Original Article

Comparison of Lung Function Changes Among Anemic and Non-Anemic Adults

Lung Function Changes Among Anemic and Non-Anemic

Aliya Waseem[1], Shahjabeen[2], Syed Adnan Ahmed[3], Saba Abrar[3], Padma Rathore[4] and Mohammad Saleh Soomro[3]

ABSTRACT

Objective: To find the correlation that exists between blood hemoglobin/ serum iron indices and lung function tests. To compare changes in lung functions amongst the anemic and non-anemic adults.

Study Design: Case control study.

Place and Duration of Study: This study was conducted at the Fatima Hospital, Baqai Medical University, Karachi and Abbasi Shaheed Hospital, Karachi from July 2017 to December 2017.

Materials and Methods: 100 males and 100 female diagnosed iron deficient anemic adults in range of 18-45 years and with no co-morbid respiratory and cardiac diseases were included. Inclusion criteria included iron deficient anemic adults with no acute emergency states and no chest and back area deformities. Blood samples were reanalyzed for blood hemoglobin (Hb) by automated cell analyzer and anemia were rechecked for confirmation of iron deficiency anemia (IDA) by doing further tests like serum iron, serum ferritin, serum Total Iron Binding Capacity (TIBC) levels by Enzyme Linked Immunosorbent Assay (ELISA). Digital spirometer was used to perform Pulmonary Function Tests (PFTs) which includes Forced Vital Capacity (FVC) and Forced Expiratory Volume in 1st second of FVC (FEV_1) in all anemic patients and lung functions were compared with lung functions of non-anemic healthy individuals.

Results: The FVC and FEV1 in male and female cases were significantly reduced($p<0.05$) as compared to that in male and female controls respectively. Whereas the FEV1/FVC ratio was significantly increased ($p<0.05$) in male and female cases. Restrictive lung changes were observed in male and female cases.

Conclusion: In the present study positive association was observed between blood Hb/serum iron indices and lung functions in anemic patients**.** The results showed restrictive lung function changes in anemic subjects**.** While no abnormal lung function changes were found in non-anemic healthy participants.

Key Words: Hemoglobin, Iron Deficiency Anemia, Pulmonary Function Tests, Forced Vital Capacity, Forced Expiratory Volume in 1st second.

Citation of article: Waseem A, Shahjabeen, Ahmed SA, Abrar S, Rathore P, Soomro MS. Comparison of Lung Function Changes Among Anemic and Non-Anemic Adults. Med Forum 2020;31(11): 29-33.

INTRODUCTION

Anemia is characterized by decreased quantity of red blood cells and/or decreased levels of hemoglobin below normal levels. Normal range of hemoglobin levels in adult males are 13.5-18.0 g/dl and in female adults are 12.0-15.0g/dl. Anemia is considered when hemoglobin levels are less than 13.5 g/dl in adult males and less than 12 g/dl in adult females[1]. Although anemia affects any gender and age but its prevalence in lower socioeconomic population is profound [2]. According to World Health Organization (WHO), around 528.7 million (29.4%) women of reproductive age are globally affected by anemia. According to this report severe anemia was found in 20.2 million women. In accordance with National Nutritional Survey conducted in 2018 in Pakistan, anemia was prevalent in 41.7% of women of reproductive age. This survey showed a slightly higher proportion in rural (44.3%) as compared to urban settings (40.2%)[3]. Molecular oxygen is necessary for proper functioning of all biological systems. In conditions like anemia where there is decrease in supply or decrease in the utilization of oxygen profound changes occur in cell metabolism. This causes accumulation of intermediary products of metabolism like lactic acid etc in the tissue. This may

[1.] Department of Physiology, Liaquat College of Medicine & Dentistry Karachi.
[2.] Department of Physiology, Fazaia Ruth Pfau Medical College Karachi.
[3.] Department of Physiology, Baqai Medical University, Karachi.
[4.] Department of Physiology, Jinnah Sindh Medical University, Karachi.

Correspondence: Aliya Waseem, Senior Lecturer, Department of Physiology, Liaquat College of Medicine & Dentistry Karachi.
Contact No: 0340-6883493
Email: aliyawaseem18@gmail.com

Received: April, 2020
Accepted: September, 2020
Printed: November, 2020

lead to increase in fatigability and decrease work output. So respiratory efforts become less powerful and respiratory muscle's weakness occurs. Earlier studies have proved that anemia has varied effects on various respiratory parameters. Larger percentage of anemia is due to IDA alone. IDA has been shown to result in impaired work capacity, lower cognition function and impaired immune response[4].

Anemic patients had significantly higher medical research council dyspnea scale and number of exacerbations than patients with normal Hb levels in a study conducted in Egypt[5]. In asthmatics, decreased concentrations of iron can initiate pathophysiologic mechanisms leading to the development of asthma. Bronchoconstriction occurred due to inflammation and muscle contraction[6].

The studies establishing relationship of blood hemoglobin/ serum iron indices and dynamic lung function tests are very limited[7]. Hence, the present study was undertaken to observe the relationship of hemoglobin/serum iron indices with dynamic ventilatory tests in iron deficient anemic patients and to compare the lung functions among anemic and non-anemic adults. By knowing the association between blood hemoglobin/ serum iron indices with lung function tests, we can detect early changes in lung functions in anemic subjects and hence by correcting anemia we can indirectly improve the function of lungs.

MATERIALS AND METHODS

The present study was carried at Fatima Hospital, Baqai Medical University, Karachi and Abbasi Shaheed Hospital, Karachi from July 2017 to December 2017. This study was approved by the Ethical committee of Baqai Medical University. An approval letter with Ref no. BMU-EC/2016-04 was issued from ethical committee of Baqai Medical University on 02-01-2017.

Patients who were attending in the hospitals were screened for the presence of lung function changes in diagnosed iron deficient anemic patients. Purposive sampling was done. Written consent was obtained from all participating individuals. 100 male and 100 female patients within the age group of 18 to 45 years and 50 Male & 50 female healthy individuals were included. Diagnosed iron deficient anemic patients confirmed by blood Hb, serum Iron, serum Ferritin, serum TIBC and serum % transferrin saturation levels were included.

The patients with any other diseases like cardiac, lung diseases, any infectious diseases, and any inflammatory disorders were excluded. Patients with back, chest deformities, other types of anemia, active smokers and pregnant women were also excluded.

All the participant's blood hemoglobin and serum iron indices (serum iron, serum ferritin, serum TIBC levels) were measured by automated cell analyzer (Sysmex Kx-21)[8] and ELISA (sandwich ELISA kit (cat # YHB2785Hu; Bio Check (Foster city, CA, USA, cat #. BC- 1025)[9] respectively.

Hemoglobin estimation was done by diluting blood in a solution containing potassium cyanide and potassium ferricyanide. Hb is converted into cyan-methemoglobin (HiCN), which is a colored-product. The color intensity is read in the colorimeter or spectrophotometer at a wavelength of 540nm, and the absorbance is proportional to the concentration of hemoglobin in the blood[10].

Serum ferritin levels were measured by ELISA. The first step is adding approximately 35 μl serum and BSA-buffer (bovine serum albumin) to each well. Then for 15 minutes, plates are allowed to stand at room temperature. Then the wells are rinsed 3 times with PBS (phosphate-buffered saline) after aspiration. Then again the plates are allowed to stand for I5 minutes after adding antiferritin to each well. Again PBS is utilized for rinsing the wells. Then the substrate solution containing p-nitrophenylphosphate (PNP) is added to each well. After keeping the wells at room temperature for 1 hr, the reaction is stopped by adding one drop of 1 M sodium hydroxide to each well. Visual estimation of the intensity of the yellow color in each well is performed. Finally, color intensity of each well is compared to ferritin standards containing 0, 20, 50, 100, 200, and 500 μg/liter[11].

Digital spirometer (Microlab 3300 electronic spirometer, Micro Medical Limited, Kent, England) was used to measure lung volumes and capacities. Three acceptable forced expiratory readings were taken for each variable and the best value was selected. Subjects were given a rest of 2-3 minutes between the tests. Nose clips were used in our study[12].

Statistical Analysis: Data for blood hemoglobin, serum ferritin, total serum iron, serum TIBC, serum % Transferrin saturation and lung function tests were analyzed by using independent sample t-test, and has given numerical values between two variables that were measured on same interval and results were calculated using SPSS 22.0 at p-value< 0.05. Pearson Correlation was used to correlate between blood Hb/serum iron indices and lung functions.

RESULTS

During study period, two hundred iron deficient anemic patients (N=200) were included, that consisted of hundred male and hundred female individuals. One hundred healthy individuals (N=100) participated as controls. These healthy subjects consisted of fifty males and the same number of females.

Table I showed that FVC in male controls was 4.05±0.05 Liters and FVC in male cases were 3.09±0.09 Liters and the t-values and p-values are 70.13 and 0.01 respectively. FVC in female controls were 3.34±0.31 Liters and FVC in female cases were 2.40±0.59 Liters and the t-values and p values are 10.54

and 0.01 respectively. FEV1 in male controls were 3.35±0.09 Liters and FEV1 in male cases were 2.80±0.06 Liters and the t values and p values are 40.46 and 0.01 respectively. FEV1 in female controls was2.70±0.97 Liters and FEV1 in female cases was 2.24±0.58 Liters and the t values and p values are 3.62 and 0.01 respectively. FEV1/FVC ratio in male controls was 0.82±0.19 % and the ratio in male cases was0.90±0.18 % and the t values and p values are -2.51 and 0.01 respectively. FEV1/FVC ratio in female controls was 0.80±0.04 % and FEV1/FVC ratio in female cases was 0.92±0.25 % and the t values and p values are -3.36 and 0.01 respectively.

Comparison of PFTs in Table I showed that The FVC and FEV1 in male and female cases were reduced significantly ($p<0.05$) than in male and female controls respectively. Whereas the FEV1/FVC ratio was increased significantly ($p<0.05$) than in male and female cases. Therefore, Restrictive lung disease was observed in anemic subjects.

Table No.1: Mean Comparison of Pulmonary Function Tests among controls and cases

Parameters	Gender	Control		Cases		t-value	p-value
		Mean	SD	Mean	SD		
FVC (L)	Male	4.05	0.05	3.09	0.09	70.13	0.01
	Female	3.34	0.31	2.40	0.59	10.54	0.01
FEV1 (L)	Male	3.35	0.09	2.80	0.06	40.46	0.01
	Female	2.70	0.97	2.24	0.58	3.62	0.01
FEV1/FVC (%)	Male	0.82	0.19	0.90	0.18	-2.51	0.01
	Female	0.80	0.04	0.92	0.25	-3.36	0.01

P <0.05 Significant
P>0.05 Non-significant

Table No.2: Mean Comparison of Biochemical parameters among Control & Case

Parameters	Gender	Control		Cases		t-value	p-value
		Mean	SD	Mean	SD		
Blood hemoglobin(g/dl)	Male	14.01	1.96	7.05	1.15	27.36	0.0001
	Female	12.06	1.89	6.05	1.32	22.64	0.0001
Serum Iron(µg/dl)	Male	144.54	50.32	20.23	2.36	24.73	0.0001
	Female	108.66	15.28	15.0	3.30	58.79	0.0001
Serum Ferritin(µg/l)	Male	156.68	25.98	9.12	1.03	56.9	0.0001
	Female	96.34	22.60	8.0	1.14	39.12	0.0001
Serum TIBC (µg/dl)	Male	349.60	51.73	625.01	10.01	-51.5	0.0001
	Female	272.84	32.77	650.50	12.04	-102.5	0.0001
% Transferrin Saturation	Male	35.4	3.13	9.99	2.56	53.12	0.0001
	Female	30.42	2.52	5.23	2.19	63.1	0.0001

P <0.05 Significant P>0.05 Non-significant

Table 2 showed that the Mean value of hemoglobin in male controls was 14.01±1.96 g/dl and mean value of hemoglobin in male cases was 7.05±1.15 g/dl and the t-values and p values are 27.36 and 0.0001 respectively. The mean value of hemoglobin in female controls was 12.06±1.89 g/dl and mean value of hemoglobin in female cases was 6.05±1.32 g/dl and the t-values and p-values are 22.6 and 0.0001 respectively. Mean value of serum Iron in male controls was 144.54±50.32 µg/dl and in male cases was 20.23±2.36 µg/dl and the t-values and p-values are 24.73 and 0.0001 respectively. Mean value of serum Iron in female controls was 108.66±15.28 µg/dl and in female cases was 15.0±3.30 µg/dl and the t-values and p-values are 58.79 and 0.0001 respectively. Mean value of serum ferritin in male controls was 156.68±25.98 µg/L and in male cases was 9.12±1.03 µg/L and the t-values and p-values are 56.9 and 0.0001 respectively. Mean value of serum ferritin in female controls was 19.34±22.60 µg/L and in female cases was 8.0±1.14 µg/L and the t-values and p-values are 39.12 and 0.0001 respectively. Mean value of serum TIBC in male controls was 349.60 µg/dl±51.73 µg/dl and in male cases was 625.01±10.01 µg/dl and the t-values and p values are -51.5 and 0.0001 respectively. Mean value of TIBC in female controls was 272.84±32.77 µg/dl and in female cases TIBC was 650.50±12.04 µg/dl and the t-values and p-values are -102.5p value and 0.0001 respectively. Mean value of % transferrin saturation in male controls was 35.4±3.13 % and in male cases was 9.99±2.56% and the t-values and p-values are 53.12 and 0.0001 respectively. Mean % transferrin saturation in female controls was 30.42±2.52 % and in female cases was5.23±2.19 % and the t-values and p-values are 63.1 and 0.0001 respectively.

Comparison of biochemical parameters among controls and cases in Table 2 showed that blood hemoglobin/serum iron indices of both genders were significantly (p=<0.05). lower in anemic group.

DISCUSSION

Millions of people around the world are affected by anemia. Profound prevalence of anemia has been observed in developing countries. Anemia hampers the normal metabolism of body due to anemic hypoxia, which could have different systemic effects. Out of which one effect is on the respiratory system. Therefore, anemic subjects are not able to blow out air at its maximum capacity because respiratory efficiency deteriorates due to prolonged anemia[13].

To the best of our knowledge, there is hardly any standardized literature documented on effects of Iron deficiency anemia on dynamic ventilator tests[14]. According to this study iron deficiency anemia was seen more commonly in suburbs of Gadap town[15].

In the present study, patients with IDA with low Hb levels had significantly lower PFT values (FVC 3.09±0.09, FEV1 2.80±0.06, FEV1/FVC ratio 0.90±0.18) in males and in females (FVC 2.40±0.59, FEV1 2.24±0.58, FEV1/FVC ratio 0.92±0.25) ($p<0.05$). Several studies have supported the current findings. A study conducted on anemic Iranian male and female healthy subjects with no history of respiratory diseases showed reduced PFT values[16].

A US based cross-sectional study revealed negative correlation between serum iron indices and FVC and FEV1[17], which is in contradiction to the current research. In the present study, FVC showed significant positive correlation with serum iron indices. Serum iron levels were found to be positively related with the FEV1 in a nationwide study conducted in Korea[18].

In a study conducted in Austria, the subject's PFTs declined with reduction in concentration of serum ferritin levels[19]. Similar significant positive ($p<0.05$) association was found in the present study between serum ferritin levels and PFTs in anemic adults.

Until recently no association has been found between serum TIBC levels and PFTs in anemic individuals. However, the present study demonstrated negative association between serum TIBC and FVC and FEV1 but showed significant positive association with FEV1/FVC ratio ($p<0.05$).

CONCLUSION

In the present study, restrictive lung function changes were found in iron deficient anemic individuals. Whereas lung functions were normal in non-anemic healthy adults.

Recommendations: It is suggested that early detection and correction of IDA in patients with reduced pulmonary functions may improve health status and prevent the development of respiratory diseases.

Author's Contribution:

Concept & Design of Study:	Aliya Waseem
Drafting:	Shahjabeen, Syed Adnan Ahmed
Data Analysis:	Saba Abrar, Padma Rathore, Mohammad Saleh Soomro
Revisiting Critically:	Aliya Waseem, Shahjabeen
Final Approval of version:	Aliya Waseem

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Nah EH, Kim S, Cho S, Cho HI. Complete Blood Count Reference Intervals and Patterns of Changes Across Pediatric, Adult, and Geriatric Ages in Korea. Ann Lab Med 2018;38(6):503-511.
2. Jamnok J, Sanchaisuriya K, Sanchaisuriya P, Fucharoen G, Fucharoen S, Ahmed F, et al. Factors associated with anaemia and iron deficiency among women of reproductive age in Northeast Thailand: a cross-sectional study. BMC Public Health 2020;20(1):102.
3. Ali SA, Khan U, Feroz A. Prevalence and determinants of anemia among women of reproductive age in developing countries. J Coll Physicians Surg Pak 2020; 30(2):177-186.
4. Salmen M, Hendriksen S, Gorlin J, Claire ML, Prekker ME. Oxygen Delivery during Severe Anemia When Blood Transfusion is refused on Religious Grounds. Ann Am Thorac Soc Vol 2017;14(7): 1216–1220.
5. Abdelaziz AO, Ghany EHA, Makram O, Aziz MO, Hoseany E, Magdy M, et al. Prevalence and impact of anemia in patients with chronic respiratory diseases. Egypt J Chest Dis Tuberc 2018;67(4): 461-70.
6. Ghio, A.J. Asthma as a disruption in iron homeostasis. Biometals 2016;29(5):751-779.
7. Nunes R, Tátá M. The impact of anaemia and iron deficiency in chronic obstructive pulmonary disease: A clinical overview. Rev Port Pneumol 2017;23(3):146-155
8. Sifatullah, Siddique AN, Rehman N, Muhammad W, Ullah MA, Haleem N, et al. Study of Anemia and its co-relation with Hematological parameters and aging in Peshawar, Pakistan. J Entomol Zool Stud 2017;5(5):31-34.
9. Alam, F, Ashraf, N, Kashif, R, Arshad, H, Fatima S S. Soluble transferrin receptor, Ferritin index in Pakistani population. Pak J Pharm Sci 2017;30(2): 537-540.
10. Whitehead Jr RD, Mei Z, Mapango C, Jefferds MED. Methods and analyzers for hemoglobin

measurement in clinical laboratories and field settings. Ann N Y Acad Sci 2019;1450(1):147–171.

11. Badem ND. Comparison of Ferritin Measurement Performance through Immunoturbidimetric and Chemiluminescence Methods in Patients with Critical Ferritin Levels. Acta Scientific Med Sci 2019;3(8):160-168.
12. Arce SC. On the 2019 Spirometry Statement. Am J Respir Crit Care Med 2020;201(5):626-627
13. Jeong YJ, Shin SR, Han AL, Lee SY, Kim JH. The Association between Pulmonary Function and Hemoglobin, Anemia in Non-Smokers Using the 6th Korea National Health and Nutrition Examination Survey. Korean J Fam Pract 2016; 6(4):371-374
14. Vasquez A, Logomarsino JV. Anemia in Chronic Obstructive Pulmonary Disease and the Potential Role of Iron Deficiency. COPD 2016;13(1): 100-109.
15. Akhtar S, Ahmed A, Ahmad A, Ali Z, Riaz M, Ismail T, et al. Iron status of the Pakistani population-current issues and strategies. Asia Pac J Clin Nutr 2013; 22(3):340-347.
16. Imanizade Z, Danesh H. The association between microcytic anemia and spirometric parameters. Adv Respir Med 2019;87(1):1–6
17. Ghio AJ, Hilborn ED. Indices of iron homeostasis correlate with airway obstruction in an NHANES III cohort. Int J Chron Obstruct Pulmon Dis 2017;12:2075-2084.
18. Kim MH, Kim YH, Lee DC. Relationships of Serum Iron Parameters and Hemoglobin with Forced Expiratory Volume in 1 Second in Patients with Chronic Obstructive Pulmonary Disease. Korean J Fam Med 2018;39(2):85-89.
19. Pizzini A, Aichner M, Sonnweber T, Tancevski I, Weiss G, Löffler-Ragg J. The Significance of iron deficiency and anemia in a real-life COPD cohort. Int J Med Sci 2020;17(14): 2232-2239.