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Original Article

Haematology Section

The Red Cell Distribution Width as a Sensitive Biomarker for Assessing the Pulmonary Function in Automobile Welders- A Cross Sectional Study

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ABSTRACT

Context: Welding fumes are considered as a risk factor for pulmonary diseases and a periodic spirometry is essential to evaluate the lung function of the welders. The Red Cell Distribution Width (RDW) is a red cell measurement which is provided by automated haematology analyzers. It reflects the range of the red cell sizes which are measured within a sample. Few studies have shown a relationship between the RDW values and the changes in the spirometry.

Aims: This study was aimed at correlating the RDW% and the spirometry FEV1/FVC ratio (%) among automobile welders (cases). Further, we have analyzed the effect of smoking on the FEV1/FVC ratio% and the RDW% in the cases.

Settings and Design: A cross sectional study was done on 50 welders and 50 non-welding office workers (controls) who were working in an automobile industry on the outskirts of Chennai, india. All the cases were arc welders and the controls were from the same production unit, who had never worked as welders. This study was conducted during the period from March 2012 to May 2012.

Methods and Material: The demographic data, smoking habits, work history and the respiratory symptoms were gathered by using a standard self -administered questionnaire. A complete haemogram study was done and pulmonary function tests were performed for both the cases and the controls. All the cases and the controls were examined in the hospital outpatients room and subsequently, their blood samples were collected. The pulmonary function tests were conducted in the spirometry room in the hospital. The statistical analysis was done using the SPSS, version 15.0.

Results: A statistically significant inverse correlation was found between the RDW% and the FEV1/FVC ratio% in the cases.

Conclusions: RDW can be used as a biomarker to identify the pulmonary compromise in automobile welders.

Key Words: RBC distribution width (RDW), FEV1/FVC ratio, Spirometry (Pulmonary Function Tests, PFT), Automobile Welders

INTRODUCTION

Welding is one of the essential components in the automobile manufacturing units. An increase in the risk of work related COPDs (Chronic Obstructive Pulmonary Diseases) in welders have been observed by many studies [1-4]. Hence, a periodic assessment of the lung function is considered as mandatory under the health surveillance program which has been designed for welders [5]. The red cell distribution width is the co-efficient of the variation of the Mean Corpuscular Volume (MCV). Though it was initially used as an index to classify microcytic anaemias [6], studies have proved its usefulness as a prognostic marker in a few non haematological entities [7-9]. A population based study which was done in the U.S. has observed an inverse relationship between the RDW and the lung function [10]. Therefore, we hypothesized that the RDW could be used as a marker to identify the magnitude of the pulmonary compromise among welders. To test the hypotheses, we analyzed the strength of the relationship between the RDW and the FEV1/FVC ratio% in automobile welders.

OBJECTIVE

Can the RDW (%) be used as a biomarker to identify the compromise in the lung function among the welders in an automobile industry?

The following questions were raised:

Q1: Can we elicit the magnitude of the RDW (%) in proportion to the magnitude of the deficit of the FEV1/FVC ratio?

Q2: Can the RDW be used as a biomarker to stratify the severity of the COPD cases based on the FEV1 (%)?

Q3: Can we estimate the magnitude of the effect of the smoking status and the RDW on the FEV1/FVC ratio% among the cases?

MATERIALS AND METHODS

Selection of the study population

The cross sectional study was performed in an automobile industry which was close to Chennai, Tamilnadu India. Seventy eight arc-welders and eighty non-welding production workers who volunteered for the study, were asked to answer a structured self – administered, socio economic and a medical history questionnaire. Based on the inclusion and the exclusion criteria, fifty automobile arc-welders and 50 age matched non-welding office workers were recruited as the cases and the controls respectively. All were males. An informed consent was obtained in the local vernacular language. The study was approved by our institutional research and ethical committee.

Characteristics			Cases			Controls		
	Range	Mean	SE	95% CI	Range	Mean	SE	95%CI
Age (Years)	22-52	32.20	0.97	30.2-34.1	21-52	33.22	1.02	31.1-35.2
Work (Years)	2-25	8.36	0.72	6.9-9.8	1-30	10.00	0.91	8.1-11.8
Smoking (Years)	0-10	3.12	0.49	2.1-4.1	0-20	4.08	0.81	2.4-5.7
Cigarettes/day	0-12	2.84	0.46	1.9-3.7	0-12	1.82	0.43	0.9-2.6
Respiratory Symptoms (years)	0-7	2.72	0.31	2.0-3.3	0-10	1.04	0.35	0.3-1.7
Hemoglobin (g/dL)	11-17	14.42	0.17	14.0-14.7	11-22	13.64	0.34	12.9-14.3
FEV1/FVC ratio (%)	59-82	69.24	0.78	67.6-70.8	64-80	71.90	0.64	70.6-73.1
FEV1%	50-85	72.86	1.50	69.8-75.8	58-86	78.48	0.98	76.5-80.4
RDW%	12.2-18.8	15.89	0.23	12.2-18.8	12.3-17.8	14.28	0.21	13.8-14.7

[Table/Fig-1]: Baseline Characteristics of Cases and Controls

Inclusion criteria:

1. Age : 20-50 years
2. Gender: Male
3. A minimum of 2 years of exposure to arc-welding (for the cases)

Exclusion criteria:

A history of

1. Respiratory diseases since child hood (repeated child hood respiratory infections, allergy and asthma)
2. Chronic alcoholism
3. Anaemia
4. Recent blood transfusions for any reason in the past one month.

Tests:

2ml of EDTA blood samples were collected from both the groups by using a vacutainer system and a complete haemogram was done by using a Sysmex KX-21 haematology analyzer, within 4 hours of sample collection. The 2-level controls were run every day in the cell counter, and the counter was maintained according to the manufacturer's instructions.

Spirometry was performed for all the cases as well as for the controls by trained personnel according to the American Thoracic Society (ATS) guidelines [11] by using a calibrated Spirovit SP 10 spirometer, after explaining the test maneouver to the participants.

Two highest values of FEV1 and FVC were taken among the 3 best maneouvers.

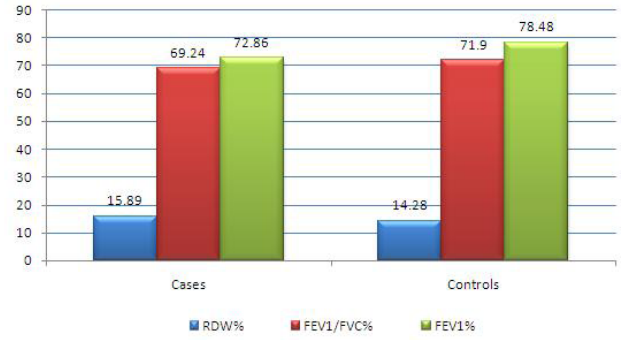
The FEV1/FVC ratio% was assessed and the post bronchodilator FEV1% of the predicted value (mentioned as FEV1%) was also evaluated as per the GOLD strategy [12].

STATISTICAL ANALYSIS

The data was analyzed by using SPSS, version 15.0 and the inferential statistics, the Student's-t-test for the independent samples, the Pearson's coefficient of correlation, the Regression coefficient and diagnostic efficacy tests were applied with a 5% level of the statistical significance.

RESULTS

[Table/Fig-1] shows the baseline characteristics of the study population. Twenty six (52.0%) welders and 22 (44%) controls were found to be current smokers. An ex-smoker status for more than 1 year was not included as a parameter. Cough, sputum production, a difficulty in breathing and chest tightness were considered as the respiratory symptoms.



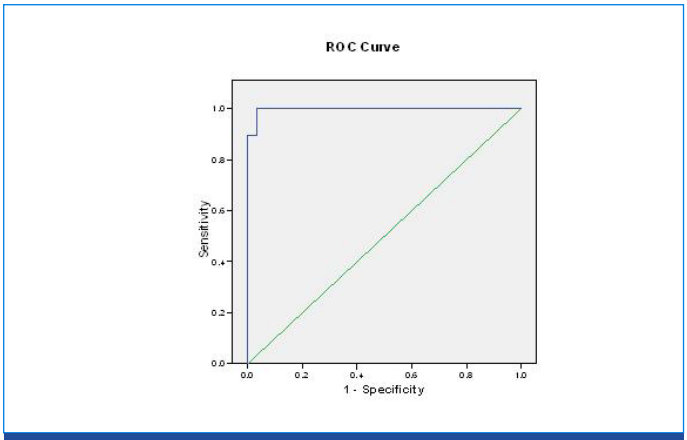
[Table/Fig-2]: Comparison for Mean % of Hypothetical Parameters

Parameter with RDW	CASES r value (p value)	CONTROLS r value (p value)
Age (Years)	+0.23 (0.101)	+0.33(0.01)*
Work (Years)	+0.74 (0.000)*	+0.26 (0.06)
Smoking status (Years)	+0.34 (0.01)*	+0.77(0.000)*
Number of cigarettes/day	+0.50 (0.000)*	+0.06 (0.80)
Respiratory symptoms (Years)	+0.58 (0.000)*	+0.43 (0.001)*

[Table/Fig-3]: Pearson Correlation of RDW with other variables in cases & controls *- Significance at 0.05 level

Statistically significant mean differences were observed for the spirometry FEV1/FVC ratio% (P=0.01), the FEV1 (%) (P=0.002) and the RDW% (P=0.000) between the cases and the controls [Table/Fig-2] The pulmonary functions, the FEV1/FVC ratio% and the FEV1(%) had a statistically significant negatively high correlation of r = -0.73(p=0.000) and r = -0.66(p=0.000) with the RDW(%) among the cases and a correlation of r = -0.79 (P=0.000) and r = -0.85(P=0.000) with the RDW(%) among the controls.

[Table/Fig-3] shows that the RDW% had a statistically significant positive correlation with the years of the work exposure, the smoking status (years), the number of cigarettes which were smoken/day and the respiratory symptoms (years) among the welders. Among the non welding production workers, there was a statistically significant correlation between the RDW% and age (years), the smoking status (years) and the respiratory symptoms (years).



[Table/Fig-4]: ROC curve for RDW% with FEV1/FVC < 70%

Q 1: From the Receiver Operator Characteristic curve (ROC) which was derived from the control for the criteria FEV1/FVC <70 [Table/Fig-4], an RDW% cut off level of 12.7% was found to yield a good correlation, r = -0.73 (p=0.000) with a sensitivity of 100%, a specificity of 26.67%, a positive predictive value of 47.62% and a negative predictive value of 100%.

Q 2: The ROC curve (area under the curve of 1.000 (P=0.007) from the controls for the criteria, FEV1% < 80, along with the FEV1/FVC ratio% of <70, showed a statistically significant moderate negative correlation of r = -0.48 (p=0.003) between the RDW% and the FEV1%. The sensitivity, specificity, positive predictive value and the negative predictive value were 85.00%, 100%, 100%, and 90.91% respectively for a cut off value of the RDW% of 14.9%.

Q3: The Bivariate Linear Regression technique [13] was employed to assess the influence of the smoking status. With the FEV1/FVC (%) as the response variable and the smoking status and the RDW% as the predictor variables, there was a statistical significance with the regression coefficient [βrdw ± se (βrdw) to be -2.45±0.36 (p=0.000)] and an insignificant regression coefficient [βSS ± SE (βSS) to be -0.047±0.17 (p=0.785)].

After adjusting for the smoking status, we obtained βRDW ± SE (βRDW) to be -2.49 ± 0.33 (p= 0.000), which was statistically significant for the FEV1/FVC ratio. The co-variation between the smoking status and RDW was observed to be a positively minimal correlation, r = +0.345 (p=0.007), with a statistically significant regression coefficient βSS ± SE (βSS) to be +0.163 ± 0.06 (p=0.014) on RDW (%).

DISCUSSION

We chose automobile welders as our cases because of their vulnerability to get obstructive lung diseases and also because a periodic spirometry was considered as mandatory for them. We had chosen two variables, namely the FEV1/FVC ratio% and the FEV1% to assess the pulmonary function in our study population. A change in the FEV1/FVC ratio% as an early indicator of COPD [14] and a post bronchodilator FEV1% of a predicted value helps in differentiating mild COPD from the moderate to the severe cases.

The aetiopathogenesis of the changes in the RDW% in individuals with a pulmonary compromise has yet to be identified. Chronic inflammation, which could leading to the release of the inflammatory cytokines [15], which was compounded with mild nutritional deficiencies and smoking [2], would have been the potential mechanism which could lead to an elevated RDW in such cases.

The present study examined the relationship between the RDW% and the FEV1/FVC ratio% in the welders of an automobile industry near Chennai. Initially, we found a statistically significant negative correlation between the RDW% and the FEV1/FVC ratio% in both the cases and the controls. The normative values of RDW in our local population has not been defined as yet and so we derived a cut-off point for the RDW from the controls, based on the sensitivity tests [16], which was 12.7%, while an FEV1/FVC ratio% of <70 was used as the criteria.. Our study showed that the RDW% was independently and negatively correlated with the FEV1/FVC ratio. This interaction was statistically significant even after adjusting for smoking, though the smoking status positively influenced the RDW values per se. This finding was in agreement with the previously published studies [2]. We could also observe that the cut off value for RDW was 14.9%, when we introduced the FEV1% of the predicted value of < 80% along with an FEV1/FVC ratio% of <70 and a statistically significant negative correlation was observed between the 2 variables among the cases.

This indicated that the RDW% values increased with decreasing lung functions, which suggested the possibility of using the RDW% as a bio marker, not only in identifying COPD, but also as a marker, to assess the severity of obstructive lung disease.

LIMITATION OF THE STUDY

A prospective cohort study with a larger sample size and other influencing factors may prove to be more useful in evaluating the role of RDW in the early diagnosis of obstructive lung disease among the welders.

CONCLUSION

This study confirmed our hypothesis that RDW could be used a marker to identify the pulmonary impairment in automobile welders. Since RDW was routinely reported as a part of the complete blood count, it was available for most of the factory workers who were undergoing periodic health checkups and so, understanding its significance would prove to be helpful in identifying the risk of the pulmonary impairment.

REFERENCES

[1] El-Zein M, Malo JL, Infante-Rivard C, Gautrin D. The prevalence and the association of the welding related systemic and respiratory symptoms in welders. *Occup Environ Med*. 2003 Sep;60(9):655-61.
[2] Nakadate T, Aizawa Y, Yagami T, Zheg YQ, Kotani M, Ishiwata K. The changes in the obstructive pulmonary function as a result of the cumulative exposure to welding fumes, as were determined by magneto pneumography in Japanese arc welders. *Occup Environ Med.* 1998;55:673–77.
[3] Luo JC, Hsu KH, Shen WS. The pulmonary function abnormalities and the airway irritation symptoms of metal fumes exposure on automobile spot welders. *Am J Ind Med*. 2006 Jun;49(6):407-16.
[4] Jani V,.Mazumdar V.S. The prevalence of respiratory morbidity among the welders in an unorganized sector of Baroda city. *Indian Journal of Occupational and Environmental Medicine*. Jan 2004;8 (1):16-21.
[5] Baxter PJ, Aw T-C, Cockcroft A, Durrington P, Harrington JM. Welding. In: Peter J Baxter, editor, Hunter's diseases of occupations 10th ed. UK,: *Hodder Arnold*; 2010; 433-34.
[6] Bessman J Gilmer PR Jr, Gardner FH., The improved classification of anemias on the basis of the MCV and the RDW, *Am J Clin Pathol.* 1983 Sep;80(3):322-26.
[7] Hampole CV, Mehrotra AK, Thenappan T, Gomberg-Maitland M, Shah SJ. The usefulness of the red cell distribution width as a prog-

nostic marker in pulmonary hypertension. *Am J Cardiol*. 2009 Sep 15;104(6):868-72.
[8] Zorlu A, Bektasoglu G, Guven FM, Dogan OT, Gucuk E, Ege MR, et al. The usefulness of the admission red cell distribution width as a predictor of the early mortality in patients with acute pulmonary embolism. *Am J Cardiol*. 2012 Jan 1;109(1):128-34.
[9] Sincer I, Zorlu A, Yilmaz MB, Dogan OT, Ege MR, Amioglu G,et al. The relationship between the red cell distribution width and the right ventricular dysfunction in patients with chronic obstructive pulmonary disease. *Heart Lung*. 2012 May;41(3):238-43. Epub 2011 Oct 11.
[10] Grant BJB, Kudalkar DP, Muti P, McCann Maurizio Trevisan SE, Freudenheim JL, Schünemann HJ. The relationship between the lung function and the RBC distribution width in a population-based study. *Chest.* 2003;124;494-500.
[11] Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A et al. The standardization of spirometry, *Eur Respir* J. 2005; 26: 319–38.
[12] Pauwels RA, Buist AS, Calverley PM, Jenkins CR, Hurd SS. The GOLD Scientific Committee. The global strategy for the diagnosis, management, and the prevention of chronic obstructive pulmonary disease. NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop summary. *Am J Respir Crit Care. Med*.2001 Apr;163(5):1256-76.
[13] Sundar Rao P.S.S,.Richard J. Linear Regression and Correlation. In: PSS Sundar Rao, J.Richard, editor, An introduction to bio statistics, 3rd edn. New Delhi: Prentice Hall of India; 2003; 45-47, 83-92.
[14] Nathell L, Nathell M, Malmberg P, Larsson K. "The COPD diagnosis is related to different guidelines and spirometry techniques". *Respiratory Research*. 2007; 8 (1): 89.
[15] Wen Y. The high red blood cell distribution width is closely associated with risk of carotid artery atherosclerosis. *Exp Clin Cardiol*. 2010 Fall; 15(3): 37–40.
[16] Sundar Rao P.S.S,.Richard J. Probability. In: P.S.S. Sundar Rao, J.Richard, editor, An introduction to bio statistics, 3rd ed. New Delhi: *Prentice Hall of India*. 2003; 45-47, 83-92.

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