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"LUNG FUNCTION TESTS IN PATIENTS OF PREDIABETES AND DIABETES"

Physiology

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ABSTRACT

Background: Prediabetes is a condition where people have blood glucose levels higher than normal but not yet high enough to be diagnosed with diabetes. WHO divides prediabetes into impaired glucose tolerance (IGT) and impaired fasting glucose (IFG). Prediabetes is a common disorder in most populations[1]. Before people develop Type 2 diabetes, they almost always have prediabetes[2]. Pulmonary Function Testing (PFT) is a complete evaluation of the respiratory system including patient history, physical examination, chest x-ray examinations, arterial blood gas (ABG) analysis and spirometry. Spirometry is the recommended objective test performed to identify abnormalities in lung volumes and air flow[3]. Accumulating evidence suggests that there is a close relationship between impaired lung function and diabetes mellitus (DM). Population-based studies have demonstrated associations between both obstructive and restrictive lung impairment and insulin resistance or DM[4, 5]. A number of Asian studies have also revealed a significant association between reduced lung function and insulin resistance, metabolic syndrome and type 2 diabetes[6,7].

Aims and objectives: To assess lung function in patients of Prediabetes and diabetes by spirometry.

Materials and methods: Our study was an observational cross sectional study. 1179 apparently healthy non-smoker adult subjects underwent fasting plasma glucose (FPG) test, 2-hr oral glucose tolerance test (OGTT) and spirometry. The spirometric parameters measured were percent predicted values of FVC (forced vital capacity), FEV_1 (forced expiratory volume in 1 second), and FEV_1/FVC .On the basis of FPG and 2 hr. OGTT the subjects were divided into NGT (normal glucose tolerance), Prediabetes and Diabetes groups.

Results: In this study 870 (74%) subjects had NGT, 177 (15%) had prediabetes and 132 (11%) had diabetes. FVC (% pred.) and FEV_1 (% pred.) were significantly lower but FEV_1/FVC (% pred.) was significantly higher in prediabetes and diabetes groups as compared to NGT group.

Conclusion: Restrictive lung disease (low lung volume) was significantly associated with prediabetes and diabetes.

KEYWORDS

Prediabetes, diabetes, lung function tests, spirometry.

1. Introduction

Prediabetes is a condition where people have blood glucose levels higher than normal but not yet high enough to be diagnosed with diabetes. It is a stage of intermediate hyperglycemia between normal glucose tolerance and type 2 diabetes .WHO divides prediabetes into impaired glucose tolerance (IGT) and impaired fasting glucose (IFG)[8]. Both IFG and IGT are the established risk factors for diabetes mellitus[9]. Prediabetes is a common disorder in most populations. Before people develop Type 2 diabetes, they almost always have prediabetes. There is progressive impairment of insulin secretion (or β-cell dysfunction) as well as worsening insulin resistance, in people with prediabetes[10], resulting in gradual increases in fasting and post-prandial plasma glucose concentrations.The higher the glucose values, the greater therisk of progression to diabetes and diabetic complications. Progression to overt diabetes from a prediabetes state occurs gradually over a period of many years and is characterized by worsening insulin resistance and insulin secretory dysfunction and gradual increase in fasting and postprandial plasma glucose concentrations[11,12,13].

Pulmonary Function Testing (PFT) is a complete evaluation of the respiratory system including patient history, physical examination, chest x-ray examinations, arterial blood gas (ABG) analysis and spirometry. Spirometry is the recommended objective test performed to identify abnormalities in lung volumes and air flow[3]. In obstructive diseases (asthma, COPD, chronic bronchitis, emphysema), FEV_1 is diminished because of increased airway resistance to expiratory flow; the FVC may be decreased as well due to premature closure of airways in expiration, but not in the same proportion as FEV_1.In restrictive diseases e.g. pulmonary fibrosis, the FEV_1 and FVC are both reduced proportionately and the value may be normal or even increased as a result of decreased lung compliance. Accumulating evidence suggests that there is a close relationship between impaired lung function and diabetes mellitus (DM). The association of reduced lung function and diabetes has been described for many years[4, 5]. Population-based studies have demonstrated associations between both obstructive and restrictive lung impairment and insulin resistance or DM. A number of Asian studies have also revealed a significant association between reduced lung function and insulin resistance, metabolic syndrome and type 2 diabetes[6,7].

2. Materials and Methods

The present study was undertaken in young Kashmiri adult population. It was a cross-sectional observational study. The group consisted of both males and females of age 18 years and above. A total of 1179 subjects participated in our study.

All the subjects underwent fasting plasma glucose (FPG) estimation, 2- hour oral glucose tolerance test (OGTT) and spirometry. Blood sugar estimation of the samples was done using automatic biochemistry analyzer Hitachi 912. On the basis of FPG and 2-hr. OGTT, subjects were classified into five categories as per American Diabetes Association criteria (ADA)[14]:

1. Isolated IFG (FPG 100–125 mg/dl and 2-h OGTT < 140 mg/dl).
2. Isolated IGT (FPG < 100 mg/dl and 2-h OGTT 140–199 mg/dl).
3. Combined IFG/IGT (FPG 100–125 mg/dl and 2-hOGTT 140–199 mg/dl).
4. Diabetes (FPG ≥ 126 mg/dl or 2-hOGTT ≥ 200 mg/dl).
5. Normal glucose tolerance [NGT] (FPG < 100 mg/dl and 2-h OGTT <140 mg/dl).

Isolated IFG, Isolated IGT and combined IFG & IGT were considered as subgroups of prediabetes. All the subjects underwent spirometry as per American Thoracic Society (ATS) standards. FVC (% pred.), FEV_1 (% pred.) and FEV_1/FVC (% pred.) were determined. FVC and FEV_1 (% pred.) ≥ 80% were considered as normal. FEV_1/FVC (% pred.) ≥ 70% was considered as normal. Pulmonary function was measured using RMS Helios 701 Spirometer.

Results

The total number of subjects in our study was 1179. Out of total 1179 subjects, 412 (35%) were males and 767 (65%) were females. Out of the total 1179 subjects, 870 (74%) had NGT, 177 (15%) had prediabetes and 132 (11%) had diabetes.

FVC (% pred.) and FEV_1 (% pred.) were significantly lower while as FEV_1/FVC (% pred.) was significantly higher in prediabetics and diabetics as compared to NGT group subjects. The trend was followed by all the three subgroups of prediabetes. Age and BMI were significantly higher in prediabetics and diabetics as compared to NGT

group subjects. These results of this study point towards a predominantly restrictive pattern (low lung volume) of lung dysfunction in prediabetic and diabetic groups as compared to NGT group.

Table 1
Distribution of study subjects according to gender

Gender	Number	Percentage (%)
Male	412	35
Female	767	65
Total	1179	100

Table 2
Comparison of Age, BMI and spirometric parameters of Prediabetic and Diabetic groups with those of NGT group.

	NGT	Prediabetes	Diabetes	p- value
Number of subjects	870	177	132	
Age(years)	39.20±13.90	47.90±14.20	48.70 ± 16.50	<0.001
BMI(kg/m^2)	23.97 ± 4.10	26.97 ± 4.57	25.95 ± 4.61	<0.001
FVC (% pred.)	108.75±13.86	83.05±12.48	76.23± 8.93	<0.001
FEV_1 (% pred.)	120.74±15.44	97.21±14.88	89.52± 10.79	<0.001
FEV_1/FVC(%pred.)	111.61±11.09	117.34±10.41	117.36± 8.63	<0.001

NGT=normal glucose tolerance; BMI=body mass index; FVC=forced vital capacity; FEV1=forced expiratory volume in 1 second.
Values are numbers or Mean±SD; p<0.05 was considered statistically significant.

Table 3
Comparison of spirometric parameters of Prediabetic subgroups with those of NGT group.

	NGT	Isolated IFG	Isolated IGT	Combined IFG& IGT	p- value
Number of subjects	870	56	54	67	
FVC (% pred.)	108.75±13.86	88.45±11.18	86.69±10.82	75.60±11.21	<0.001
FEV_1 (% pred.)	120.74±15.44	102.63±14.14	99.98±13.25	90.45±14.33	<0.001
FEV_1/FVC(% pred.)	111.61±11.09	116.25±10.36	115.30±10.40	119.91±10.11	<0.001

NGT=normal glucose tolerance; FVC=forced vital capacity; FEV_1=forced expiratory volume in 1 second; IFG=impaired fasting glucose; IGT=Impaired glucose tolerance Values are numbers or Mean±SD; p<0.05 was considered statistically significant.

Discussion

Prediabetes is a global health problem. The prevalence of prediabetes is in fact higher than the diabetes prevalence. The person who develops prediabetes is going to become diabetic if he/she goes untreated in an appropriate manner[15].Diabetes is a micro- macrovascular disorder with debilitating effects on many organs. It is known to cause target organ diseases like nephropathy, retinopathy and neuropathy. The alveolar capillary network in the lungs is a large microvascular unit and may be affected by microangiopathy. However because of its large reserve, substantial loss of the microvascular bed can be tolerated without developing dyspnea. As a result pulmonary diabetic microangiopathy may be under- recognized clinically. Reduced elastic recoil, reduced lung volume, diminished respiratory muscle performance, chronic low grade inflammation[16], decrease in pulmonary diffusion capacity for carbon monoxide, autonomic neuropathy involving respiratory muscles are some of the important changes occurring in DM.

The mechanism by which impaired glycemic control may lead to a reduction in lung function is uncertain, though it has been suggested that the increased systemic inflammation associated with diabetes may result in pulmonary inflammationand hence airway damage[17].

Alternatively, a reduction in antioxidant defenses resulting from increased oxidative activity associated with diabetes may lead to a secondary reduction in the antioxidant defenses of the lung and hence increased susceptibility to environmental oxidative insults, resulting in subsequent loss of lung function. While IFG is characterized by predominantly hepatic insulin resistance and normal muscle insulin sensitivity, IGT shows normal to slightly reduced hepatic insulin sensitivity and moderate to severe muscle insulin resistance. Both IFG and IGT are associated with impairment of insulin secretion.

The histopathological changes in the lungs of diabetics are associated with the thickening of the alveolar epithelium and the pulmonary capillary basal lamina and also reduced recoiling of the lung. This is caused by biochemical alteration of connective tissue constituents, particularly collagen and elastin. There is increased cross-linkage formation between polypeptides of collagen which leads to thickening, leading to restriction of lung volume and alveolar gas transport, reduced membrane diffusion capacity and pulmonary capillary blood volume.

Our study results are consistent with the study results of Takashi Yamane, Akihito Yokoyama, Yoshihiro Kitahara, et al (2013), [18] that low % FVC but not low FEV_1/FVC ratio was significantly associated with increased prevalence's of diabetes and prediabetes in the cross-sectional study. Our study results are in agreement with the study results of Yulan Li, Masafumi Saito, Satoshi Tobimatsu et al(2013),[19] which showed that the prevalence of low FVC increased significantly with progression from NGT to diabetes, whereas the prevalence of low FEV_1/FVC did not. Not only diabetes but also prediabetes was significantly associated with low FVC, compared with NGT. Isolated IFG, combined IFG & IGT, and diabetes were significantly associated with low FVC.

Cross sectional study results of Mahadeva Murthy, et al (2012)[20] showed that the spirometric values were consistently lower in subjects with Type 2 diabetes mellitus than in non-diabetics. The differences reached statistical significance only for FVC, but the trend was seen across all parameters. The results of our study also demonstrated that the spirometric findings were consistently lower in diabetics than in non-diabetics. However our study results reached statistical significance for FEV_1 also.

Our study results are in agreement with the study results of Bram van den Borst, Harry R. Gosker, Maurice P. Zeegers, et al(2010)[21], that in the absence of covert pulmonary comorbidity both type I and type II diabetes are associated with a modest, albeit statistically significant, impaired pulmonary function in a restrictive pattern. However, we did not categorize diabetics into Type I and Type II.

Muhammad Irfan, Abdul Jabbar, Ahmad Suleman Haque, et al(2011)[22],on studying the effects of DM on lung function concluded that there was a significant reduction in FVC and FEV_1 in diabetics as compared to controls and there was no significant difference in FEV_1/FVC between two groups. Our study also demonstrated a significant reduction in FVC and FEV_1 in diabetics but in our study FEV_1/FVC was significantly higher in diabetics as compared to controls.

CONCLUSION

Restrictive lung disease (low lung volume) was significantly associated with prediabetes and diabetes. The severity of lung restriction increased gradually with progressively increasing blood glucose levels. Spirometry remains a cost effective; a simple non-invasive method for assessing extent of pulmonary involvement in prediabetics and diabetics and its judicious use can help in measuring the response to treatment in these states.

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