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Relationship between Pulmonary Function Tests and Common Haematological Parameters (RDW, Hb, MCH, MCHC, MCV) In Healthy Non-Smokers

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***Abstract*-** BACKGROUND: The pulmonary function tests (PFT) are known predictors of clinical outcome in respiratory disorders. Several recent studies have shown inverse correlation between PFT and certain haematological parameters like red cell distribution width (RDW) independent of confounding factors like smoking. This study was taken up to find out if there is any direct correlation between PFT and certain haematological parameters in healthy non-smokers. METHODS: The study was carried out on 200 healthy non-smokers aged between 20 and 55 years. In all the subjects PFTs were performed and common haematological parameters like haemoglobin, RDW, MCV, MCH, MCHC and derived ratios were determined. The correlation between PFT and haematological parameters were statistically analysed. RESULTS & CONCLUSIONS: Despite the absence of pulmonary illness, the mean values for PFT in the study subjects were lower than the predicted range. There was no correlation between PFT and any one of the haematological parameters studied. In healthy non-smokers, PFT does not appear to have a direct effect on any one of the haematological parameters or *vice versa*

***Index Terms*-** haematological parameters; predictors of outcome; pulmonary function tests; red cell distribution width;

I. Introduction

Recently, many studies have been published assessing the potential of common laboratory investigations to act as predictors of outcome in various illnesses. The ultimate aim of such studies is not only to find new biomarkers but also to find simple, quick, cost-effective alternatives to the current, more expensive, time consuming investigations that are used as biomarkers. Most of these studies have focussed on common haematological parameters that are part of complete blood count. The parameters that have been explored include *haematocrit* in chronic obstructive pulmonary disease (COPD) (Arnaud Chambellan, 2005); *red cell distribution width* (RDW) in such diverse ailments as heart disease (Ola Hammarsten, 2010), inflammatory bowel disease (Mehmet ARHAN, 2011) and respiratory disease (Nathan et al., 2013; Schunemann HJ, 2000); derived parameters such as *RDW/MCV* ratio in diabetic ketoacidosis(Liu DS, 2013); and *Hb/MCHC, Hb/RDW and MCHC/RDW* ratios in grading the severity in hereditary spherocytosis (Rocha S, 2011).

In one such cross-sectional study performed on a random population, Grant et al (Grant et al., 2003) found an inverse correlation between an established predictor of mortality like pulmonary function tests (PFT) (Schunemann HJ, 2000), and RDW that was independent of confounding factors like smoking and ethnicity. They even suggested that RDW can be used as an alternative biomarker of clinical outcome in respiratory illness. The findings of this publication prompted us to take up the present study to find out if there are any direct correlations between PFT and certain haematological parameters (including RDW) *per se* in non-smoking healthy individuals and whether this correlation is significant enough to justify these parameters being used as biomarkers.

II. Materials and Methods

The present study was carried out on 200 non-smoking healthy, clinically asymptomatic adult subjects, with no respiratory complaints, attending the Master Health Check-up Clinic at Chettinad Hospital and Research Institute, Chennai. The study population consisted of 180 males and 20 females aged between 20 and 55 years. The subjects were inducted to the study after obtaining informed consent. The study was initiated after getting clearance from the Institutional Ethics Committee.

On all the subjects, the pulmonary functions tests consisting of FEV1 (forced expiratory volume in 1 second in litres), FVC (Forced Vital Capacity in litres), %FEV1 (Percentage of the predicted value for FEV1), %FVC (Percentage of the predicted value for FVC) and FEV1/FVC ratio were performed using Chestgram HI-105 Spirometer. From all the subjects, venous blood was collected in K2EDTA vacutainers for the estimation of haemoglobin, RDW (CV) (red cell distribution width – coefficient of variation), MCH (mean corpuscular haemoglobin), MCHC (mean corpuscular haemoglobin concentration), and MCV (mean corpuscular volume) using Beckman Coulter HMX Haematology Analyser. From these parameters, the following ratios were calculated: HB/RDW, MCV/RDW, MCH/RDW and MCHC/RDW.

Results were analysed using the statistical package SPSS version 21. Besides the mean and the standard deviation of all the results, independent samples t-test was performed to test the gender differences; one-way ANOVA to test the differences in the values between different age groups and Pearson's correlation coefficient to determine the relationship between PFT

and various haematological parameters. A "p" value of 0.05 was accepted as significant.

III. Results and Observations

Gender based summary statistics and the results of the student t-test are given in table 1.

The results of PFT and haematological investigations in various age groups along with results of one-way ANOVA are summarised in table 2.

Correlation between PFT and various haematological parameters are summarised in tables 3, 4 and 5

PFT. As expected, the values for FEV1 and FVC showed statistically significant difference ($p < 0.001$) between the genders, with higher values in men (Table 1). However, the mean values for FEV1 (2.09L) in women and FVC (2.79L and 2.14 L) in both sexes were below the predicted normal value (Pierce R, 2008). One-way ANOVA was done to highlight the differences between the age groups (Table 2). Although the values for FEV1 and FVC remained the same across all age groups, %FEV1 and %FVC were significantly higher and FEV1/FVC ratio was significantly lower in the age group 30-34 compared to the age group 20 – 24.

Haematological parameters: As expected, mean value for haemoglobin (Hb) was significantly higher in males than in females. In addition, one of the derived parameters, Hb/RDW, significantly differed in men and women (Table 1); it was significantly higher in men. The study subjects in the age group 20 – 24 exhibited significantly higher mean values for Hb, MCH and Hb/RDW ratio (Table 2); similarly, study subjects of the age group 30-34 had significantly higher mean values for RDW and significantly lower values for MCV, MCV/RDW, MCH/RDW, and MCHC/RDW than subjects who were 45 years or older.

Correlation between PFT & haematological parameters: There was no correlation between any of the pulmonary function tests and haematological parameters. Within PFT, FEV1 and FVC showed strong positive correlation as expected (r=0.975). Within haematological parameters, RDW showed negative correlation with Hb (r=-0.377), MCH (r=-0.415), MCV (r=-0.323), MCHC (r=-0.577), MCHC/RDW (r = -.949), MCV/RDW (r = -0.837), MCH/RDW (r = -0.836), and HB/RDW (r = -0.816). As expected, there was positive correlation among other haematological parameters.

Table 1. Mean and SD of all the parameters & gender differences

Parameters	Normal Range*	Sex				Independent Samples t-test	
		Male (180)		Female (20)			
		Mean	SD	Mean	SD	t-value	Sig.(p)
Height		168.17	6.43	155.80	5.48		
Weight		65.83	13.32	56.85	9.66		
FEV1 (L)	2.23 – 4.54	2.65	.68	2.09	.87	3.396	**.001**
FVC (L)	2.85 – 5.42	2.79	.76	2.14	.89	3.613	**.000**
FEV1_FVC	> 70%	95.21	5.97	97.86	2.47	-1.963	.051
% FEV1	80 – 120%	70.76	17.42	76.44	37.60	-1.190	.236
% FVC	80 – 120%	62.96	16.14	67.45	32.77	-1.034	.302
Hb	12.1 – 17.2 g/dL	14.78	1.31	12.35	1.45	7.797	**.000**
RDW (CV)	12.8 ±1.2%	12.61	1.34	13.08	2.18	-1.387	.167
MCH	27 to 31 pg/cell	29.29	2.85	27.92	4.08	1.945	.053
MCHC	32 to 36 gm/dL	33.30	1.03	32.96	1.08	1.397	.164
MCV	80 to 95 fL	87.78	7.34	84.58	10.79	1.754	.081
Hb / RDW		1.19	.17	.97	.20	5.372	**.000**
MCV / RDW		7.05	.97	6.64	1.24	1.749	.082
MCH / RDW		2.35	.36	2.20	.45	1.829	.069
MCHC / RDW		2.67	.31	2.58	.40	1.199	.232

*(Pierce R, 2008; Stanojevic S, 2008) (http://www.nlm.nih.gov/medlineplus/ency/article/003642.htm);

Note: [FEV1 = forced expiratory volume in 1 second in litres; FVC = Forced Vital Capacity in litres; %FEV1 = Percentage of the predicted value for FEV1; %FVC = Percentage of the predicted value for FVC; Hb= haemoglobin; RDW (CV) = red cell distribution width coefficient of variation); MCH = mean corpuscular volume; MCHC = mean corpuscular volume concentration; MCV = mean corpuscular volume]

Table 2: Summary statistics of Pulmonary function and haematological function parameters and one way ANOVA

	Age												One way ANOVA	
	20 – 24 (n = 52)		25 – 29 (n = 61)		30 – 34 (n = 36)		35 – 39 (n = 24)		40 – 44 (n = 17)		45 or more (n = 10)			
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	F	p value
FEV1	2.49	.90	2.61	.64	2.71	.49	2.67	.70	2.63	.70	2.29	.89	.814	.541
FVC	2.57	1.00	2.74	.72	2.88	.57	2.86	.73	2.80	.75	2.44	.90	1.136	.343
FEV1_FVC	**97.65**	3.31	95.62	5.18	**94.54**	6.86	93.34	5.97	94.58	6.58	93.37	9.65	2.814	**.018**
% FEV1	**63.43**	21.37	70.73	16.79	**75.29**	13.16	76.90	24.66	79.68	25.45	74.25	24.21	2.987	**.013**
% FVC	**57.42**	20.20	62.74	15.50	**67.28**	12.45	68.62	20.97	70.25	21.89	60.50	23.60	2.423	**.037**
HGB	**14.83**	1.29	14.81	1.59	**13.82**	1.91	14.55	1.38	14.41	.74	14.17	.86	2.678	**.023**
MCH	**29.85**	2.72	29.11	3.13	**27.76**	3.77	29.43	2.05	29.18	2.39	29.97	2.33	2.357	**.042**
RDW (CV)	12.45	1.13	12.57	1.41	**13.25**	2.04	12.90	1.33	12.50	.87	**11.83**	.99	2.385	**.040**
MCHC	33.23	.84	33.40	.96	32.99	1.21	33.19	.80	33.19	.61	33.82	2.19	1.340	.249
MCV	89.71	6.96	86.95	7.90	**83.52**	9.27	88.37	5.45	87.86	7.26	**90.10**	6.37	3.250	**.008**
HB / RDW	**1.21**	.17	1.19	.17	**1.08**	.24	1.14	.15	1.16	.09	1.20	.10	2.867	**.016**
MCV / RDW	7.26	.82	7.01	.97	**6.48**	1.30	6.92	.79	7.04	.53	**7.70**	1.20	3.919	**.002**
MCH / RDW	2.42	.30	2.35	.36	**2.16**	.48	2.31	.29	2.34	.20	**2.56**	.43	3.089	**.010**
MCHC / RDW	2.69	.26	2.69	.30	**2.55**	.40	2.60	.26	2.67	.22	**2.89**	.48	2.488	**.033**

. Table 3: Correlation coefficients between PFT and haematological Parameters

	FEV1	**FVC**	**FEV1/ FVC**	**% FEV1**	**% FVC**	**HGB**	**RDW**	**MCH**	**MCHC**	**MCV**
FEV1	1									
FVC	**.975****	1								
FEV1/FVC	-.120	***-.324*****	1							
% FEV1	**.813****	**.779****	-.045	1						
% FVC	**.763****	**.776****	***-.252*****	**.933****	1					
HGB	.068	.066	-.029	-.078	-.070	1				
RDW	-.105	-.096	.001	-.106	-.110	***-.377*****	1			
MCH	-.036	-.048	.063	-.077	-.091	**.558****	***-.415*****	1		
MCHC	-.022	-.038	.078	-.013	-.030	**.390****	***-.577*****	**.597****	1	
MCV	-.050	-.060	.050	-.098	-.107	**.502****	***-.323*****	**.969****	**.448****	1

Note: Values with ** indicates significance at 5% level of significance (red = positive; green = inverse)

Table 4: Correlation coefficients between PFT and haematological Ratios

	FEV1	**FVC**	**FEV1/ FVC**	**% FEV1**	**% FVC**	**HB / RDW**	**MCV / RDW**	**RDW / HB**	**MCH / RDW**	**MCHC / RDW**
FEV1	1									
FVC	**.975****	1								

FEV1/FVC	-.120	***-.324*** **	1							
% FEV1	**.813** **	**.779** **	-.045	1						
% FVC	**.763** **	**.776** **	***-.252*** **	**.933** **	1					
HB / RDW	.095	.082	.015	-.006	-.002	1				
MCV / RDW	.024	.009	.054	-.009	-.014	**.800** **	1			
MCH / RDW	.026	.009	.063	-.004	-.013	**.813** **	**.989** **	***-.784*** **	1	
MCHC / RDW	.062	.046	.049	.064	.059	**.800** **	**.856** **	***-.760*** **	**.873** **	1

Note: Values with ** indicates significance at 5% level of significance (red = positive; green = inverse)

Table 5: Correlation coefficients between haematological Parameters

	HGB	**RDW**	**MCH**	**MCHC**	**MCV**	**HB / RDW**	**MCV / RDW**	**MCH / RDW**	**MCHC / RDW**
HGB	1								
RDW	***-.377*** **	1							
MCH	**.558** **	***-.415*** **	1						
MCHC	**.390** **	***-.577*** **	**.597** **	1					
MCV	**.502** **	***-.323*** **	**.969** **	**.448** **	1				
HB / RDW	**.813** **	***-.816*** **	**.557** **	**.573** **	**.467** **	1			
MCV / RDW	**.479** **	***-.837*** **	**.797** **	**.642** **	**.755** **	**.800** **	1		
MCH / RDW	**.503** **	***-.836*** **	**.816** **	**.710** **	**.741** **	**.813** **	**.989** **	1	
MCHC / RDW	**.349** **	***-.949*** **	**.462** **	**.750** **	**.347** **	**.800** **	**.856** **	**.873** **	1

Note: Values with ** indicates significance at 5% level of significance (red = positive; green = inverse)

IV. Discussion

The need for simple, cost-effective and quick predictors of outcome has sparked a flurry of new studies trying to identify such biomarkers. Some of the common haematological parameters like RDW, haematocrit and absolute indices have emerged as probable candidates. RDW in particular has shown great promise as a predictor outcome in several disease states (Koma et al., 2013; Ola Hammarsten, 2010). There is a prospect of its being considered as an effective alternative to pulmonary functions tests (PFT) which have been recognised for some time as a long-term predictors of mortality (Schunemann HJ, 2000). In a cross-sectional study conducted on a random population, Grant and his associates (Grant et al., 2003), found a inverse correlation between RDW and PFT. This correlation persisted even when the confounding factors like smoking and ethnicity, which normally influence RDW, were accounted for.

The present study was taken up to find out if there is any direct relationship between haematological parameters like RDW, Hb, MCV, MCH, MCHC and pulmonary function tests in a healthy population. The study was carried out on ethnically homogeneous, controlled, healthy population in whom confounding factor like smoking was used as an exclusion criteria. All the subjects were attending routine master heath check-up with no history of respiratory ailment.

Despite the lack of any respiratory problem, mean values of PFT (FVC in both sexes and FEV1 in women) were below the predicted normal range for white population. This is in agreement with the study of Fulambarker et al (Fulambarker, Copur, Javeri, Jere, & Cohen, 2004) who found that the mean values for PFT in Asians are 20 – 28% lower than those for white population. In addition, we also noticed a higher mean values for FEV1 and FVC in the age group 30 – 34 than all other age groups. This is somewhat unusual as the age related reduction in pulmonary function is progressive and linear (Pruthi & Multani, 2012).

There was no correlation between any one of the Routine haematological parameters (RDW, Hb, MCH, MCHC and MCV) and PFT in our study. We also failed to find any correlation between the derived ratios (HB/RDW, MCV/RDW, MCH/RDW and MCHC/RDW) with PFT. This was in marked contrast to the findings of Grant et al (Grant et al., 2003) who found a significant inverse correlation between RDW and PFT in a population based study. However, the investigators were not sure whether the pulmonary function directly influenced RDW or vice versa, as other factors like nutrition that can influence both pulmonary function and RDW were not accounted for in their study. They hypothesized that micronutrients may play a role in this correlation. In our study, RDW showed an inverse correlation with other haematological parameters including Hb, MCH, MCHC, MCV and derived ratios. This is significant as

Hb, MCH, MCV, and MCHC are indirect indicators of the nutritional status of the individual and the latter is known to affect RDW values. Surprisingly, there was no correlation between these indirect indicators and PFT.

From our study, it appears that the pulmonary function does not directly influence RDW and other haematological parameters, and vice versa, in healthy non-smokers. The significant correlation observed between PFT and RDW in the previous study (Grant et al., 2003) is probably due to an as yet unidentified factor that has independent effect on both these parameters. This factor may be nutritional as suggested by Grant et al. Further study required to elucidate this relationship.

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