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Original Article

Correlation of Surfactant Protein D with Insulin Resistance and Body Mass Index

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Abstract

Objective: This study assessed the correlation among insulin resistance, serum surfactant protein D (SP-D) and body mass index (BMI).

Methods: It was a cross-sectional work carried out at The Institute of Molecular Biology & Biotechnology, The University of Lahore, Pakistan from February 2022 till December 2022. 80 patients were participated in research work. BMI, serum surfactant protein D, insulin and fasting blood sugar levels were measured using commercially available kits. The values of FBG and homeostatic model assessment of insulin resistance (HOMA-IR) were measured via formula and analysed by using Spearman's correlation test SPSS version 18.

Results: The results indicate a significant negative connection between blood SP-D levels and HOMA-IR. The correlation between HOMA-IR and BMI is statistically insignificant. The SP-D levels and BMI had a negative connection. The association was found among insulin resistance, BMI and surfactant protein D levels in self reported healthy Pakistani people.

Conclusion: Serum surfactant protein D (SP-D) levels were found to be decreased in individuals with higher levels of obesity and insulin resistance. A significant association was observed between serum SP-D levels and insulin resistance.

Keywords: Surfactant Protein D, Insulin Resistance, Body mass index, HOMA-IR

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Introduction

The complex protein known as SP-D is made up of collagen protein and belongs to the calcium-dependent lectin family. Clara cells and type 2 alveolar cells produce it. After identifying the pathogen, SP-D performs a variety of tasks as the respiratory tract's first line of defense against it, including balancing hemostasis and influencing aggregation and lymphocytic activity.[1,2] Prostate glands, genitourinary tract, gastrointestinal tract, heart, salivary glands, blood, fat, skin and liver are among the extrapulmonary tissues where it has been detected. Even though SP-D is secreted in the lungs and is well-known for preventing pulmonary infections, it is also a wonderful protein with a trimeric shape that contributes to extrapulmonary cell-mediated innate immunity and hemostasis.

The function of SP-D in pathogen recognition through the carbohydrate recognition domain is well-known. According to recent studies, the same carbohydrate recognition domain binds to glucose in individuals with uncontrolled glycemic levels. When it comes to binding with CRD, glucose competes with the sugar molecules found in pathogenic cell walls. Accordingly, research has indicated heightened vulnerability to infections brought on by microorganisms that are known to connect with CRD. Diabetics are therefore thought to be more susceptible to infections.

BMI was calculated on basis of height and weight as calculated as kg/m². Low BMI was considered below 18.5. Normal BMI was considered between 18.5 - 24.5. Overweight non-obese were considered between 25.0 - 29.9. Grade I obesity was considered when BMI was between 30.0 - 34.9. Grade II obesity was considered when BMI was between 35.0 - 39.9. Grade III obesity was considered when BMI was more than 40.[3] Many studies revealed association of

insulin resistance and BMI.[4] Increased level of fats in obese persons promote formation of many compounds which are involved in insulin resistance condition such as glycerol, non-esterified fatty acids, cytokines, pro-inflammatory markers and hormones.[5] Insulin is linked with metabolism of glucose in tissues and insulin resistance depicts opposite or impaired mechanism in tissues of adipose, liver and muscles.[6] Production of insulin is increased as a result of insulin resistance in body, which leads to hyperinsulinemia, which promotes weight gain.[7] This whole mechanism leads to calculation of HOMA-IR.[8] Due to this pathology, levels of glucose rise in insulin resistance patients equal to diabetes mellitus.[9]

Abnormal gain in weight is crucial health hazard common all over the globe and obesity is the contributing factor in progression of diseases and affects around 0.3 billion population in America and 1 billion are obese with other complications such as insulin resistance, dyslipidaemia and hypertension. Incidence of obesity is increased with insulin sensitivity variations such as fat distribution, fat mass and body weight.[10,11] The signaling axis of IRS proteins and other pathways mediate the majority of insulin's metabolic actions, such as promoting glucose transport in adipose tissue and muscle and reducing glucose synthesis in the liver. Because of alterations in protein levels and the activities of transcription factors, enzymes, and signaling molecules, this pathway is known to be disrupted at multiple stages in insulin resistance brought on by obesity, a condition characterized by excessive fat production.[12,13] Correlation between BMI, SP-D and insulin resistance has been the subject of intermittent research. It is proposed that SP-D function may be impacted in insulin-resistant people with a history of diabetes. Hyperglycemia-induced glucose may function as a preferential ligand for SP-D's carbohydrate recognition domain, hence reducing its capacity to interact with a wide range of pathogens.[2] Old studies confirmed association of SP-D with obesity and diabetes.[8]

Methods

The study was undertaken following ethical approval from the Institute of Molecular Biology & Biotechnology, The University of Lahore. This cross-sectional study was conducted at the Institute of Molecular Biology and Biotechnology, The University of Lahore, Pakistan, from February 2022 to December 2022. A non-probability convenience sampling technique was employed to recruit study participants.

Written informed consent was obtained from all participants prior to enrollment. Demographic information was collected using a structured questionnaire (Annex A), along with measurements of height and weight. The study was conducted in accordance with the ethical principles of the 1964 Declaration of Helsinki and its subsequent amendments and was approved by the relevant institutional and national research ethics committees.

A total of 80 participants were enrolled in the study, with a mean age of 34.72 ± 12.00 years. Based on previous studies, the mean serum surfactant protein D (SP-D) level was reported to be 139.9 in patients with type 2 diabetes mellitus (T2DM) and 99.4 in healthy individuals. The estimated standard deviation was 20.25, with a variance of 4.5, which was used for sample size estimation.

Participants aged 18 years and above who provided informed consent were enrolled in the study. Individuals with congenital disorders, obesity, a body mass index (BMI) below 18 kg/m², confirmed COVID-19 infection, or pregnancy were excluded from the study.

The sample size was calculated using the following World Health Organization (WHO) formula for sample size determination:

n=Z1−α/22×P(1−P)d2n = \frac{Z^2_{1-\alpha/2} \times P(1-P)}{d^2}n=d2Z1−α/22×P(1−P)

(Sample Size Determination in Health Studies, WHO, 2012).

Body mass index (BMI) was calculated by dividing body weight (kg) by the square of height (m²). A **5 mL** venous blood sample was collected from each participant into vacutainer tubes. The samples were centrifuged at **1,000 rpm for 10 minutes** to separate the serum for subsequent biochemical analysis.

Spectrophotometry was used to calculate blood glucose levels. Chemiluminescence immunoassay was used to calculate serum insulin. For the measurement of HOMA-IR, blood was obtained by venipuncture in aseptic environment in vials. HOMA-IR was measured by following formula:

HOMA-IR = (insulin X glucose) / 405 for glycemia in mg/dL. In both cases the insulin is in mU/L

OR

HOMA-IR = (insulin X glucose) / 22.5 for the glucose concentration in mmol/L

SP-D levels were calculated via ELISA kit [23].

Data was analysed via P.A.S.W 18.0 (formerly SPSS). Mean ± S.E.M was used for weight, size and quantitative parameters. Spearman's correlation test was also used for correlation among these parameters. A p-value≤0.05 was considered statistically significant.

Results

Table 1 and **Figure 1** present the demographic characteristics of the study cohort, comprising 48 men with a mean age of **33.64 ± 12.07 years** and 32 women with a mean age of **31.50 ± 20.00 years**. The mean and median values for waist circumference, body mass index (BMI), serum insulin, fasting blood glucose, surfactant protein D (SP-D), and homeostatic model assessment of insulin resistance (HOMA-IR) are also presented. The distribution of these variables was assessed using the **Shapiro–Wilk test**, with a **p-value ≤ 0.05** considered statistically significant.

Table 1: *Baseline & demographic data of 80 persons.*

Sr.#	Parameters	Frequency	Percentage	p*
1	Gender	48 Men	60.00%	
		32 Women	40.00%	
		Mean ± SD	**Median ± IQR**	
2	Age (years)	33.64 ± 12.07	31.50 ± 20.00	0
3	BMI (kg/m^2)	27.14 ± 7.35	26.50 ± 14.50	<0.001
4	Waist circumference in inches	38.71 ± 12.21	36.00 ± 20.0	<0.001
5	Fasting blood sugar in mg/dL	36.20 ± 47.45	7.05 ± 74.60	<0.001
7	HOMA-IR	49.51 ± 82	16.57 ± 40.42	<0.001
8	SP-D	1.50 ± 0.631	1.03 ± 0.94	<0.045

**p value for Shapiro Wilk test*

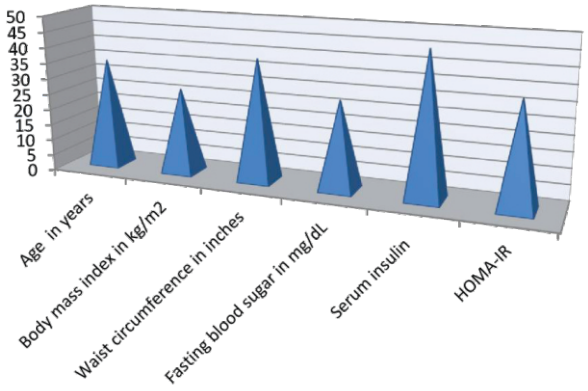

Figure 1: *Mean values of various variables*

Current study is based on correlation among BMI, HOMA-IR and SP-D levels. This study revealed correlations among HOMA-IR, SP-D and BMI. Results via spearman's correlation coefficient (SCC) is -0.0539 showed significant negative correlation of HOMA-IR with SP-D levels because p-value is less than 0.05, SCC is 0.191 showed statistically insignificant with BMI because p-value is not less than 0.05. Similarly, results via SCC is -0.36 showed statistically insignificant negative correlation between SP-D and BMI levels because p value is not less than 0.05, SCC is -0.124 showed statistically insignificant negative correlation between gender and HOMA-IR levels because p-value is not less than 0.05, SCC is 0.742 showed significant positive correlation between age and BMI levels because p-value is less than 0.05. Table 2 shows the SCC between SP-D and various metabolic and anthropometric variables.

Table 2: *SCC showing correlation between SP-D and other parameters*

Ser#	Variables	Correlation Coefficient	P-value
1	Age	0.113	0.317
2	Gender	0.001	0.996
3	Body Mass Index	-0.036	0.754
4	Waist Circumference	-0.163	0.176
5	Fasting Blood Sugar	-0.581	0
6	Serum Insulin Level (Fasting)	-0.221	0.49
7	HOMA-IR	-0.538	0

Discussion

Several studies showed varying results when analysing correlation among BMI, insulin levels, glycaemic control and SP-D levels. Some studies showed association of reduced SP-D levels in diabetic patients with reduced insulin resistance and increased insulin sensitivity.[14,15] A study also revealed association of SP-D with atherosclerosis and inflammation in diabetic patients.[16]

A study found that people with high BMI had reduced serum SP-D levels. The decline in SP-D expression may be due to inflammation associated with obesity. Research indicates a positive relationship between age and serum SP-D levels. According to a different study, elevated elastase activity and elevated blood glucose levels lead to a reduction in serum SP-D level functioning. Research indicates that variations in glucose absorption and metabolism, which are linked to insulin sensitivity, are associated with serum SP-D

deficit.[17,18] A study of Sindh, Pakistan suggested reduced SP-D levels as being causative factor for infections in obese and diabetic patients.[19,20]

According to a Chinese study, men typically have higher serum surfactant protein D levels than women. Serum surfactant protein D levels appear to positively correlate with age, according to another study done on the Danish population. According to data from another investigation, people with high BMIs who were known to have type 2 diabetes mellitus had higher serum surfactant protein D levels.[21,22]

Current study predicted correlation among BMI, HOMA-IR and SP-D levels because BMI influences level of adipokines.[22] Research findings depicted the answer to research question in current study. Increase in insulin resistance was found with decreased level of SP-D. Insulin resistance is very much linked to raised glycemia and cause pathology. Hyperglycemia was found in blood and in walls of pathogens with reduced level of SP-D at the same time. Some studies also suggested lower level of SP-D in obese patients. Some data also revealed association of low level of SP-D with high values of BMI. Still much work is required in this research area due to unknown mechanisms involved with them.[23,24]

Hence, SP-D acts as pathogen proteins recognizer especially in patients having impaired glucose and insulin mechanisms.[25] In current study, sample size was not large and patients data, such as obese and type 2 diabetes mellitus is also required with long follow up to understand mechanism fully and this data should be compared with data of healthy persons mentioned in this study. Moreover, lifestyle and diet improvement data can be helpful to reveal underlying mechanisms. Because healthy lifestyle and better diet helps in controlling obesity and improve glycaemic control.

Conclusion

The present study demonstrated a significant association between insulin resistance, body mass index (BMI), and surfactant protein D (SP-D) levels. The findings also revealed age- and gender-related variations in SP-D concentrations among the Pakistani population, along with their relationship to other components of metabolic syndrome. Furthermore, the results are consistent with previously proposed pathophysiological mechanisms, suggesting that individuals with diabetes and insulin resistance are more susceptible to recurrent infections because of reduced levels and impaired function of the immunomodulatory protein SP-D. This functional impairment may result from elastase-mediated degradation and competitive inhibition of the carbohydrate recognition domain of SP-D by elevated blood glucose levels.

Ethical Approval: The IRB/EC approved this study via letter no. Ref- IMBB/BBBC/22/050 dated January 10, 2022.

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Authors' Contribution

AM: Conception.

HF, MM: Design of the work.

SA,ZH,FH: Data acquisition, analysis, or interpretation.

SA,ZH,MM,FH: Draft the work.

AM,HF: Review critically for important intellectual content.

All authors approve the version to be published.

All authors agree to be accountable for all aspects of the work.

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