

Respiratory tract infections in diabetic and non-diabetic individuals are linked with serum surfactant protein-D

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Abstract

Objective: To find out the rate of respiratory tract infections in diabetic and non-diabetic individuals and their relation with surfactant protein D.

Methods: The cross-sectional study was conducted at Dow University of Health Sciences, Karachi, from September 2011 to April 2012, and comprised subjects of both genders between ages of 30 and 60 years. The subjects were divided into four groups: diabetic obese, non-diabetic obese, diabetic non-obese, and non-diabetic-non-obese. A structured questionnaire was used to collect information about respiratory tract infections. Serum surfactant protein D levels were analysed using human surfactant protein D enzyme-linked immunosorbent assay kit. Statistical analysis was performed using SPSS 16.

Results: Of the 90 subjects, there were 20(22.2%) diabetic obese, 30(33.3%) non-diabetic obese, 10(11.1%) diabetic non-obese, and 30(33.3%) non-diabetic-non-obese. The overall mean age was 36.6 ± 10.3 years. Among the diabetic obese, 15(75%) had respiratory tract infections which was higher than the other study groups, and patients having respiratory tract infections had lower surfactant protein D levels than those who did not have infections ($p=0.01$).

Conclusion: Diabetic obese subjects had greater rate of recurrent respiratory tract infections and had lower concentration of serum surfactant protein D compared to subjects without respiratory tract infections.

Keywords: SP-D, Innate immunity, Diabetes mellitus, Respiratory tract infections. (JPMA 65: 1210; 2015)

Introduction

Diabetes mellitus (DM) and obesity have always been considered to be associated with carrying a high risk for community-acquired infections. Despite the large number of studies, the pathogenesis of respiratory tract infections (RTIs) in both conditions is still elusive. It is only recent that we find laboratory findings consistent with the hypothesis that subjects with obesity and DM may have variations in immune system that may predispose them to infections.¹ Various studies have been carried out to find out the relationship between DM and the risk of acquiring upper respiratory tract infections (URTIs). The increased number of infections in both conditions may be associated with a decrease in T-cell-mediated immunity as well as an impairment in function of neutrophils.² DM patients are mostly affected by streptococcus pneumoniae, influenza virus, legionella, mycobacterium tuberculosis, staphylococcus aureus, mucor and gram-negative bacterial infections. Therefore, DM is considered to confer an increased risk of lower respiratory tract infections (LRTIs).³

Quite obviously, LRTIs are due to impairment in pulmonary host defences.³ During respiration, lots of micro-organisms are inhaled along with air daily, which may be harmful to the respiratory epithelium and lungs. Our innate system fights against them by increasing the secretion of proteins; one such protein implicated in pulmonary host defence system is surfactant protein D (SP-D), which is secreted by type-II pneumocytes and prevents further invasion by microbes.⁴ In addition to synthesis and secretion by alveolar and bronchiolar epithelial cells, the lining epithelial cells of many exocrine ducts and the mucosa of gastrointestinal tract (GIT) and genitourinary tract also express SP-D.⁵ It is proved to be an important component of pulmonary host defence which helps to clear the pathogens, micro-organisms and organic antigens inhaled into the respiratory tract and, hence, regulates the immune and inflammatory response of the lung.^{5,6} On the other hand, deficiencies in proteins playing a part in immune system have been detected in cases of impaired glucose metabolism, impaired insulin action and inflammation.⁴ Hence, it is suggested that LRTIs occur with more frequency due to compromise in pulmonary host defence at multiple levels.⁵

Studies and observations showing a high risk of infections in diabetics exist as this topic is still being debated upon.⁷ Impaired lung function and glucose intolerance, insulin resistance, type 2 diabetes and obesity have been

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proposed to be linked to each other.⁴

The current study was planned to explore the relationship between levels of SP-D and RTIs in obese and diabetic individuals.

Subjects and Methods

The cross-sectional study was conducted at the National Institute of Diabetes and Endocrinology (NIDE), Dow University of Health Sciences (DUHS), Karachi, from September 2011 to April 2012. The sample size was calculated by Open Epi Sample Size Calculator with prevalence (p) 13%, error (e) 7% and confidence interval (CI) of 95% and was confirmed by formula

$$n = Z^2_{1-\alpha/2} (P(1-P)) / e^2.^8$$

(n = sample size; Z = standard normal Z value at 95% CI = 1.96).

Subjects in the age range of 30-60 years of either gender were included with non-probability convenient sampling. Diabetic subjects were enrolled from the NIDE outpatient department (OPD) and non-diabetics were DUHS employees. All relevant information regarding basic characteristics and history of RTIs of the subjects were recorded on a detailed proforma. Details about the episodes of RTIs and symptoms like cough, sputum production, and shortness of breath, wheeze, coryza, and fever during this illness were inquired about. A new episode of infection was defined if a patient was free of signs or symptoms for a 30-day period. Second episode occurring >30 days after the initial episode was considered to be a recurrence. Number of visits to doctors (an episode could include at least one or more visits to doctor) and use of antibiotic for respiratory tract symptoms during the preceding 6 months were also noted. Rate of RTIs in study subjects were evaluated on the basis of above information. Subjects with known history of other endocrine disorders, liver diseases, neuromuscular diseases, malignancy, cardiopulmonary diseases, drug addicts and smokers were excluded. After

taking informed written consent from those included, the subjects were divided into four groups: diabetic obese, non-diabetic obese, diabetic non-obese, and non-diabetic-non-obese. Blood samples of all participants were obtained to analyse SP-D. Blood was allowed to clot for 30 minutes, for serum extraction, to determine SP-D levels, which was estimated by enzyme-linked immunosorbent assay (ELISA) method by commercially available Human SP-D ELISA kit (De-medi-tec Laboratory, Germany).

Statistical analysis was performed using SPSS 16. Mean $\pm$ standard deviation (SD) was calculated for normally distributed quantitative variables (age and SP-D levels). Frequencies and percentages were calculated for qualitative variables (gender and RTIs). Chi square test was used for comparison of proportions (categorical variable). RTIs were analysed as a dichotomous outcome (absence versus presence). Association between the categorical variables (DM and RTIs) was evaluated by binomial logistic regression analysis; and results were expressed as odds ratio (OR), 95% CI and P value. Odd ratios and 95% CI were given as an approximation of the relative risk (RR). $P < 0.05$ was considered statistically significant.

Shapiro-Wilk's test and Levene's test were performed to check normality and homogeneity of the variance prior to analysis of variance (ANOVA). As both tests were insignificant, which indicated that the data was normally distributed. ANOVA was applied to compare SP-D levels between the groups. Tukey post hoc test was performed for multiple comparisons.

Results

Initially 120 subjects were approached, but 30(25%) had to be excluded as they did not meet the inclusion criterion. Of the 90 subjects, there were 20(22.2%) diabetic obese, 30(33.3%) non-diabetic obese, 10(11.1%) diabetic non-obese, and 30(33.3%) non-diabetic-non-obese. The overall mean age was 36.6 ± 10.3 years. Among

Table-1: Frequencies and percentages of respiratory infections in study groups (n=90).

Groups	Total No. (n=90)	Subjects with infections		Subjects without infections	
		Frequency	Percentage %	Frequency	Percentage%
Diabetic Obese	20	15	75	5	25
Non Diabetic Obese	30	21	70	9	30
Diabetic-Non Obese	10	4	40	6	60
Non Diabetic-Non Obese	30	8	26.6	22	73
P Value			0.0002*		0.0002*

Comparison of percentages of respiratory tract infections by X2 test in study groups.

P-Value < 0.05 was considered as statistically significant.

Table-2: Binomial logistic regression analysis to evaluate the independent effect of diabetes mellitus on respiratory tract infections.

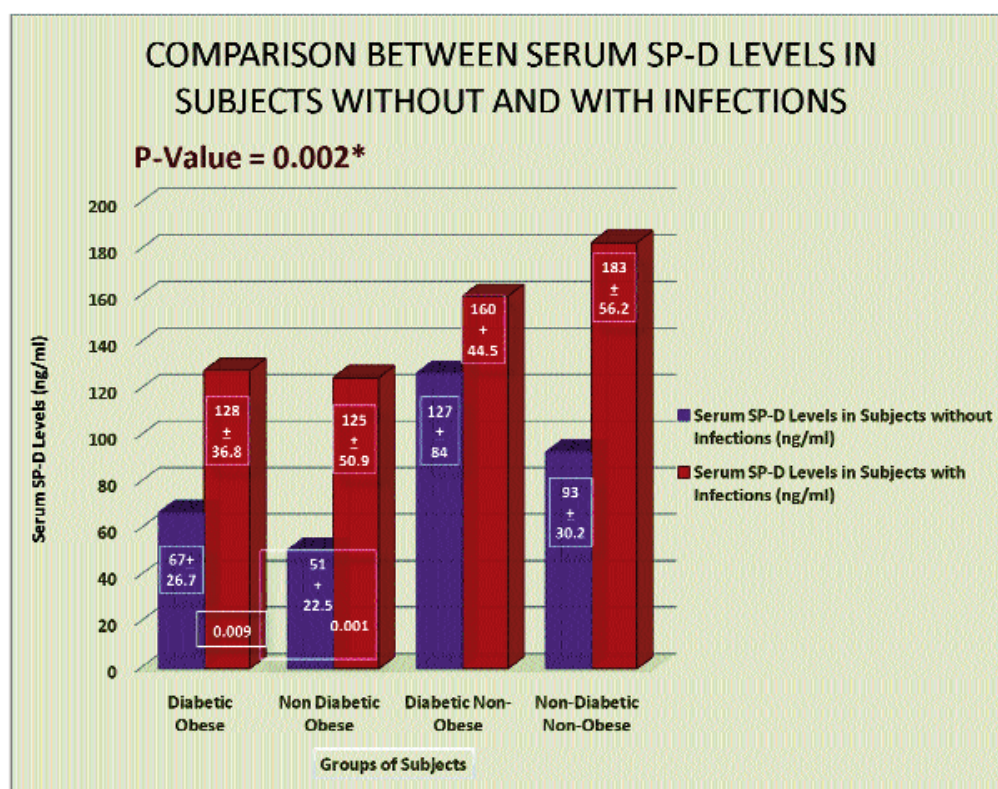
Groups	Odd Ratio (OR)	P- Value	95% CI
Diabetic obese	-	0.008*	-
non Diabetic obese	5.44	0.045*	1.039 -28.533
Diabetic normal weight	1.556	0.573	0.334 - 7.235
Non diabetic normal weight	7.667	0.012*	1.555 - 37.796

P-Value < 0.05 was considered as statistically significant.

the diabetic obese, 15(75%) had respiratory tract infections which was higher than the other study groups (Table-1), and patients having respiratory tract infections had lower surfactant protein D levels than those who did not have infections ($p=0.01$) (Table-2). Statistically significant difference was found in mean SP-D levels of subjects of different groups ($p=0.002$) (Figure). There was significant difference in mean SP-D of non-diabetic obese with and without infections ($p=0.001$), and between the mean SP-D of diabetic obese with infections and non-diabetic obese without infections ($p=0.009$).

Discussion

The growing prevalence of type 2 diabetes is because of increasing incidence of obesity worldwide.⁹ And DM, in turn, is believed to be an independent risk factor for recurrent RTIs and associated with impaired immunity. In previous studies, attention has been largely focused towards the consequences of metabolic disorders, like renal problems and cardiovascular diseases,¹⁰ but their effect on immune functions and RTIs have been poorly characterised. Much has been studied in the recent past about their association with RTIs, but it has always remained a biased hypothesis.¹ These chronic conditions compromise the immune system by impairing the neutrophil function as well as T-cell-mediated immunity. They also depress antioxidant system and humoral immunity.^{7,10} SP-D secreted by type II pneumocytes is hypothesised to be associated with pulmonary host defences. Several studies have also linked the risk of RTIs in diabetic and obese individuals with levels of SP-D. We conducted this study in order to find out the rate of RTIs in diabetic and non-diabetic individuals and, furthermore, their relation with SP-D.



Comparison of Serum surfactant protein D (SP-D) levels in study groups
Mean values $\pm$ SD of groups compared by analysis of variance.
Post hoc was applied for multiple comparisons
 $P < 0.05$ was considered statistically significant.

Figure: Serum SP-D levels of study groups.

Our study indicates that 73.7% of diabetic obese patients and 70% of non-diabetic obese subjects had history of recurrent RTIs. Besides, the diabetic obese and non-diabetic obese have greater rate of infections compared to normal-weight diabetic and non-diabetic individuals. This result is in accordance with a study⁷ that showed greater risk of RTI in diabetic patients compared to the non-diabetic. The current study further indicates that diabetic patients had a greater risk for recurrence than non-diabetic obese (OR=5.44; p=0.045) and non-diabetic normal-weight subjects (OR=7.667; p=0.012). These findings were confirmed by a study² which also reported higher relative risk of RTIs in diabetic subjects than non-diabetic subjects (OR=1.64; p=0.010).

Decreased levels of SP-D were noticed in subjects having RTIs than subjects without RTIs in our study which shows that diabetic obese and non-diabetic obese subjects having RTIs have the lowest levels of serum SP-D compared to the other groups. This finding is consistent with a study which stated that the level of SP-D expressed decreased in association with obesity and impaired glucose tolerance (IGT).⁶

In terms of limitations, the study, though it achieved its aim, had financial and time constraints. The small sample size, also an offshoot of financial limitations, may not represent the whole population. There is a need for additional research on a large scale to elucidate the role of SP-D in RTIs.

Conclusion

Diabetic patients had greater rate of recurrent RTIs than

non-diabetic subjects and DM was an independent predictor of RTIs. Subjects with RTIs had lower concentration of serum SP-D compared to subjects without RTIs. RTIs in diabetics as well as non-diabetic individuals was linked to SP-D.

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