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Prediabetes is associated with restrictive pattern of lung disease in otherwise asymptomatic adults: a cross-sectional study

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Abstract

Background: Very few studies have been conducted to study the effects of prediabetes on lung functions. Evidence suggests that prediabetes causes mechanical changes in the periphery of lungs which may have adverse affects on the lung functions.

Material and methods: In this observational cross sectional study, 800 apparently healthy adult subjects were selected who underwent spirometry, fasting plasma glucose analysis and 2-h oral glucose tolerance test. Spirometric indices such as percent predicted values of forced vital capacity, forced expiratory volume in 1 second, and forced vital capacity/forced expiratory volume in 1 second were considered. Based on fasting plasma glucose and 2 hr oral glucose tolerance test the subjects were further divided into two groups, i.e. subjects with normal glucose levels and those with prediabetics.

Results: It was observed that 400 (50%) subjects had normal glucose levels, 400 (50%) had prediabetes. Furthermore it was observed that as compared to the control group, forced vital capacity (% pred.) and forced expiratory volume in 1 second (% pred.) were significantly lower but forced vital capacity/forced expiratory volume in 1 second (% pred.) was significantly higher in prediabetes group.

Conclusion: Based on the results of spirometry it may be concluded that restrictive lung pattern (low lung volume) may be in prediabetes itself before the development of type 2 diabetes mellitus.

Key words: prediabetes, restrictive lung diseases, forced vital capacity, forced expiratory volume in 1 second, low lung volume

ПРЕДИАБЕТ ЕРЕСЕК БЕЛГІСІЗ НАУҚАСТАРДА ӨКПЕ АУРУЫНЫҢ ШЕКТЕУЛІ ТҮРІМЕН БАЙЛАНЫСТЫ: КӨЛДЕНЕҢ ЗЕРТТЕУ

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ТҰЖЫРЫМДАМА

Кіріспе: Преддиабеттің өкпенің жұмысына әсері туралы өте аз зерттеулер жүргізілген. Қол жетімді деректер преддиабет өкпенің перифериясында механикалық өзгерістер тудыратындығын көрсетеді, бұл өкпенің жұмысына теріс әсер етуі мүмкін.

Материалдар мен әдістер: Бұл тәжірибелік көлденең зерттеуге спирометрия, плазмалық глюкоза анализі және 2 сағат ішінде ауыз қуысы арқылы глюкозаға төзімділік сынақтарынан өткен 800 клиникалық сау ересектер қатысты. Өкпенің тездетілген тіршілік сыйымдылығының және тездетілген тірлішілік сыйымдылығының болжамды пайызы, 1 секундтағы тездетілген ауа шығару көлемі/1 секіндтағы тездетілген ауа шығару көлемі секеілді спирометриялық көрсеткіштер қарастырылды. Аш қарынға плазмадағы глюкоза таладуыі мен 2 сағаттық глюкозаға төзімділік сынағының негізінде субъектілер екі топқа бөлінді, яғни қалыпты глюкоза деңгейі бар субъектілер және қант диабетімен ауыратын субъектілері.

Нәтижелер: 400 (50%) субъектілерде глюкозаның қалыпты деңгейі, 400 (50%) -да преддиабиет ауруы бар екендігі анықталды. Сонымен қатар, бақылау тобымен салыстырғанда, тездетілген тіршілік сыйымдылығының мәні (% алдыңғы) және 1 секундқа тездетілген ауа шығару көлемі (% пред.) айтарлықтай төмен болды, бірақ 1 секунд ішінде (% алдыңғы) тездетілген тіршілік көлемі/ тездетілген ауа шығару көлемінің мәні преддиабет тобында едәуір жоғары болды.

Қорытынды: Спирометрияның нәтижелеріне сүйене отырып, өкпе ауруының шектеулі түрі (өкпенің шағын көлемі) 2 типті қант диабеті дамымай тұрып, преддиабиет ауруы жағдайында пайда болуы мүмкін деген қорытынды жасауға болады.

Негізгі сөздер: преддиабиет, өкпе ауруының шектеулі түрі, тездетілген тіршілік сыйымдылығы, 1 секундтағы тездетілген ауашығару көлемі, өкпенің кіші көлемі

ПРЕДДИАБЕТ СВЯЗАН С РЕСТРИКТИВНОЙ ФОРМОЙ ЗАБОЛЕВАНИЯ ЛЕГКИХ У ВЗРОСЛЫХ БЕССИМПТОМНЫХ ПАЦИЕНТОВ: ПОПЕРЕЧНОЕ ИССЛЕДОВАНИЕ

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РЕЗЮМЕ

Введение: Проведено очень мало исследований по изучению влияния преддиабета на функции легких. Имеющиеся данные свидетельствуют о том, что преддиабет вызывает механические изменения на периферии легких, которые могут оказывать неблагоприятное воздействие на функции легких.

Материалы и методы: В настоящем экспериментальном поперечном исследовании приняло участие 800 клинически здоровых взрослых людей, которые прошли спирометрию, анализ глюкозы в плазме натощак и пероральный тест на толерантность к глюкозе в течение 2 часов. Рассмотрены такие спирометрические показатели, как прогнозируемые в процентах значения форсированной жизненной емкости, объема форсированного выдоха за 1 секунду и форсированной жизненной емкости / объема форсированного выдоха за 1 секунду. На основании анализа глюкозы в плазме натощак и перорального теста на толерантность к глюкозе в течение 2 часов, субъекты были разделены на две группы, т.е. субъекты с нормальным уровнем глюкозы и субъекты, предрасположенные к диабету.

Результаты: Было отмечено, что у 400 (50%) субъектов был нормальный уровень глюкозы, у 400 (50%) был преддиабет. Кроме того, было отмечено, что по сравнению с контрольной группой, значения форсированной жизненной емкости (% пред.) и объем форсированного выдоха за 1 секунду (% пред.) были значительно ниже, но значение форсированная жизненная емкость / объем форсированного выдоха за 1 секунду (% пред.) было значительно выше в группе преддиабета.

Заключение: На основании результатов спирометрии можно сделать вывод о том, что рестриктивная форма заболевания легких (малый объем легких) может иметь место в случае преддиабета до развития сахарного диабета 2 типа.

Ключевые слова: преддиабет, рестриктивная форма заболевания легких, форсированная жизненная емкость, объем форсированного выдоха за 1 секунду, малый объем легких

Introduction

Prediabetes is a condition, which precedes diabetes mellitus, characterized by high blood glucose levels (100-125mg/dl) than the normal (70-99mg/dl). However these high levels of blood glucose are not sufficient enough to meet the required criteria for a diagnosis of diabetes mellitus [1]. Prediabetes may be divided into impaired glucose tolerance (IGT) characterized by fasting blood glucose <126mg/dl or 2-h blood glucose levels in between 140 mg/dl to 200mg/dl and impaired fasting glucose (IFG) characterized by a fasting blood glucose level of 110mg/dl- 125mg/dl or 2-h blood glucose level of < 140 mg/dl. Both IFG and IGT are known risk factors for diabetes mellitus and both of them increase in prevalence with age [2,3]. The prevalence of prediabetes is increasing all over the world and it is estimated that >470 million people will have prediabetes by 2030 [3].

Because IFG and IGT vary among populations with different ethnic backgrounds, prevalence of prediabetes varies [4]. Prediabetes is asymptomatic and can often go undiagnosed for many years with a yearly conversion rate of 5-10% into full fledged diabetes mellitus [5]. IFG and IGT can occur as separate entities or they can occur simultaneously [6]. Some individuals may remain with prediabetes throughout their life and in some reversion from prediabetes to normoglycaemia may occur [7]. Literature suggests that in people with prediabetes, there is progressive impairment of insulin secretion or as worsening of insulin resistance which ultimately causes a gradual increase in fasting and post-prandial plasma glucose levels [8]. Decreased level of HDL cholesterol, increased level of LDL cholesterol, triglycerides and hypertension, are present more frequently among prediabetic individuals hence they are at a heightened risk of cardiovascular diseases [9]. Microvascular and macrovascular complications start during the toxic state of pre¬diabetes and much of the cardiovascular disease burden is already evident during prediabetes [10]. It is a known fact that elevated glucose levels damage endothelial cells, which can lead to microvascular disease [10]. There is data that suggests increased presence of restrictive lung disease (RLD) in prediabetes that is usually characterized by breathlessness [11]. These changes during prediabetes suggest that there are some mechanical changes in the periphery of lungs prior to effects on the pulmonary capillary bed which lead to a decreased forced vital capacity (FVC) in patients with prediabetes [12,13].

Thus, this study was conducted with the aim to see whether there was any impact on the lung function tests in recently diagnosed cases of prediabetes or not.

Material and methods

After getting clearance from the Institutional Ethical Committee, this cross sectional observational study was carried in the Department of Physiology Government Medical College & SMHS hospital, Srinagar, J&K, India from January 2019 to January 2020. In this study a total of 800 adult subjects participated. They were further divided into healthy controls who had normal blood glucose levels (400 subjects) and those who had prediabetes (400 subjects).

Exclusion criteria

- Subjects aged < 18 years.
- Subjects who could not perform the spirometry correctly.
- Subjects having history of any obstructive or restrictive lung disease.
- Subjects with a history of smoking.
- Subjects previously diagnosed with type 1or type 2 diabetes mellitus.
- Subjects who were pregnant.
- Subjects with diseases or on drugs which affect blood glucose levels and lung function.

Study protocol

Anthropometric measurements: Written consent was taken from all the participants before the commencement of study. Weight of subjects was measured by a digital weighing scale (Omron-HN 289, Japan). Height was measured using a stadiometer in all the subjects. Body mass index (BMI) was calculated by Quetlet's index expressed as kg/m². BMI of 25kg/m² or more was considered as overweight and 30kg/m² or more was considered as obesity [14].

Blood sugar levels: Fasting blood glucose (FBG) estimation and 2-h oral glucose tolerance test (OGTT) was done in all the subjects. Analysis of blood sugar levels of the samples was done using automated analyzer (Roche Hitachi

912, USA). Based on the results of FBG and 2-h OGTT and the criteria set by American Diabetes Association [15] subjects were categorized into

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

Isolated IFG, Isolated IGT and combined IFG & IGT were considered as subgroups of prediabetes [15].

Spirometry: All the subjects underwent spirometry using RMS helios701 spirometer in accordance with the American Thoracic Society (ATS) standards [16]. Spirometry of all the subjects was done in a sitting position. Indices such as forced vital capacity [FVC (% pred.)], forced expiratory volume at the end of 1 minute [FEV1 (% pred.)] and ratio of FEV1/FVC (% pred.) were determined. FVC and FEV1 (% pred.) ≥ 80% and FEV1/FVC (% pred.) ≥ 70% was considered as normal [16].

Statistical analysis

Statistical analysis was done using GraphPad 7 (San Diego, CA, USA). All the anthropometric and biochemical data variables were expressed in terms of Mean±SD. Normality was checked by D'Agostino-Pearson test. Chi- square test was used for nominal data (gender). For comparing the anthropometric parameters between the two groups Student's unpaired t-test was used. Indices of spirometry between the controls and various subtypes of prediabetes were compared by ANOVA test. P value <0.05 was considered as statistically significant.

Results

A total of 800 subjects were selected for this study in which 400 (50%) were healthy controls whereas 400 (50%) were cases diagnosed with prediabetes. Furthermore 455 (57%) were males and 345 (43%) were females as shown in Table 1. There was no significant difference in age between the two groups however BMI of the case group was significantly higher than the control group as shown in Table 2. In this study it was observed that FVC (% pred.) and FEV1 (% pred.) were significantly lower where as FEV1/FVC (% pred.) was significantly higher in prediabetics (IFG, IGT & combination of both) as compared to the control group as shown in Table 3.

Table 1 Distribution of subjects on the basis of gender.

Gender	Number	Percentage
Male	455	57%
Female	345	43%
N	800	100%

Chi- square test for gender distribution; N: total number of subjects.

Table 2 Anthropometric measurements of controls vs cases.

	Controls	Cases	P value
Age (Years)	42.20 ± 6.91	43.32 ± 7.22	0.12
BMI (kg/m^2)	22.91 ± 3.21	27.21 ± 2.36	<0.001♣

BMI: body mass index; kg: kilogram; m^2: meter square
Data expressed as Mean ± SD
♣: highly significant.

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

	Controls	Isolated IFG	Isolated IGT	Combined IFG& IGT	p- value
Number of subjects	400	166	140	94	
FVC (% pred.)	108.75±13.86	88.45±11.18	86.69±10.82	75.60±11.21	<0.001♣
FEV1 (% pred.)	120.74±15.44	102.63±14.14	99.98±13.25	90.45±14.33	<0.001♣
FEV1/FVC(% pred.)	111.61±11.09	116.25±10.36	115.30±10.40	119.91±10.11	<0.001♣

FVC: forced vital capacity; FEV_1: forced expiratory volume at the end of 1 second; % pred: percentage predicted; IFG: impaired fasting glucose; IGT: impaired glucose tolerance.
Data expressed as Mean ± SD
♣: highly significant

Discussion

Literature suggests that the number of prediabetics is increasing at an alarming pace which makes it a potential health hazard [4]. Prevalence of prediabetes is in varies considerably due to the various types of diagnostic criteria, population studied and selection of tests [17]. It has been seen that prediabetes progresses to overt T2DM in approximately 25% of prediabetics over a span of 3-5 years and almost 70% of prediabetics develop T2DM within their life span [18,19]. Prediabetes has been reported to reduce lung function but the exact mechanism by which it affects lung function is yet to be ascertained although it is postulated that there may be mechanical changes in the periphery of lungs due to hyperglycemia before the development of T2DM [12]. Prediabetes has a strong association with obesity. Study conducted by Rahmanian K et al [20] in a sample of 788 subjects, 360 men and 428 women, showed that subjects with prediabetes had higher BMI, p<0.05. In a cross sectional study conducted by Fernando GR et al [21], they observed that prevalence of obesity was 45.9% in prediabetes. Findings in our study were similar. In a cross sectional study by Sanchez E et al [22] lung function tests of about 3455 subjects were done out of which 1093 (31.6%) had prediabetes and 2362 subjects were taken as healthy controls. They observed that subjects with prediabetes showed a significantly lower FVC (FVC:93 [82;105] vs 96 [84;107]% of predicted, p<0.001), FEV_1 (FEV_1: 95[82; 108] vs 97[85; 109]% of predicted, p=0.004) in comparison with the controls. It was also observed that in subjects with prediabetes exhibited FVC<80% (20.7% vs 16.3%) and FEV_1 <80% (19.7% vs 16.6% [p<0.001]). They concluded that restrictive pattern of lung disease is present in prediabetes. Our findings were consistent with their findings. Li Y et al [23] in a cross-sectional study of 1237 subjects demonstrated that there is a significant association of restrictive pattern of lung disease in prediabetics. In another cross sectional study Yamane T et al [24]

demonstrated that prediabetes was significantly associated with low % FVC. They observed that IGT subtype of prediabetes was associated with restrictive pattern of lung disease. Our findings were similar but we observed that both IGT and IFG were associated with restrictive pattern of lung disease.

Conclusion

Thus it may be concluded that prediabetes, in otherwise asymptomatic subjects, is significantly associated with restrictive pattern of lung disease. Thus, frequent monitoring of blood glucose levels especially in obese people, for timely diagnosis of prediabetes, is of paramount significance so that the complications related to prediabetes could be minimized which will ultimately increase the quality of life in prediabetics.

The main lacunae of this study are the scarcity of literature because fewer studies have been conducted to assess the lung function tests in prediabetes.

Disclosures: There is no conflict of interest for all authors.

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