first attempt to study cytological changes in order to demonstrate the association between cigarette smoking and cytopathological changes in the Kingdom of Saudi Arabia (KSA), as far as the authors know. Passive smoking could be more harmful than directly inhaled smoke\textsuperscript{(3,4)}. Results of this study conducting a sputum cytology screening among university students reveal many cytological abnormalities among our participants with smoking duration more than five years and those exposed to passive smoking. A finding of particular interest was the proportion of participants who presented abnormal cytological changes; their occurrence percentage (mild, moderate, metaplastic and severe dyskerosis) was 17.1\% for different cytological abnormalities.

Many previous studies have reported that individuals with these cytological changes are at high risk for the development of lung cancer\textsuperscript{(4,5,6)}. Our study population represents a group of active and passive smokers who could ultimately benefit from routine cytology-based screening for this disease. It is well known that persons diagnosed with lung cancer by sputum cytology have better outcomes in terms of treatment and survival\textsuperscript{(14,15)}.

Similar findings have also been reported in other studies that assess cytopathological changes in patients with clinical suspicious of lung cancer who were diagnosed clinically\textsuperscript{(15)}. During this work we could not obtain sputum samples from patients with clinical symptoms of chest diseases, as this study was mainly screening. Future studies are needed to include these important groups in screening in order to put base for screening program. Both univariate and multivariate analysis suggest that smoking habit increased the severity of cytological diagnosis, and that those individuals with mild to moderate dyskerosis were more likely to be active and/or passive smokers compared to those with normal sputum cytology. Definitive explanations for these unanticipated findings are not possible at this time due to the relatively small study sample size and limitations in the types of data that were collected. A potentially important data omission was information on clinical symptoms. Many individuals either quit smoking or reduced their cigarette consumption rate after the onset of respiratory symptoms linked with the effects of long-term smoking on the lungs (cough, wheezing, and sputum production). Accordingly, there may have been a higher prevalence of such
symptoms in those study participants who were passive, or who had attempts of smoking history. Such symptoms could have an influence on cytological outcome. Future studies are needed to further evaluate this issue. In general, smokers and participants of the screening program need to be offered annual sputum cytological examinations as well as being monitored for changes in clinical status. Moreover, screening program participants with cytology of moderate to severe dyskerosis and metaplastic changes are advisable to be subjected to lung cancer early detection methods. Many of these methods require collections of other samples, e.g., urine, serum, sputum, bronchial biopsy material and brushings, and tumor tissue if needed. The data that will emerge from these assessments will provide new information on the prognostic significance of cytological changes that is needed in pre- and early lung neoplasia. Due to the high yield of abnormal cytology findings in our study sample among university students with different smoking habits (current smokers and passive smokers), this study recommends that such individuals be considered as suitable volunteers for research investigations focusing on lung cancer prevention and early detection.

1.4.2 Conclusions and recommendations

The initiation of a sputum cytology screening program is recommended as this study concluded that smokers and passive smokers have a high prevalence of premalignant dyskerosis that is detectable through sputum cytology, and should be targeted for research programs focusing on lung cancer prevention. Early detection and exploratory biomarker studies as well as application of screening sputum cytology on large scales is highly recommended for early diagnosis and improved prognosis.
REFERENCES


