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RESEARCH ARTICLE

Serum interleukin-6 and body mass index among diabetic patients in Manipur

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ABSTRACT

Background: Diabetes mellitus has emerged as a state of low-grade chronic inflammation. Interleukin-6 (IL-6) has evolved as a regulator of glucose homeostasis apart from it is immunoregulatory action. Body mass index (BMI) is always being used as a qualitative and quantitative measurement of normal healthy life. Any association between these two parameters will give us a direction toward living a healthy disease free lifestyle. **Aims and Objectives:** Present study was aimed to (i) estimate serum IL-6 level and BMI among diabetic patients, (ii) compare them with healthy subjects, and (iii) study correlation between them. **Materials and Methods:** A cross-sectional study was done with 60 diabetes mellitus patients and 60 controls. Further, each group was divided into three BMI categories: Normal (BMI <25), overweight (BMI 25–29), and obese (BMI >29) categories. Weight and height were measured; BMI was calculated as kg/m^2. All blood samples were analyzed by enzyme-linked immunosorbent assay (ELISA) method using human IL-6 ELISA kit. Data analysis was done using SPSS, version 21. Mean ± standard deviation values of variables were analyzed using student's independent *t*-test. Correlation was found out using Pearson's correlation test. **Results:** In all three BMI categories, serum IL-6 were found to be higher among cases than controls, but the difference was significant among normal BMI category (P = 0.00). On the other hand, correlations between serum IL-6 and BMI were found to be positive among all three BMI categories but were not statistically significant. **Conclusion:** Positive correlation was found between serum IL-6 and BMI. However, the results were not statistically significant. Increased BMI may be responsible for inducing hyperglycemic state, but IL-6 may not be a reliable tool to study the effect of BMI among diabetic patients.

KEY WORDS: Interleukin-6; Body Mass Index; Diabetes Mellitus

INTRODUCTION

Type II diabetes is a major global health problem affecting 415 million people. It is considered that this number will rise to 642 million in 2040.[1] The rise has been dramatic in India from 11.9 million in 1980 to 64.5 million at present.[2]

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The trend in the prevalence of obesity documented over the past few decades has been alarming with morbid obesity affecting 5% of our country's population. As individuals become obese and their adipocytes enlarge, adipose tissue undergoes molecular and cellular alterations affecting systemic metabolism. Compared with that of lean individuals, adipose tissue in obese persons shows higher expression of proinflammatory proteins, including tumor necrosis factor-α, interleukin-6 (IL-6), monocyte chemotactic protein 1, inducible nitric oxide synthase, transforming growth factor β1, and procoagulant proteins such as plasminogen activator inhibitor Type 1, tissue factor, and factor VII.[3] In fact, adipose tissue macrophages are responsible for the significant amount of IL-6 production in the body. IL-6, in addition to

its immunoregulatory action, has also been implicated in glucose homeostasis and metabolism directly and indirectly by its action on skeletal muscle cells, adipocytes, hepatocyte, pancreatic beta cells, and neuroendocrine cells.[4] Hence, any increase than normal range can be taken as a predictor of altered glucose regulation.

On the other hand, body mass index (BMI) is taken as a qualitative as well as quantitative measurement of normal healthy lifestyle. Obesity is associated with higher incidence of diabetes mellitus. A variation in anthropometric indexes influences the outcome of diabetes mellitus. Studies have shown that the prevalence of complications is more among those diabetics who are obese than non-obese ones.

In spite of increasing number of diabetes and rapid progress of science and technologies in its management and treatment, there has not been much studies on IL-6 and its correlation with BMI among diabetics. That is why any association between these two parameters will give us a direction toward living a healthy disease free lifestyle. The vicious cycle of obesity, chronic inflammation, and insulin resistance must be broken to have a permanent and successful weight loss.[5] Hence, the present study was aimed to find out the serum IL-6 level and BMI among the patients suffering from diabetes mellitus; to compare them with normal healthy subjects and to find out any possible correlation between them.

MATERIAL AND METHODS

It was a cross-sectional study, which was conducted in the Departments of Physiology and Medicine, Regional Institute of Medical Sciences (RIMS), Imphal during a period of 5 months (July 2016 to November 2016). 120 subjects, ranging from 18 to 60 years, were recruited for the study, out of which 60 were known diabetic patients, who were selected on the basis of guidelines according to American Diabetes Association[6] and 60 were controls.

Exclusion Criteria

1. Patients with complaints of chronic cough, sputum, or breathlessness,
2. Patients having cardiorespiratory illness or any other major disease,
3. Patients with history of smoking and alcoholism,
4. Any physical disabilities that may affect lung function such as kyphoscoliosis, pectus excavatum, and pectus carinatum and
5. Unwilling to participate.

Further, each group was divided into three categories based on BMI: Normal (BMI <25), overweight (BMI 25–29), and obese (BMI >29) categories. Weight and height of the subjects were measured, and BMI was calculated as kg/m^2. Written consent was obtained from subjects willing to participate in the study.

All blood samples were analyzed by enzyme-linked immunosorbent assay (ELISA) machine (Model SR NO. 120710 Scan EM, Transasia Bio-Medical Ltd., Mumbai) using human IL-6 ELISA kit (Cat. No. KB 1068, Krishgen biosystems, CA 90603). Ethical approval was taken from Research Ethics Board, RIMS, Imphal.

Data were collected entered in SPSS, version 21. Mean ± standard deviation values of variables were estimated and analyzed using student's independent *t*-test. Correlation between two categories was analyzed using Pearson's correlation test.

RESULT

Table 1 summarizes that the mean BMI was 24.73 ± 4.22 and 26.19 ± 3.05, respectively, among cases and controls with a $P = 0.018$; whereas mean serum IL-6 levels were 33.6 ± 6.3 pg/ml and 10.6 ± 3.6 pg/ml among them, respectively, with a $P = 0.024$.

Table 2 summarizes the mean BMI among normal, overweight, and obese categories. The mean BMI of normal category was 21.5 ± 2.6 and 23.6 ± 0.99 among cases ($n = 31$) and controls ($n = 23$), respectively, with a statistically significant difference ($P = 0.00$). The mean BMI of overweight category was 26.7 ± 1.2 and 26.4 ± 1.1 among cases ($n = 20$) and controls ($n = 28$), respectively; but the difference was statistically insignificant ($P = 0.202$); the mean BMI of obese category was 31.2 ± 2.2 and 31.8 ± 2.4 among cases ($n = 9$) and controls ($n = 9$), respectively; but the difference was statistically insignificant ($P = 0.356$).

Table 3 summarizes the mean serum IL-6 level among normal, overweight, and obese categories. In normal category, the mean values were 33.6 ± 7.1 pg/ml and 10.6 ± 3.6 pg/ml, respectively, among cases and controls ($P = 0.024$). The mean serum IL-6 levels in overweight category were 33.9 ± 4.3 pg/ml and 10.7 ± 3.7 pg/ml, respectively, with insignificant differences ($P = 0.992$). The obese category had mean serum IL-6 levels of 33.6 ± 8.1 pg/ml and 10.6 ± 4.1 pg/ml, respectively, among cases and controls with insignificant differences ($P = 0.333$).

Table 4 summarizes the correlation between serum IL-6 and BMI among cases and controls of respective categories. In normal BMI category both these parameters were positively but insignificantly correlated among both cases ($r = 0.134$, $P = 0.471$) and controls ($r = 0.367$, $P = 0.085$). Among overweights, correlations were again positive but insignificant for cases ($r = 0.311$, $P = 0.181$) as well as controls ($r = 0.309$, $P = 0.109$). In obese category, correlations were again positive

Table 1: BMI and serum IL-6 levels among cases and controls

Parameter	Case (*n*=60)	Control (*n*=60)	*P*
BMI	24.73±4.22	26.19±3.05	0.018*
Serum IL-6 (pg/ml)	33.6±6.3	10.6±3.6	0.024*

*=Significant (*P*<0.005). BMI: Body mass index, IL: Interleukin

Table 2: Mean±SD values of BMI among subjects

BMI categories	BMI		*P*
	Cases	Controls	
Normal	21.5±2.6 (*n*=31)	23.6±0.99 (*n*=23)	0.000*
Overweight	26.7±1.2 (*n*=20)	26.4±1.1 (*n*=28)	0.202
Obese	31.2±2.2 (*n*=9)	31.8±2.4 (*n*=9)	0.356

N.B: *=Significant. SD: Standard deviation, BMI: Body mass index

Table 3: Mean±SD values of IL-6 among subjects

BMI Categories	IL-6 levels		*P*
	Cases	Controls	
Normal	33.6±7.1 (*n*=31)	10.6±3.6 (*n*=23)	0.030*
Overweight	33.9±4.3 (*n*=20)	10.7±3.7 (*n*=28)	0.992
Obese	33.6±8.1 (*n*=9)	10.6±4.1 (*n*=9)	0.333

N.B: *=Significant. SD: Standard deviation, IL: Interleukin, BMI: Body mass index

Table 4: Correlation of serum IL-6 and BMI among subjects of different BMI categories

BMI categories	Subjects	Pearson correlation (*r*)	*P*
Normal	Case (*n*=31)	0.134	0.471
	Control (*n*=23)	0.367	0.085
Overweight	Case (*n*=20)	0.311	0.181
	Control (*n*=28)	0.309	0.109
Obese	Case (*n*=9)	0.369	0.328
	Control (*n*=9)	0.317	0.406

IL: Interleukin, BMI: Body mass index

but insignificant for cases ($r = 0.369$, $P = 0.328$) as well as for controls ($r = 0.317$, $P = 0.406$).

DISCUSSION

The present study had found that BMI was positively correlated with serum IL-6 levels among diabetics, but this correlation was not statistically significant.

Our results were found to be quite similar to the studies by Malenica *et al*.,[7] Goyal *et al*.,[8] Wegner *et al*.,[1] and Mirza *et al*.,[9] where all of them found a positive correlation between BMI and serum IL-6. However, none of them tried to evaluate the correlation between BMI and IL-6 among different categories of BMI as done in the present study. Study by Malenica *et al*. found a significant positive correlation ($P = 0.007$) between BMI and IL-6 among female Type II diabetic patients. Study by Goyal *et al*. found an increased level of serum IL-6 among obese diabetics compared to non-obese diabetics (38.2 ± 3.8 vs. 34.9 ± 4.1 pg/ml), but they did not do any correlation between BMI and serum IL-6. Study by Wegner *et al*. found a positive correlation between BMI and serum IL-6 ($r = 0.427$, $P < 0.05$). Study by Mirza *et al*. also found a significant positive correlation between serum IL-6 and BMI ($r = 0.16$).

Contrary to the present study, Darko *et al*.[10] and Nadeem *et al*.[11] had not found any correlation between the two parameters. Study by Darko *et al*. found no association of BMI with IL-6. Likewise Nadeem *et al*. have also not found any correlation between BMI and serum IL-6, but the values were higher among cases compared to control ($P = 0.001$). Diabetes is regarded as a state of low-grade chronic inflammation, leading to release of many inflammatory markers over time. One of such is IL-6, whose secretion is thought to increase from the enlarged adipose tissue. Hence, body fat percentage, rather than BMI, would be a better alternative to assess it is a relation with IL-6 among diabetics.

Strength of the study is that it tried to evaluate each and every possibility of comparing and correlating serum IL-6 and BMI. It divided the subjects according to their BMI and then performed the necessary computations among different BMI categories so that a stronger result could be obtained. However, there are some inherent limitations also associated with this study. The cases and controls were not age and sex matched. Moreover, it did not divide the diabetic patients into Type I and Type II and look for the above correlations among these categories. Hence, a large-scale study is needed to be conducted to determine pitfalls of the present study.

CONCLUSION

We conclude that IL-6 acts as a marker of diabetes mellitus and may be an important parameter for assessing complications. Increased BMI may be responsible for inducing hyperglycemic state, but IL-6 may not be a reliable tool to study the effect of BMI among diabetic patients.

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