# Relationship between C-Reactive Protein and Body Mass Index in Nigerians with Type II Diabetes Mellitus

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**Abstract**

**Background.** C-reactive protein is an acute-phase protein synthesized in the liver and its release is stimulated by cytokines (interleukin 6 and tumour necrosis factor alpha). Baseline levels of C-reactive protein in apparently healthy men and women predict long-term risk of a first myocardial infarction. In older men and women, elevated level CRP was found to be associated with a 10-year risk of coronary heart disease regardless of the presence or absence of cardiac risk factors. Studies have shown a significant correlation between CRP and body mass index (BMI). But data regarding CRP and BMI in our Nigerian population is lacking hence the decision to conduct this study.

**Method.** The study design was cross-sectional comprising 125 consecutive subjects consisting of 75 patients with type II diabetes mellitus with or without hypertension attending medical outpatient clinic of the Obafemi Awolowo University Teaching Hospitals complex (OAUTHC) Ile Ife, Osun State (in southwestern Nigeria), and 50 apparently healthy age- and sex-comparable controls from the hospital staff and patient relatives who were themselves not relatives of the study patients were recruited. Measurement of C-reactive protein was based on the principle of solid phase enzyme-linked immunosorbent assay (ELISA).

**Results.** Body mass index differed significantly between patients and controls as well as the C-reactive protein level. There was a positive and significant correlation between serum CRP and body mass index among both patients and controls.

**Conclusion.** C-reactive protein was found to be significantly higher in diabetics compared to controls. In addition, there was a positive and significant correlation between body mass index and C-reactive protein even after adjusting for hyperglycaemia.

**Key words**: C-Reactive Protein, Body Mass Index, Type II diabetes Mellitus.

## Introduction

C- reactive protein was first identified by Tilet and Francis in1930 in the plasma of patients with pneumonia and was named for its ability to bind and precipitate the capsular polysaccharide of pneumococcus.[1] It is synthesized in the liver and is normally present as a trace constituent of serum or plasma at levels 0.25-1.5µg/ml.[2] Its release is stimulated by cytokines (interleukin 6 and tumour necrosis factor alpha). Studies have shown that elevated levels of CRP is a risk factor for coronary heart disease (CHD).[4-6] Baseline levels of CRP in apparently healthy men and women predict long-term risk of a first myocardial infarction.[5]

In older men and women, elevated CRP was found to be associated with a 10-year risk of CHD regardless of the presence or absence of cardiac risk factors.[6] A single CRP measurement provides information beyond conventional risk assessment, **especially among men with intermediate Framingham risk and women with high Framingham risk[6]**

C-reactive protein induces complement activation thus leading to vascular and myocardial damage. It also promotes secretion of inflammatory mediators by vascular endothelium,

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increases cell adhesion molecules expression, opsonises low-density lipoprotein cholesterol (LDL) for uptake by macrophages.[7] C-reactive protein decreases endothelial nitric oxide synthase expression[8], activates vascular smooth muscles cells proliferation and attenuates endothelial progenitor cells survival, differentiation and function.[9]

Elevated CRP levels have also been linked to an increased risk of later development of diabetes mellitus.[10] Furthermore, CRP levels are **higher in obese individuals and in diabetics compared** with normal individuals.[11] Obesity is associated with a number of risk factors for atherosclerosis and CHD. These include systemic hypertension, insulin resistance, glucose intolerance, hypertriglyceridaemia, reduced HDL cholesterol, and elevated fibrinogen.[12] It remains to be determined if CRP levels will parallel the degree of obesity (adiposity) in type II diabetic. We therefore decided to conduct the study to determine the relationship between C-reactive protein and body mass index in Nigerians with type II diabetes mellitus.

## Methods

The study design was cross-sectional comprising 125 consecutive subjects consisting of 75 patients with type II diabetes mellitus with or without hypertension attending medical out patient clinic of the Obafemi Awolowo University Teaching Hospitals complex (OAUTHC) Ile Ife, Osun State (southwestern Nigeria), and 50 apparently healthy age- and sex-comparable controls from the hospital staff and patient relatives who are themselves not relatives of the study patients were recruited.

Using a structured pre-evaluated questionnaire, the demographic data, history of cigarette smoking, alcohol consumption, duration of diabetes, and duration of hypertension were recorded. The diagnosis of diabetes mellitus was based on the reported history and medical records.

Diabetics with chronic kidney disease, chronic liver disease, congestive cardiac failure or systemic infection were excluded from the study. Also excluded from the study were diabetics on oral contraceptive pills, analgesics or anti-inflammatory drugs and those on HMGcoA reductase inhibitor (statins). Diabetics aged less than eighteen years and those that did not consent were also excluded from the study.

Ethical clearance was obtained from the **Ethics and Research** Committee of the Obafemi Awolowo University Teaching Hospitals Complex, and all participating subjects signed the informed consent form after being clearly explained to them.

The following investigations were carried out: Fasting blood glucose and 2-hour post prandial, fasting lipid profile, serum electrolytes, urea and creatinine. Urinalysis was done using dip-stick while measurement of CRP was based on the principle of solid phase enzyme-linked immunosorbent assay (ELISA).

### Data Analysis

The Statistical Package for Social Sciences version 11.0 (SPSS Chicago Ill. USA) was used for all statistical analysis. Data was presented as mean ± standard deviation (SD). Student t-test was used to determine the significance of differences between mean values of continuous variables and Spearman's correlation coefficient was performed to determine the association between variables. Statistical significance was set at p (probability) value less than 0.05.

## Results

### *Demographic and Clinical Characteristics of the Study Population*

125 consecutive subjects were recruited comprising 75 patients with type II diabetes mellitus with or without hypertension and 50 apparently healthy age-and-sex comparable controls. Forty-five (60.0%) patients and 31 (62.0%) controls were females with mean ages ± SD of 57.2 ± 9.4 years and 56.6 ± 7.8 years, respectively (p = 0.804). Thirty (40.0%) patients and 19 (38.0%) controls were male with mean ages of 58.3 ± 10.3 years and 58.3 ± 7.3 years,

respectively (p = 0.995). Body Mass Index (BMI) differed significantly between patients and controls. The mean BMI of the patients and controls were 26.0±5.1 kg/m$^2$ and 21.9±1.6 kg/m$^2$, respectively (p = 0.000). Thirty (40.0%) patients and 48 (96.0%) controls had normal BMI (Fishers exact test, p = 0.000). 27 (36.0%) patients and 2 (4.0%) controls were overweight (Fishers exact test, p = 0.000); 12 (15.0%) patients were obese and the remaining 6 (8.0%) were underweight.

The mean waist circumference of the female patients and controls were 92.5 ± 10.0. cm and 81.5 ± 2.7 cm, respectively (p = 0.000). Similarly, the mean waist circumference of the male patients and controls were 95.3 ± 7.2 cm and 92.8 ± 2.4 cm, respectively (p = 0.162). Fifty-two (69.3%) patients were hypertensive-diabetic and 23 (30.7%) were normotensive-diabetic. Thirty-four (65.38%) out of the 52 hypertensive-diabetic were females, while the remaining 18 (34.61%) were males. There was a significant difference between the mean systolic and diastolic blood pressures of the patients and controls. The mean systolic blood pressure of the patients and controls were 144.0 ± 12.2 mmHg and 120.2 ± 9.1 mmHg, respectively (p = 0.000). In addition, the mean diastolic blood pressure of the patients and controls were 87.1 ± 8.0mmHg and 79.8 ± 8.2 mmHg, respectively (p = 0.000).

***Laboratory Parameters of the Study Population***

The mean fasting blood glucose of the patients was 9.3 ± 2.4 mmol/L and was significantly higher than that of the controls 4.5 ± 1.0 mmol/L (p = 0.000). Similarly, the mean serum CRP level of the patients was significantly higher than that of the controls 2.5 ± 0.5 µg/mL and 1.5 ± 0.4 µg/mL, respectively (p = 0.000). There was a positive and significant correlation between serum CRP and BMI in the patients and controls (r = 0.942, p = 0.000) and (r = 0.893, p = 0.000) respectively. On regression analysis, BMI was found to be strongly associated with CRP than systolic blood pressure, diastolic blood pressure or fasting blood glucose among patients (beta value 0.642, p = 0.000), (beta value 0.409, p = 0.001), (beta = 0.162, p = 0.032) and (beta = 0.119, p = 0.036), respectively. Similar results was also observed among controls (beta = 0.765, p = 0.000), (beta = 0.602, p = 0.001) (beta = 0.689, p = 0.001) and (beta = 0.375, p = 0.000), respectively.

**Discussion**

This study showed that type II diabetics have significantly higher BMI compared to the healthy controls, which could be responsible for their insulin resistance. Similarly, both systolic and diastolic blood pressures were significantly higher in diabetics compared to the controls implying that diabetics are likely to have multiple coronary heart disease risk factors**.** Type II diabetic patients appear to have defects in both endothelial-dependent vasodilatation and smooth muscle function[13, 14] which may be responsible for the association between hypertension and diabetes mellitus.

A positive and significant correlation between serum CRP and BMI was observed in this study. On regression analysis, BMI was found to have a stronger association with CRP than systolic blood pressure, diastolic blood pressure or fasting blood glucose among patients and controls. This finding is similar to that previously reported by other workers.[11,15] The reason for the apparent association between CRP and BMI is not clear but a possible explanation is that individuals with obesity are at increased risk of various chronic diseases that could be associated with high CRP levels. Secondly, sub-clinical diseases may have been responsible for the observed association. The pathophysiologic mechanisms linking obesity with elevated CRP levels include increased expression of tumour necrosis factor alpha (TNFα) and circulating interleukin 6 from adipocytes which stimulates the production of CRP.[16]

**Conclusion**

This study showed that CRP is significantly higher in type II diabetics compared to the apparently healthy controls, and also shows a significant positive correlation with BMI.

**References**


1. Macy EM, Hayes TE, and Tracy RP. Variability in the measurement of C-reactive protein in healthy subjects. Implication for reference interval and epidemiological applications. Clin Chem 1997; 43:52-58.
2. U.S Biological C-reactive protein, human bio-Assay TM ELISA kit. Catalogue No-C7907-01. Swampscott, Massachusetts 01907
3. Kushner I. C-reactive protein in rheumatology. Arthritis Rheum 1991; 34:1065-1068.
4. Soinio M, Marniemi J, Laasko M, Letho S, Ronnemaa T. High sensitivity C-reactive protein and coronary heart disease mortality in patients with type II diabetes. A 7-year follow up U.S study. Diabetes Care 2006; 29:329-333.
5. Albert MA, Robert J, Glynn RJ, and Ridker PM. Plasma concentration of C-reactive protein and the calculated Framingham coronary heart disease risk score. Circulation 2003; 108:161-165.
6. Mcolhoun H, Schalkwijk C, Rubens MB, Stehouwer Coen DA. C-reactive protein in type I diabetes and its relation to coronary calcification. Diabetes Care 2002; 25:1813-1817.
7. Pasceri V, Willerson JT and Yeh Edward TH. Direct Proinflammatory Effects of C - reactive protein on Human Endothelial cells. Circulation 2000; 102:2165-2168.
8. Venugopal SK, Devaraj S, Yuhanna I, et al. Demonstration That C-Reactive Protein Decreases eNOS Expression and Bioactivity in Human Aortic Endothelial Cells. Circulation 2002; 106:1439-1441.
9. Verma S, Kuliszewski MA, Shu-Hong Li, et al. C - reactive protein Attenuates Endothelial Progenitor Cell Survival, Differentiation, and Function: Further Evidence of a Mechanistic Link between C - reactive protein and Cardiovascular Disease. Circulation 2004; 109:2058-2067.
10. Pradhan AD, Manson JE, Rifai N, et al. C-reactive protein, Interleukin 6, and the risk of developing type 2 diabetes mellitus. JAMA 2001; 286:327-334.
11. Ford ES. Body mass index, Diabetes, and C-reactive protein among U.S adults. Diabetes care 1999; 22:1971-1977.
12. Forniguera X, Canton A. Obesity, Epidemiology and Clinical aspects. Best prac research in clinic gastroenterol 2004; 18:1125-1146.
13. McVeigh GE, Brennan GM, Johnston GD, et al: Impaired endothelium-dependent and independent vasodilatation in patients with type 2 (non–insulin-dependent) diabetes mellitus. Diabetologia 1992;35:771-776
14. Williams SB, Cusco JA, Roddy MA, et al: Impaired nitric oxide–mediated vasodilatation in patients with non–insulin-dependent diabetes mellitus. J Am Coll Cardiol 1996;27:567-574
15. Visser M, Bouter LM, Mcquillan GM, et al. Elevated CRP levels in over weight and obese adults. JAMA 1999; 282:2131-2135.
16. Warren RS, Starnes HF Jr, Gabrilove JL, Oettgen HF and Brennan MF. The acute metabolic effects of tumour necrosis factor administration in humans. Arch of surg 1987; 122:1396-1400.

**Table 1: Demographic and clinical characteristics of the study population**

| Parameters | Patients | Controls | P-Value |
|---|---|---|---|
| **Age** | | | |
| Male | 58.3±10.3 | 58.3±7.3 | 0.995 |
| Female | 57.2±9.4 | 56.6±7.8 | 0.804 |
| **Sex** | | | |
| Male | 30(40.0%) | 19(38.0%) | 0.822 |
| Female | 45(60.0%) | 31(62.0%) | 0.822 |
| **Waist circumference** | | | |
| Male | 95.3±7.2 | 92.8±2.4 | 0.162 |
| Female | 92.5±10.0 | 81.5±2.7 | 0.000* |
| **SBP (mmHg)** | 144.0±12.2 | 120.2±9.1 | 0.000* |
| **DBP (mmHg)** | 87.1±8.0 | 79.80±8.2 | 0.000* |

DBP = Diastolic Blood Pressure, SBP = Systolic Blood Pressure
* = Significant at P < 0.05

**Table 2: Showing the BMI distribution among study population**

| BMI(kg/m$^2$) | Patients | Controls | P-Value |
|---|---|---|---|
| <18.5 | 6 (8.0%) | 0 (0.0%) | 0.080 |
| 18.5-24.9 | 30 (40.0%) | 48 (96.0%) | 0.000* |
| 25-29.9 | 27 (36.0%) | 2 (4.0%) | 0.000* |
| 30-34.9 | 8 (10.7%) | 0 (0.0%) | 0.021* |
| 35-39.9 | 3 (4.0%) | 0 (0.0%) | 0.274 |
| >40 | 1 (1.3%) | 0 (0.0%) | 1.000 |

BMI = Body Mass Index, * = Significant at p < 0.05

**Table 3: Laboratory parameters of the study population.**

| Parameters | Patient | Controls | p-value |
|---|---|---|---|
| **FBG (mmol/L)** | 9.3±2.4 | 4.5±1.0 | 0.000* |
| **CRP (µg/mL)** | 2.5±0.5 | 1.5±0.4 | 0.000* |
| **Total cholesterol (mmol/L)** | 5.7±1.3 | 3.9±1.2 | 0.000* |
| **LDL cholesterol (mmol/L** | 4.0±0.7 | 2.1±0.4 | 0.000* |
| **HDL cholesterol (mmol/L)** | 0.9±0.2 | 1.8±0.2 | 0.000* |
| **Triglycerides (mmol/L)** | 2.3±0.5 | 1.4±0.2 | 0.000* |
| **Serum sodium (mmol/L)** | 134.6±3.2 | 137.1±3.5 | 0.000* |
| **Serum potassium (mmol/L)** | 3.9±4.2 | 4.1±4.9 | 0.793 |
| **Serum bicarbonate (mmol/L)** | 22.8±2.7 | 24.5±2.4 | 0.000* |
| **Serum urea (mmol/L)** | 5.3±6.6 | 3.6±0.6 | 0.075 |
| **Serum creatinine (µmol/L)** | 90.6±37.5 | 58.2±8.5 | 0.000* |

FBG = Fasting Blood Glucose, CRP = C - reactive protein, LDL = Low Density Lipoprotein, HDL = High Density Lipoprotein, * = Significant at $p < 0.05$

**Table 4: Correlation between CRP and systolic blood pressure, diastolic blood pressure, body mass index and fasting blood glucose in the study patients.**

| Parameters | Spearman correlation Coefficient (r) | P-value |
|---|---|---|
| **SBP (mmHg)** | 0.667 | 0.000* |
| **DBP (mmHg)** | 0.438 | 0.000* |
| **BMI (kg/m$^2$)** | 0.942 | 0.000* |
| **FBG (mmol/L)** | 0.656 | 0.000* |

BMI = Body Mass Index, DBP = Diastolic Blood Pressure, SBP = Systolic Blood Pressure, FBG = Fasting Blood Glucose

**Table 5: Correlation between CRP and systolic blood pressure, diastolic blood pressure, body mass index and fasting blood glucose among controls.**

| Parameters | Spearman correlation coefficient (r) | P-value |
|---|---|---|
| **SBP (mmHg)** | 0.738 | 0.000* |
| **DBP (mmHg)** | 0.686 | 0.000* |
| **BMI (kg/m$^2$)** | 0.893 | 0.000* |
| **FBG (mmol/L)** | 0.551 | 0.000* |

BMI = Body Mass Index, SBP = Systolic Blood Pressure, DBP = Diastolic Blood Pressure, FBG = Fasting Blood Glucose

**Table 6: Multiple regression analysis between CRP and BMI, systolic blood pressure, diastolic blood pressure and fasting blood glucose among study patients.**

| Parameters | Beta value | P-value |
|---|---|---|
| **BMI (kg/m$^2$)** | 0.642 | 0.000* |
| **SBP (mmHg)** | 0.409 | 0.000* |
| **DBP (mmHg)** | 0.162 | 0.032* |
| **FBG (mmol/L)** | 0.119 | 0.036* |

BMI = Body Mass Index, SBP = Systolic Blood Pressure, DBP = Diastolic Blood Pressure, FBG = Fasting Blood Glucose

**Table 7: Multiple regression analysis between CRP and BMI, systolic blood pressure, diastolic blood pressure and fasting blood glucose among study controls.**

| Parameters | Beta value | P-value |
|---|---|---|
| **BMI (kg/m$^2$)** | 0.765 | 0.000* |
| **SBP (mmHg)** | 0.602 | 0.001* |
| **DBP (mmHg)** | 0.689 | 0.001* |
| **FBG (mmol/L)** | 0.375 | 0.000* |

BMI = Body Mass Index, SBP = Systolic Blood Pressure, DBP = Diastolic Blood Pressure, FBG = Fasting Blood Glucose