

## Oxidative stress related organ damage assessed using the serum Ischemia Modified albumin levels and Malondialdehyde among male cigarette smokers

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### Abstract:

**Introduction:** Cigarette smoking induces lung inflammation, repeated injury and followed by repair. The oxidative stress and an excess of proteinase in lung further modify lung inflammation. This increase in oxidative stress can be seen as the change in levels of markers like lipid peroxidation and oxidative protein products. **Aim:** The present study aimed to measure and correlate the serum levels of Ischemia Modified Albumin (IMA) with Malondialdehyde (MDA) in cigarette smokers and non-smokers. **Material and Methods:** The present study was conducted at Father Muller Medical College hospital, Mangalore. A total of 480 individuals are recruited for the study after taking the informed consent. Subjects were divided into two groups, Group-I: 340 male healthy smokers aged between 20-60yrs, who smoked cigarette more than 10 each day and Group-II: Included 140 number of age sex matched healthy non-smokers. **Results:** Total number of 480 subjects were selected for the study & grouped into case which are cigarette smokers (n=340) and controls as non-smokers (n=140). There is a significant higher mean of IMA and MDA among the smokers compared to non-smokers. ( $p < 0.001$ ) The strength of association of MDA and IMA with the spirometry is negative with significant good strength of association, whereas a significantly great strength of association is found between the oxidative marker like the MDA and the IMA in the blood levels of the individuals ( $r = 0.912$ ). The Receiver Operator Characteristics (ROC) graph has shown a good relation to identify the spirometric changes using both the variables as the biomarkers with AUC (Area under the ROC curve) of 0.761 & 0.745 for MDA and IMA respectively in the plasma of the study individuals. **Conclusion:** The present study found a significant higher mean level of MDA and IMA among the smokers compared to non-smokers, with these markers predicting the oxidative stress among the smokers.

**Keywords:** Ischemia Modified Albumin (IMA), Malondialdehyde (MDA), Smoker, Oxidative stress.

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### I. Introduction:

Smoking is most common among the men aged 15 and above accounting for 51%. Globally about 18% of adolescent boys use tobacco. Smoking is one among the most important risk factor for developing chronic obstructive pulmonary disease (COPD).<sup>1</sup> In India, an estimated 82.3% males with COPD are smokers.<sup>2</sup> Tobacco specific nitrosamines (TSNs) are recognised carcinogens that can have a direct mutagenesis effect on human oral mucosal cells in both smoking and smokeless forms. Cell culture studies have shown that, in addition to carcinogenic TSNs, reactive oxygen species (ROS) produced from tobacco and oxidative DNA damage are important in the pathophysiology of tobacco-induced malignancies. These radicals contribute to the formation of cancer by inducing DNA damage, activating procarcinogens, changing the cellular antioxidant defence system, and acting as initiators and/or promoters of carcinogenesis.<sup>3,4</sup> Oxidative stress via free radical generation in smokers has been widely investigated, as they cause lipid peroxidation, oxidation of proteins and even damage to tissues mainly Lung.<sup>5</sup>

Cigarette smoking induces lung inflammation, repeated injury and followed by repair. The oxidative stress and an excess of proteinase in lung further modify lung inflammation. This increase in oxidative stress can be seen as the change in levels of markers like lipid peroxidation and oxidative protein products. Malondialdehyde (MDA) is one of the markers for assessing the free radical induced lipid peroxidation.<sup>6</sup> Ischemia Modified Albumin (IMA) is a new protein that has been widely explored in ischemic heart disorders, and its assessment for the amount of myocardial ischemia has been authorised by the Food and Drug Administration (FDA). The present study aimed to measure and correlates the serum levels of IMA with MDA in cigarette smokers and non-smokers with the changes in the pulmonary function.

## II. Material and Methods:

Study was conducted at Father Muller medical college hospital, Mangalore, Karnataka, India, total of 480 individuals are recruited for the study after taking the informed consent for the duration of 1 year from June 2015-May 2016. Subjects were divided into two groups, Group-I: 340 male healthy smokers aged between 20-60yrs, who smoked cigarette more than 10 each day and Group-II: Included 140 number of age sex matched healthy non-smokers. The subject with Diabetes Mellitus, Chronic alcoholism, asthma, Chronic kidney disease (CKD), and other systemic illnesses were excluded from the study. 2ml blood was collected with necessary aseptic precautions from all the study subjects and subjected for centrifugation at 3000rpm for 10-12 mins, the serum was used for analysis of the parameters, which include the Serum Malondialdehyde (MDA) is quantified by Thiobarbituric acid (TBA) method,<sup>10</sup> and serum Ischemia Modified Albumin (IMA) by Albumin Cobalt binding method,<sup>8</sup> based on spectrophotometer, in UV visible spectrophotometer (Systronics 117), the lung function is assessed using the spirometer EasyOne<sup>TM</sup>.<sup>9</sup> The present study was approved by the Institutional Ethics Committee (IEC) for the final permission.

### Statistical analysis:

Statistical analysis was performed using the institutional licensed SPSS version 23. The Descriptive data is given as Mean, standard deviation (SD), the mean difference was analysed using unpaired student t-test and Pearson's correlation to assess the strength of association between the variables.

## III. Results:

Total number of 480 subjects were selected for the study & grouped into case which are cigarette Smokers (n=340) and controls as non-smokers (n=140)(Table 1). With mean age of participants was 45.62 yrs of age with no significant difference in the mean between the groups. There is a significant higher mean of IMA and MDA among the smokers compared to non-smokers(p<0.001)(Table 2).

**Table 1:** Agewise distribution of study subjects.

| Age in years | Smokers<br>(n=340) | Non-smokers<br>(n=140) |
|--------------|--------------------|------------------------|
| 20 – 30      | 62                 | 27                     |
| 31 – 40      | 97                 | 48                     |
| 41 - 50      | 121                | 42                     |
| 51 – 60      | 60                 | 23                     |
| Total        | 340                | 140                    |

**Table 2:** Showing the descriptive details and t-test result of IMA and MDA in smokers and Non-smokers

|  | Smokers      | Non-smokers  | p Value | Significance |
|--|--------------|--------------|---------|--------------|
| Age in years   | 45.4±12.0    | 46.1±11.0    | 0.654   | NS           |
| MDA(nmol/dL)   | 926.6±253.57 | 301.2±100.38 | <0.001  | HS           |
| IMA (ABSU)   | 0.516±0.022  | 0.322±0.030  | <0.001  | HS           |
| Spirometry-FEV <sub>1</sub> (%)  | 77.6 ± 7.9   | 58.5 ± 12.0  | <0.001  | HS           |
| The above table showing the t-test result of MDA & IMA in smokers and non-smoker showing the mean difference which is significant. p value <0.001.<br>HS: Highly significance (HS)<br>IMA- Ischemia Modified albumin<br>MDA- Malondialdehyde |              |              |         |              |

The strength of association of MDA and IMA with the spirometry is negative with significant good strength of association, whereas a significantly great strength of association is found between the oxidative marker like the MDA and the IMA in the blood levels of the individuals (r=0.912) (Table 3 & Figure 1).

| Table 3: Showing the strength of association among the variables in smokers and non-smokers |            |                         |                      |         |
|---|------------|-------------------------|----------------------|---------|
|   |            | r (Pearson correlation) | R <sup>2</sup> value | p-value |
| MDA   | IMA        | 0.912*                  | 0.831                | <0.001  |
| MDA   | Spirometry | -0.604*                 | 0.419                | <0.001  |
| IMA   | Spirometry | -0.648*                 | 0.364                | <0.001  |

Above table showing the strength of association by Pearson correlation between the IMA, MDA & spirometric changes in smokers and non-smokers.  
 IMA- Ischemia Modified albumin  
 MDA- Malondialdehyde

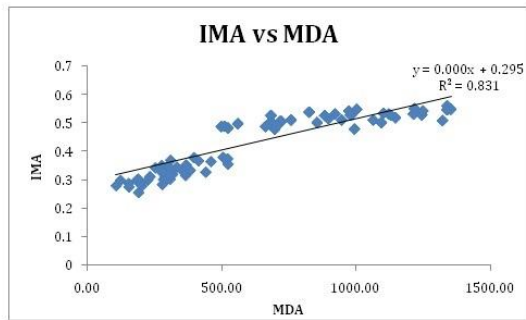


Fig 1A

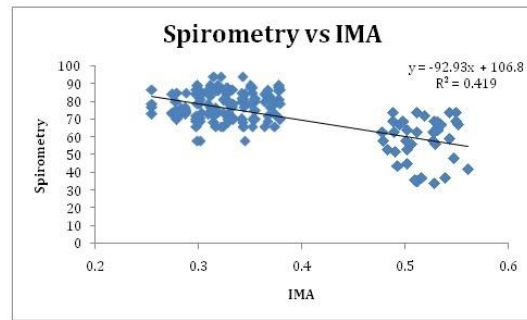


Fig 1B

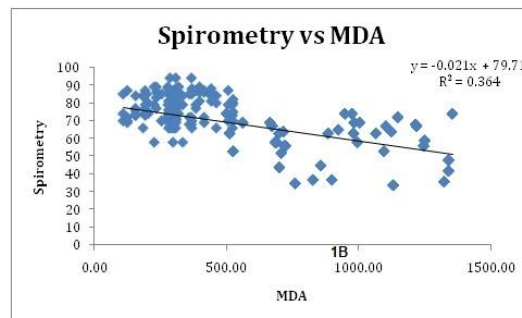
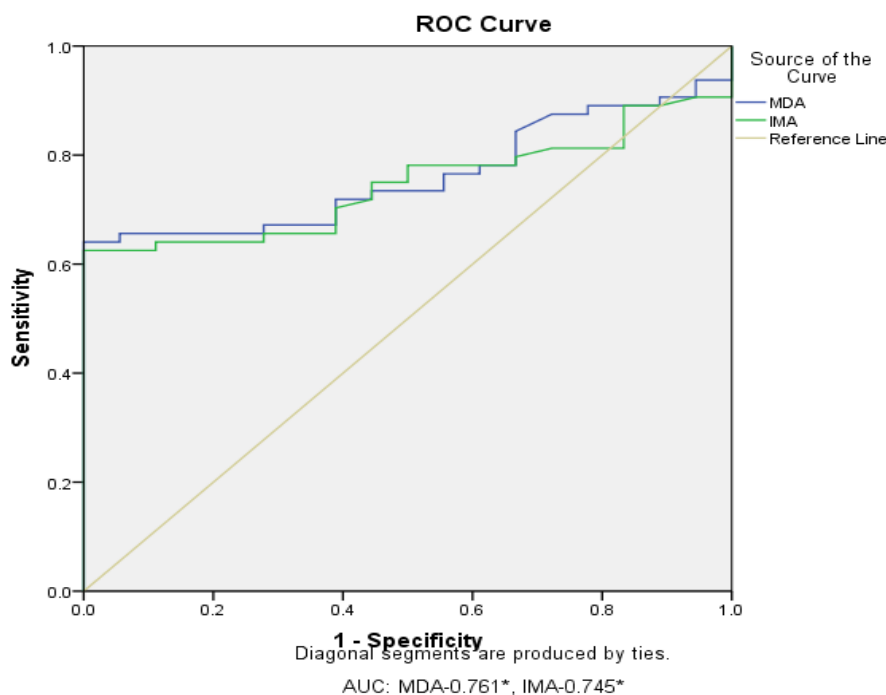


Fig 1C

**Figure 1:** 1A-regression analysis between the MDA and IMA ( $R^2=0.831$ ); 1B - regression analysis showing the relation of IMA with spirometry changes ( $R^2=0.419$ ); 1C – regression analysis showing the relation of MDA with spirometry changes ( $R^2=0.364$ ).

The ROC has shown a good relation to identify the Spirometric changes using both the variables as the biomarkers with AUC of 0.761 & 0.745 for MDA and IMA respectively in the plasma of the study individuals (Figure 2).



**Figure 2: ROC graph representing the relation between IMA and MDA among study subjects.**

#### IV. Discussion:

Co-relation between the oxidative stress and the smoking of cigarette with the acute and the chronic complication is an established relation from the long time.<sup>10</sup> Heavy tobacco smokers have the higher incidence of the cardiac events, peripheral vascular diseases, and the compromise in the lung capacity due to the damage related to the oxidative stress and the reactive oxygen (ROS) in the cases. It's always a need for the time to use the markers to identify extent of the oxidative damage in the person with the cigarette smoking. The lipid peroxidation is measured using the MDA levels in the person, the smokers on hand has the higher level of the MDA when compared to the non-smokers. This correlate with the various studies which assessed MDA as the oxidative markers.<sup>6</sup> The Possibility of the damage caused by the cigarette smoking is due the formation of the ROS in the smokers in excess when compared to the non-smokers. The generation of the ROS will modify the N-terminal region of the Albumin, leading to increased levels of the IMA.<sup>8</sup> As a result, additional research in this area is required, using more sensitive methodologies and more standardised circumstances, to corroborate the findings of this study and show that IMA might be an early marker of tobacco-related oxidative stress.

**Limitations of the study:** Study has limitations which include, it being a single centric study with male participants only. Findings of the study can be generalised by conducting larger multicentric study including participants of both gender.

#### V. Conclusion:

Study found a significant higher mean level of MDA and IMA among the smokers compared to non-smokers, with these markers predicting the oxidative stress among the smokers. The IMA and MDA levels are an important marker that is elevated after exposure to tobacco which cause oxidative stress. Apart from the pulmonary diseases, smokers are at the higher risk at cardiovascular diseases, cancer and other illnesses.

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