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TO STUDY THE EFFECT OF EXPOSURE TO FORMALDEHYDE IN DISSECTION HALL ON PULMONARY FUNCTION TESTS OF 1ST YEAR MBBS STUDENTS

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ABSTRACT: Introduction: 1st year M.B.B.S. students are exposed to Formaldehyde, used as a component of embalming mixture for Anatomy Dissection classes and to preserve organ specimen. Formaldehyde is known to cause irritation of respiratory tract and causes inflammation, mediators released like histamine, serotonin cause contraction of smooth muscle of bronchi. Lung Function Tests such as FVC, FEV1, and FEV1/FVC % are used to analyze respiratory health since they are reliable indices that aid in early detection of pulmonary disorders. **Materials and Methods:** The effect of formaldehyde (due to exposure to formalin) with respect to 3 parameters (FVC, FEV1 & FEV1/FVC%) of Pulmonary Function Tests among 150 healthy first year M.B.B.S. students aged 17 to 23 years (72 Females, 78 Males) was studied in the Physiology Department of Government Medical College, Patiala from December 2022 to December 2023. Spirometry was performed at the beginning of the session (before the start of anatomy dissection or classes on preserved organ specimen) to get the pre-exposure (0 month) values of FVC, FEV1 & FEV1/FVC% and then followed-up after 1, 5 & 9 months of exposure. **Results:** Although the range of data and means (both pre- and post-exposure) remained within physiological limits, MAXIMUM REDUCTION of mean with shift of the entire range of data was observed AT 1 MONTH OF EXPOSURE (along with an increase in the no. of students in "HIGH RISK" category & a decrease in "SAFE" category), w.r.t. all 3 PFT parameters. Thereafter, some amount of tolerance was observed, PFT parameters progressively increasing after 5 months & 9 months of exposure (along with a decrease in the no. of students in "HIGH RISK" category & an increase in "SAFE" category), though still not fully returning back to pre-exposure level till 9 months, w.r.t. all 3 PFT parameters studied. **Conclusion:** In this study, we found statistically significant effect of inhalation of formaldehyde vapours on Pulmonary Function Tests (FVC, FEV1, and FEV1/FVC %) of 150 healthy subjects studying in 1st year MBBS (aged 17 to 23 years) due to exposure to formalin during Anatomy Dissection and classes on preserved organ specimen. Although the range of data and means (both pre- and post-exposure) remained within physiological limits, the general trend in our study shows maximum reduction of mean with deviation of the entire range of data at 1 month of exposure. Thereafter, the trend showed some amount of tolerance progressively after 5 months & 9 months of exposure, but still not fully returning back to pre-exposure level till 9 months, having a statistically highly significant difference w.r.t. all 3 PFT parameters studied (FVC, FEV1, and FEV1/FVC%), before exposure vs after 1, 5 & 9 months of exposure to formaldehyde among females as well as males.

INTRODUCTION: 1st year M.B.B.S. students are exposed to Formaldehyde, used as a component of

embalming mixture for Anatomy Dissection classes and to preserve organ specimen. Formaldehyde is known to cause irritation of respiratory tract and causes inflammation, mediators released like histamine, serotonin cause contraction of smooth muscle of bronchi. The vapours when inspired, bind to endogenous proteins forming haptens which trigger immune response in the respiratory tract leading to spasm of smooth muscles

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(bronchoconstriction due to hypersensitivity reaction) and can cause obstructive symptoms. It often penetrates lung parenchyma, damages it and also results in restrictive conditions^{19, 35}. Formaldehyde vapours are adsorbed on dust particles. When they reach a critical size, they can enter the lung parenchyma, change the lungs' cytoarchitecture, and occasionally cause damage to Type II pneumocytes. This results in a decrease in surfactant release, an increase in surface tension, and an overall reduction in the ease of airflow. The respiratory tract's mucociliary clearance is frequently reduced^{14, 18, 35, 41}. Lung Function Tests such as FVC, FEV1, and FEV1/FVC % are used to analyze respiratory health since they are reliable indices that aid in early detection of pulmonary disorders.

By turning ingested formaldehyde into formate, red blood cell enzymes promote the cross-linking of nucleic acids and amino acids, which ultimately results in cell death. The metabolism of formate produces carbon dioxide, which is then exhaled¹⁸. Immunological hypersensitivity, defined as elevated levels of circulating IgG and IgE autoantibodies against human serum albumin and a lower proportion of T-cells, indicating a changed immune response, is linked to long-term formaldehyde exposure^{13, 19}.

METHODOLOGY: The effect of formaldehyde (due to exposure to formalin) with respect to 3 parameters (FVC, FEV1 & FEV1/FVC%) of Pulmonary Function Tests among 150 healthy first year M.B.B.S. students aged 17 to 23 years (72 Females, 78 Males) was studied in the Physiology Department of Government Medical College, Patiala from December 2022 to December 2023. Students with pre-exposure PFT parameters beyond Physiological limits and those with potential confounding factors were excluded from the study.

OBSERVATIONS AND RESULTS:

Physiological Range	Females		Males		
	Lower Limit	Upper Limit	Lower Limit	Upper Limit	
FVC (L)	3.25	3.75	4.75	5.5	& ≥ 80% of Predicted FVC
FEV1 (L)	2.5	3.25	3.5	4.5	& ≥ 80% of Predicted FEV1
FEV1/FVC %	>70		>70		

Since FVC's or FEV1's *Normal Range for Females and Males do not overlap*, Females & Males had to be grouped SEPARATELY to get normal distribution (mean = median = mode) in each month, which is essential criteria for parametric (Quantitative) tests. Normal distribution was confirmed by Bell-shaped Frequency Distribution, Quantile-Quantile Plot & Normal Probability Plot, for the data-sets of all 3 parameters for females & males separately.

Spirometry was performed at the beginning of the session (before the start of anatomy dissection or classes on preserved organ specimen) to get the pre-exposure (0 month) values of FVC, FEV1 & FEV1/FVC% and then followed-up after 1, 5 & 9 months of exposure.

Study-subjects were selected by Random Sampling, with the following criteria:

Inclusion Criteria for Subject Selection:

- 1st year M.B.B.S. students (aged 17-23 years) in the academic year 2022-2023.
2. Healthy, non-smoker, BMI within normal limits ($18.5 \text{ kg/m}^2 - 24.9 \text{ kg/m}^2$).
3. Baseline Pre-Exposure FVC, FEV1 & FEV1/FVC Ratio within Physiological Limits (Table below).

Exclusion Criteria for Subject Selection:

1. Baseline Pre-Exposure FVC, FEV1 & FEV1/FVC Ratio NOT within Physiological Limits (Table below).
2. Smokers.
3. $\text{BMI} < 18.5 \text{ kg/m}^2$ or $\geq 25 \text{ kg/m}^2$.
4. Subjects suffering from respiratory ailments.
5. Subjects displaying apprehension, or having a with history of anxiety or depressive disorder.
6. Subjects with severe cardiopulmonary morbidity, neurological impairment, recent musculoskeletal injury and vocal cord dysfunction.
7. Subjects on bronchodilator medication.

Quantitative Analysis: Repeated Measures ANOVA & Bonferroni Post-hoc Tests were used to study the difference across 0, 1, 5 & 9 months of exposure to formaldehyde vapours w.r.t. all 3 PFT parameters, among females & males separately.

Paired t-Test was used to properly analyze at 1, 5 & 9 months of exposure (each at a time), the difference vs pre-exposure, w.r.t. all 3 PFT parameters, among females & males separately.

Since, the normal ranges for females & males are very different quantitatively, females vs males cannot be compared quantitatively, hence the need to define Statistical cut-offs for Qualitative Categorization within the Physiological range.

In the existing literature, categorization only exists in Pathological range, which is beyond the scope of this study.

For Qualitative Categorization within the Physiological range, 2 Statistical Cut-offs based on pre-exposure data-set were established for this study, w.r.t. each PFT parameter (FVC, FEV1 & FEV1/FVC %) as:

☐ “Lower Cut-off” at (Mean – 2 SD) of Pre-exposure data-set

Thresholds for statistical significance				
P-value < 0.01	:	Statistically Highly Significant	:	Confidence > 99 %
0.01 ≤ P-value < 0.05	:	Statistically Significant	:	99 % ≥ Confidence > 95 %
0.05 ≤ P-value	:	Statistically Insignificant	:	95 % ≥ Confidence

Results: Although the range of data and means (both pre- and post-exposure) remained within physiological limits, maximum reduction of mean with shift of the entire range of data was observed AT 1 month of exposure (along with an increase in the no. of students in “HIGH RISK” category & a decrease in “SAFE” category), w.r.t. all 3 PFT parameters.

Thereafter, some amount of tolerance was observed, PFT parameters progressively increasing after 5 months & 9 months of exposure (along with a decrease in the no. of students in “HIGH RISK” category & an increase in “SAFE” category), though still not fully returning back to pre-exposure level till 9 months, w.r.t. all 3 PFT parameters studied as shown in **Diagram 1, 2, 3, 4.**

☐ “Upper Cut-off” at (Mean – 1 SD) of Pre-exposure data-set

For Females and Males separately, thereby dividing each month’s data-set into three Qualitative Categories within the Physiological range, henceforth “nicknamed” as:

☐ “HIGH RISK” (< “Lower Cut-off”)

☐ “LOW RISK” (≥ “Lower Cut-off” & < “Upper Cut-off”)

☐ “SAFE” (≥ “Upper Cut-off”).

Qualitative Analysis: Chi-Square (χ^2) Test was used to compare the association of females vs males with poor tolerance to formaldehyde inhalation in a particular month.

McNemar Test was used to study month vs month change (1/5/9 vs 0 month) within a particular gender-group.

Study Period	:	From December, 2022 to December, 2023.
Statistical Tools	:	SPSS software, DataTab application, Microsoft Excel.

Quantitative Analysis: Repeated Measures ANOVA & Bonferroni Post-hoc Tests showed highly significant difference w.r.t. all 3 PFT parameters, across 0, 1, 5 & 9 months of exposure to formaldehyde vapours among females as well as males as shown in **Diagram 1, 2, 3, 4.**

Quantitative Analysis: Paired t-Test showed highly significant difference w.r.t. all 3 PFT parameters, before exposure vs after 1, 5 & 9 months of exposure to formaldehyde vapours among females as well as males as shown in **Diagram 1, 2, 3, 4.**

Qualitative Analysis: McNemar Test (same group, before vs after):

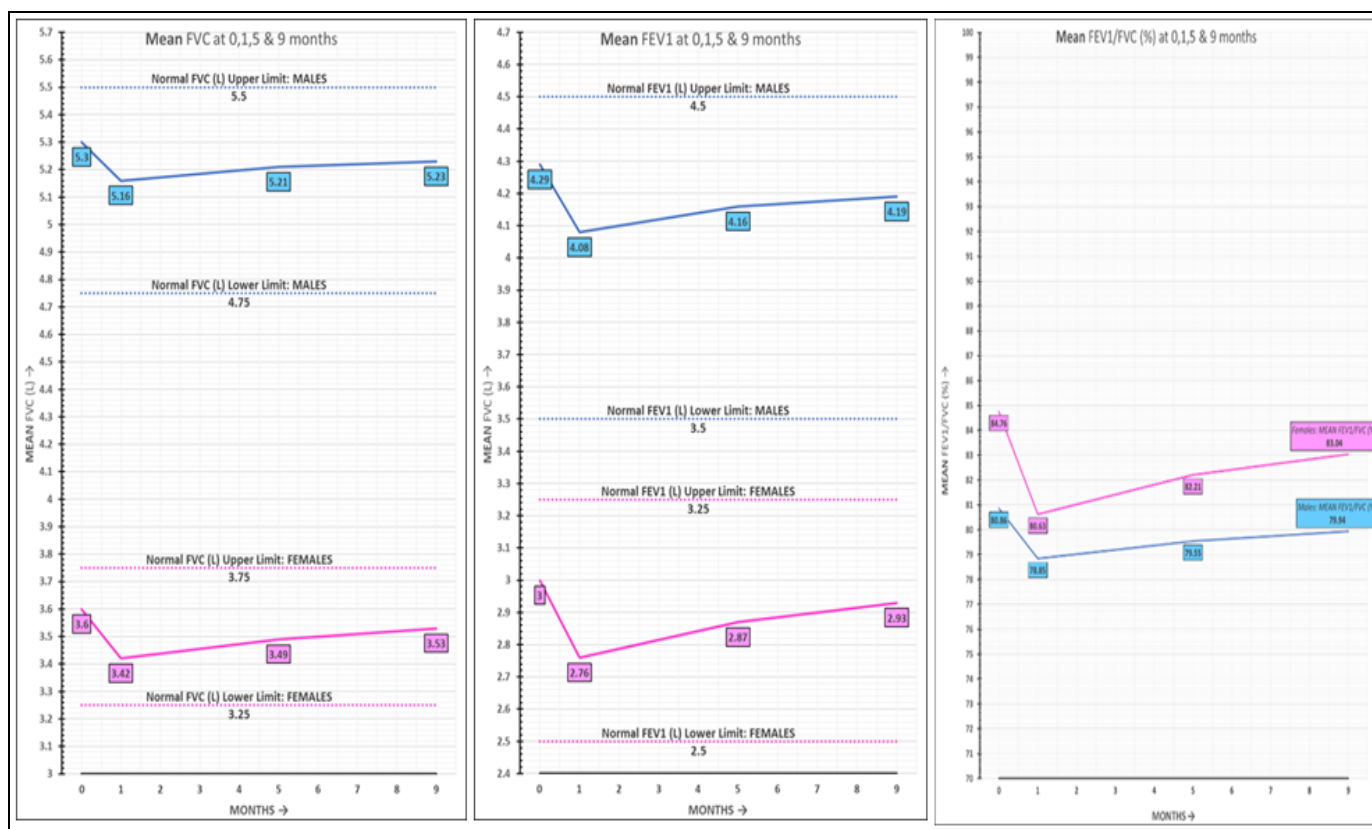


DIAGRAM 1: THE GENERAL TREND SHOWS MAXIMUM DEVIATION OF MEANS AT 1 MONTH OF EXPOSURE AND THEREAFTER SHOWING SOME AMOUNT OF TOLERANCE, ALTHOUGH STILL NOT FULLY RETURNING BACK TO PRE-EXPOSURE LEVELS TILL 9 MONTHS. Note: In the case of FVC & FEV1, Means are higher for Males than Females. In the case of FEV1/FVC %, the range of values from 0 Month to 9 Month for Females (77% to 87%) & Males (77% to 82%) Overlap with each other. However, the Mean for Males was 4.6 % less than the Mean for Females at 0 Month, 2.2 % less at 1 Month, 3.8 % less at 5 Month & 3.7 % less at 9 Months. Although within physiological limits, this SLIGHTLY less FEV1/FVC % for Males, EVEN PRE-EXPOSURE (at 0 Month), is probably due to some amount of Pulmonary Obstructive tendency (vs Females) caused by (1). Increased exposure to vehicular air pollution; (2). Although tobacco smokers (more prevalent among Males) were already excluded from this study, some students may not have disclosed their smoking habit and (3). Passive smokers (more prevalent among Male hostellers) couldn't be excluded from the study.

DISCUSSION:

Comparison with Existing Literature:

FVC: The results of our study are in ACCORDANCE with Shrivastava *et al* 13, Dhar *et al* 14, Kumar *et al* 17, Hajra *et al* 37, Patil *et al* 39, Dehagi *et al* 41 and Anjum *et al* 43 who concluded there was a significant decrease in FVC after 1 month of exposure to formaldehyde in anatomy dissection hall and then gradually it returned back towards normal value in subsequent months due to adaptive compensatory changes in respiratory system. Our results are also in Accordance with study by Khanzadeh *et al* 30 which reported a significant decrease in FVC following exposure to formaldehyde in anatomy dissection hall. The results are in CONTRAST to findings of Chia *et al* 29 & Raharjo *et al* 42 which showed no significant difference in pre- and post-exposure mean FVC.

The results are also in CONTRAST to findings of Mankar *et al* 38 in which the male group of students showed no significant change in FVC after exposure, while the female group did.

FEV1: The results of our study are in ACCORDANCE with Shrivastava *et al* 13, Dhar *et al* 14, Kumar *et al* 17, Hajra *et al* 37, Patil *et al* 39, Dehagi *et al* 41 and Anjum *et al* 43 who concluded there was a significant decrease in FEV1 after 1 month of exposure to formaldehyde in anatomy dissection hall and then gradually it returned back towards normal value in subsequent months due to adaptive compensatory changes in respiratory system. The results are also in Accordance with Khanzadeh *et al* 30. It showed a significant decrease in FEV1 following exposure to formaldehyde in anatomy dissection hall.

The results are in Contrast with findings of Chia *et al*²⁹, which showed no significant difference in pre- and post-exposure mean FEV1. The results are in Accordance with Mohammadpour *et al*³⁴ who concluded insignificant variation when comparing FEV1 between boys and girls.

FEV1/FVC%: The results of our study are in ACCORDANCE with Shrivastava *et al*¹³, Dhar *et al*¹⁴ and Anjum *et al*⁴³ who concluded there was a significant decrease in FEV1/FVC% after 1 month of exposure to formaldehyde in anatomy dissection hall and then gradually it returned back towards normal value in subsequent months due to adaptive compensatory changes in respiratory system. Our results are also in Accordance with Khanzadeh *et al*³⁰ who reported a significant decrease in FEV1/FVC% following acute exposure to

formaldehyde in anatomy dissection hall. Our results are in Contrast to those of Binwara *et al*³³, Suhas *et al*³⁶, Patil *et al*³⁹, which demonstrated no significant alteration in FEV1/FVC% following acute formalin exposure.

Our study is also in Contrast to Kumar *et al*¹⁷ who concluded an increase in FEV1/FVC%. Our results are in Accordance with Mohammadpour *et al*³⁴ who concluded insignificant variation when comparing FEV1/FVC% between boys and girls

FVC Summary: The general trend shows maximum deviation of Mean & the entire Range of Data at 1 month of exposure & thereafter showing some amount of TOLERANCE, although still not fully returning back to Pre-Exposure level till 9 months.

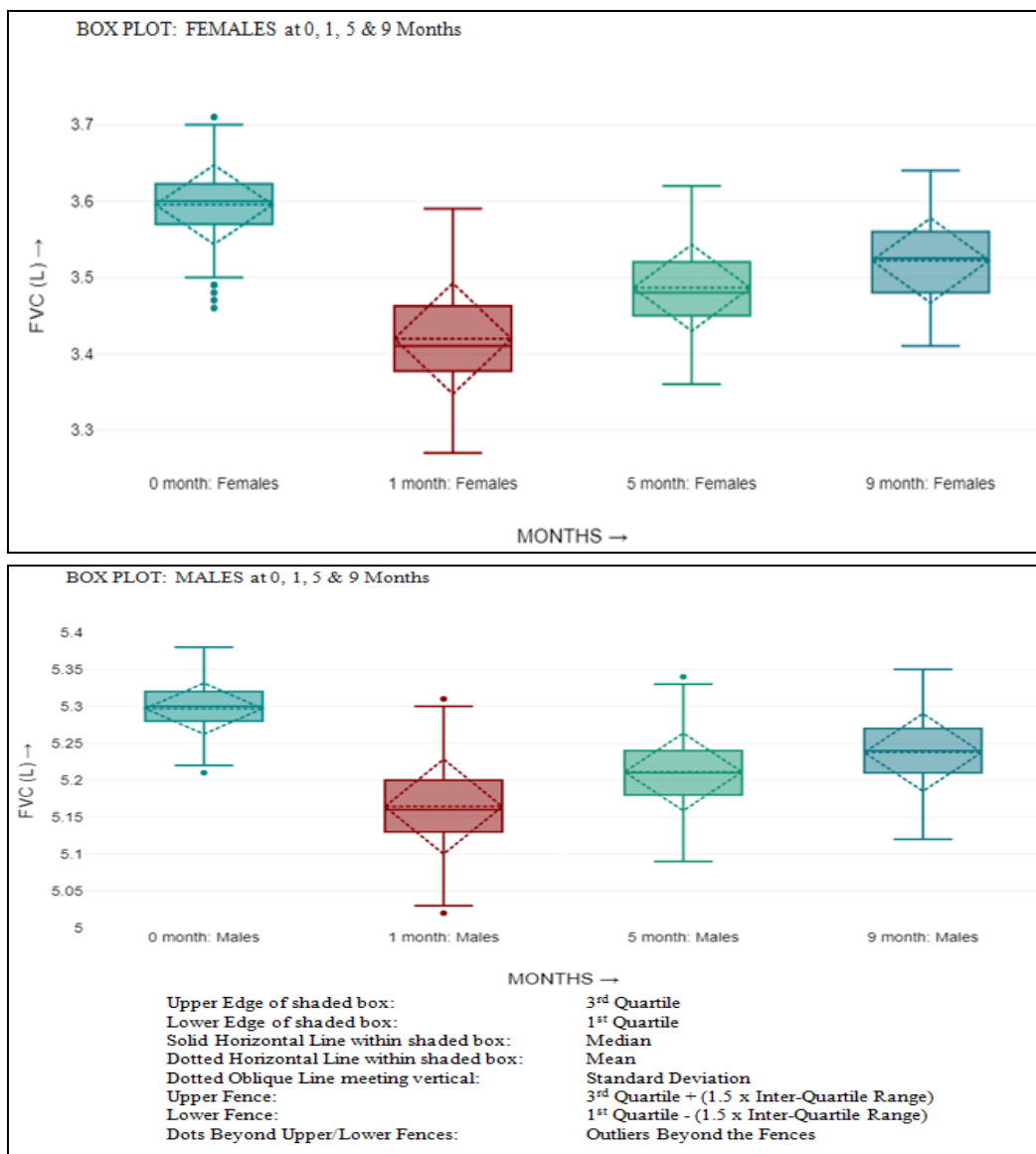


DIAGRAM 1: FVC

FEV1 Summary: The general trend shows maximum deviation of Mean & the entire Range of Data at 1 month of exposure & thereafter showing

some amount of TOLERANCE, although still not fully returning back to Pre-Exposure level till 9 months.

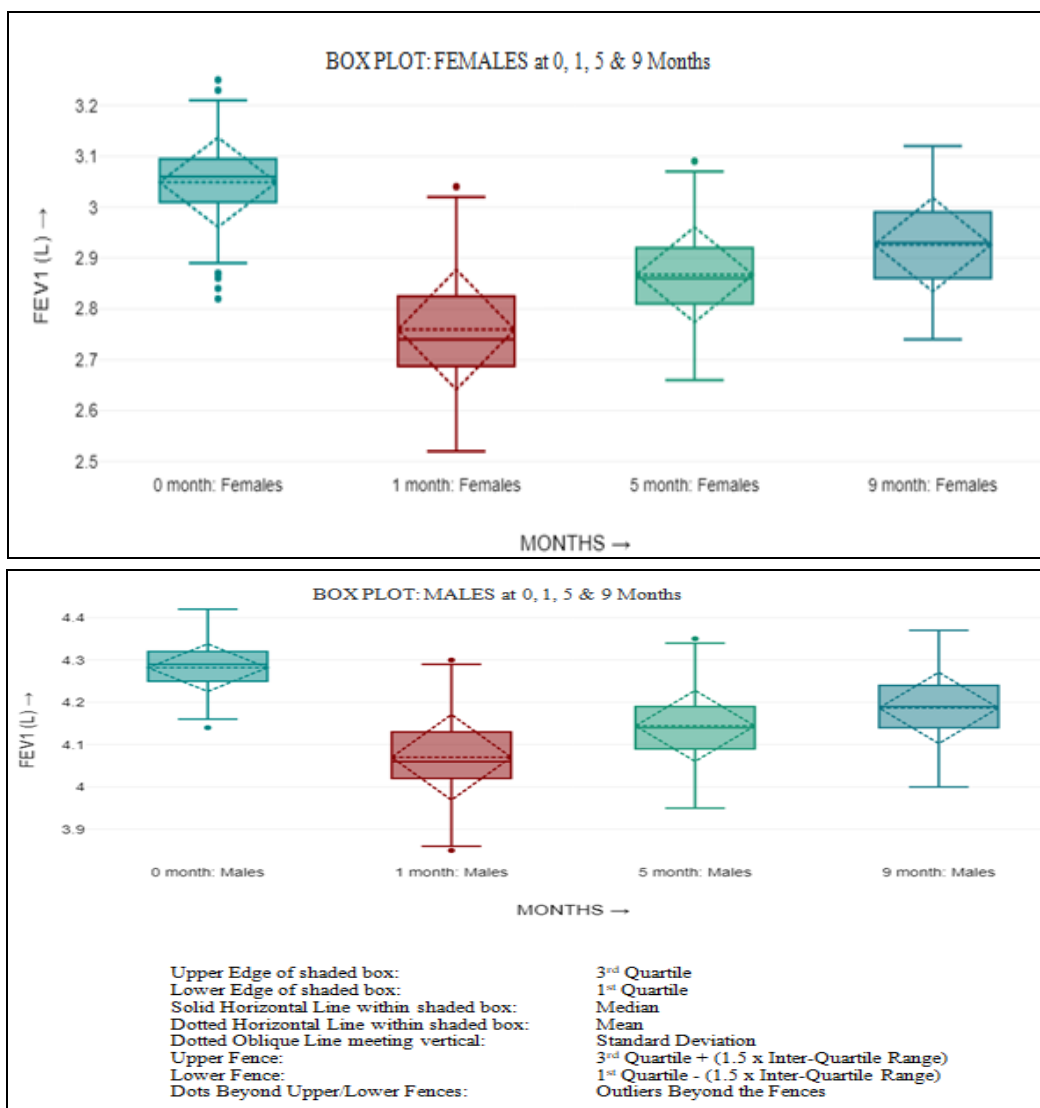


DIAGRAM 2: FEV1

FEV1/FVC % Summary: The general trend shows maximum deviation of Mean & the entire Range of Data at 1 month of exposure & thereafter showing some amount of TOLERANCE, although still not fully returning back to Pre-Exposure level till 9 months.

Similar results were reported by many studies like immediate and long-term health hazards linked to exposure to formaldehyde, specifically its contribution to the exacerbation of pulmonary inflammatory conditions like asthma and bronchitis⁴⁶. Another study suggested that even low-dose formaldehyde exposure in occupational settings is associated with a higher prevalence of allergic

rhinitis, allergic dermatitis, and irritation-related symptoms, particularly among workers with higher relative exposure levels⁴⁷. Another study suggested that Formaldehyde, a well-known carcinogen and prevalent indoor air pollutant found in household products, poses risks of chronic inhalation leading to Upper respiratory tract injuries⁴⁸. Another recent study suggested high prevalence of respiratory symptoms, such as cough and wheezing among hospital laboratory staff thus emphasizing the importance of continuous exposure monitoring and the implementation of effective control measures in hospital laboratory departments with formaldehyde emission⁴⁹.

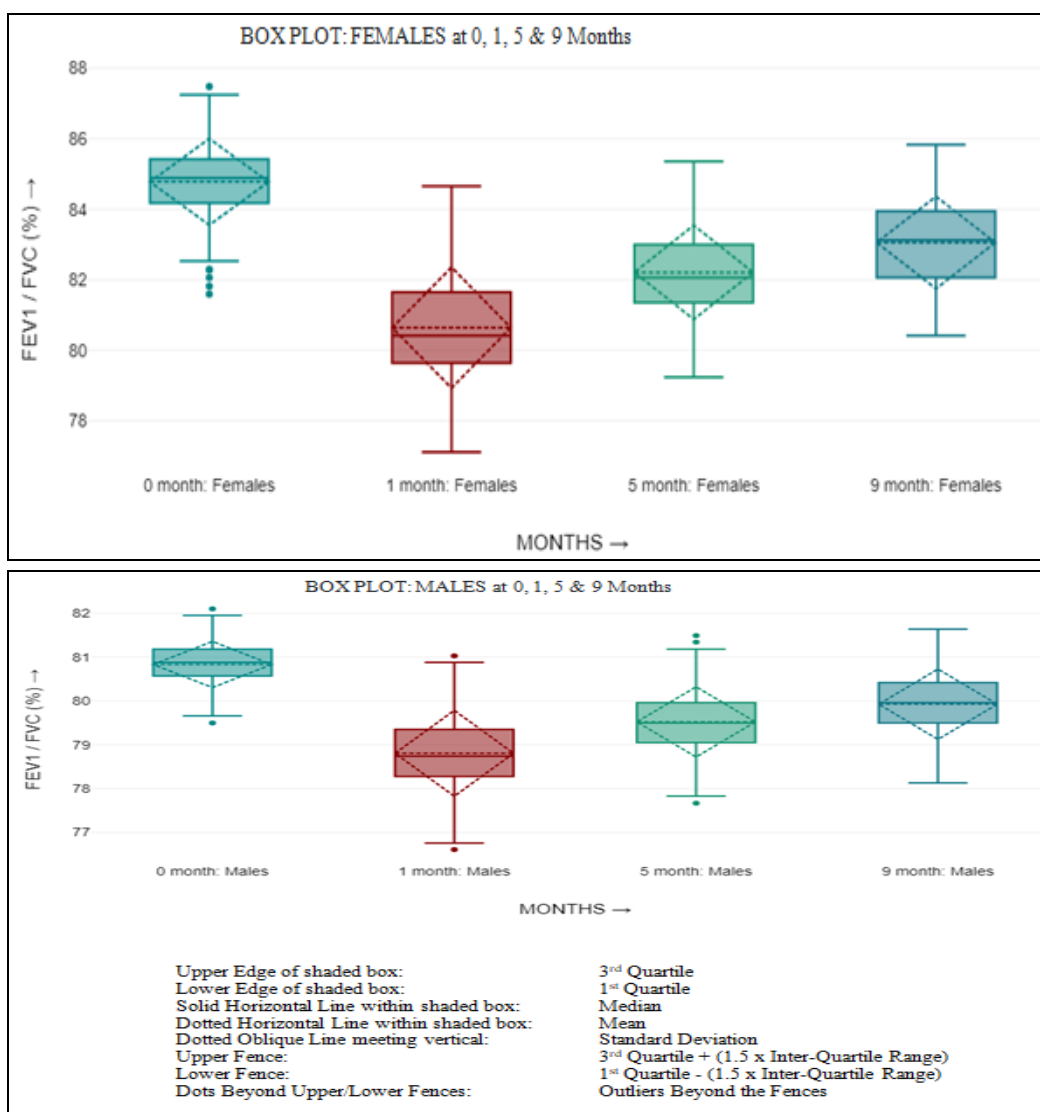


DIAGRAM 3: FEV1/FVC%

CONCLUSION: In this study, we found statistically significant effect of inhalation of formaldehyde vapours on Pulmonary Function Tests (FVC, FEV1, and FEV1/FVC %) of 150 healthy subjects studying in 1st year MBBS (aged 17 to 23 years) due to exposure to formalin during Anatomy Dissection and classes on preserved organ specimen.

Although the range of data and means (both pre- and post-exposure) remained within physiological limits, the general trend in our study shows maximum reduction of mean with deviation of the entire range of data at 1 month of exposure. Thereafter, the trend showed some amount of tolerance progressively after 5 months & 9 months of exposure, but still not fully returning back to pre-exposure level till 9 months, having a statistically highly significant difference w.r.t. all 3

PFT parameters studied (FVC, FEV1, and FEV1/FVC %), before exposure vs after 1, 5 & 9 months of exposure to formaldehyde among females as well as males.

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CONFLICTS OF INTEREST: Nil

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