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Original Article

Elevated adiponectin but varied response in circulating leptin levels to *falciparum* malaria in type 2 diabetics and non-diabetic controls

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ABSTRACT

Background: To investigate effects of *falciparum* malaria on circulating levels of leptin and adiponectin in type 2 diabetes mellitus (T2DM) and non-diabetic controls in relation to measures of adiposity.

Methods: Levels of leptin and adiponectin were measured in 100 type 2 diabetics and 100 age-matched controls before and during *falciparum* malaria in a 2-year prospective study. Also, waist circumference (WC), weight, height and hip circumference were measured. Body mass index (BMI) and waist-to-hip ratio (WHR) were computed.

Results: At baseline, diabetics had significantly ($p < 0.05$) higher WC and BMI but lower WHR, leptin and adiponectin levels. Baseline leptin correlated positively with WC ($r = 0.633$; $p < 0.001$) and BMI ($r = 0.63$; $p < 0.001$) in diabetics but only BMI (0.562; $p < 0.001$) in non-diabetic controls. Baseline leptin and adiponectin correlated positively ($r = 0.249$; $p = 0.029$) in non-diabetic respondents only. Adiponectin correlated negatively with WC ($r = -0.58$; $p = 0.006$) in diabetic males only. During malaria, mean levels of leptin and adiponectin were comparable ($p > 0.05$) between diabetics and controls. However, compared to baseline levels, significant ($p < 0.001$) elevation of adiponectin was found in both study groups. In respect of leptin, significant ($p < 0.001$) rise but decline was observed in diabetics and controls respectively. Malaria-induced leptin correlated negatively with adiponectin ($r = -0.694$; $p < 0.001$) in non-diabetic controls only.

Conclusion: Diabetics and controls exhibited increased adiponectin levels due to *falciparum* malaria but differed in response in terms of leptin levels.

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At a glance commentary

Scientific background on the subject

Little is known regarding how leptin and adiponectin respond to infectious agents. With sub-Saharan Africa shouldering over 80% of global malaria burden and predicted to accommodate the highest burden of T2DM by 2030, investigating the response of these adipocytokines to malaria and implications of its interaction with T2DM is paramount.

What this study adds to the field

Falciparum malaria increased cardiovascular disease (CVD) risk of diabetics and non-diabetic controls through elevation of adiponectin levels independent of adiposity. In terms of leptin, elevation and reduction in levels were observed in diabetics and control respondents respectively suggesting different mechanisms for malaria-induced CVD risk in the study groups.

In spite of a seeming decline of global malaria cases, the condition still affects millions of people in the world [1]. In the case of type 2 diabetes mellitus (T2DM), a recent International Diabetes Federation (IDF) report suggests continued elevation of incidence of the disease across the various continents of the globe [2]. In both conditions, sub-Saharan Africa contributes over 80% to the reported cases globally, suggesting a possible inevitable coexistence of malaria and T2DM in the same individual; a situation that may pose additional health challenge that ought to be investigated. Leptin and adiponectin are important adipocytokines that have been mostly associated with T2DM and other chronic non-communicable diseases [3,4].

Leptin, a 167-amino acid sequence protein with structural similarities to the cytokine family, has been studied extensively in various conditions since its discovery as a satiety signal in 1994 through positional cloning [5]. It is expressed by various tissues including adipocytes, liver, placenta, ovaries, skeletal muscle, pituitary and stomach [6]. Leptin suppresses food intake and stimulates energy expenditure by interacting with its receptors in the hypothalamic region of the brain [5]. Also, it is involved in the regulation of immune cells, blood cells, pancreatic beta cells, muscle, insulin sensitivity and adipocytes [5,7]. In relation to human disease, leptin has been associated with diabetes mellitus, reduced bone mass, atherosclerosis and cancer [3,8–12].

Adiponectin, discovered in the mid-90s by four different groups, is a 30-kDa monomeric polypeptide of 247 amino acid residues synthesized by white adipose tissue [5]. It improves insulin sensitivity and exhibits anti-atherogenic, anti-inflammatory and anti-diabetic properties [4,13–15]. High or low circulating adiponectin levels has been associated with mortality in apparently healthy elderly cohort [16]. However, in patients suffering from chronic kidney disease, cardiovascular disease or type 2 diabetes, high baseline level of circulating adiponectin has been linked to mortality [17–20]. These observations suggest that the exact impact of these biomolecules depends on their circulating levels and the underlying health condition of the individual.

The pleiotropic roles of leptin and adiponectin make them suitable candidates to be studied under varied disease and health conditions. To this end, leptin and adiponectin have been studied extensively in chronic non-communicable diseases such as diabetes, cancer and cardiovascular disease [4,12,18,20]. However, little is known about how these adipocytokines respond to infectious agents such as the *Plasmodium* parasite and its consequence to cardiovascular health of the affected. With sub-Saharan Africa predicted to shoulder the highest burden of type 2 diabetes mellitus by 2030, it may be important to examine the role that *Plasmodium* infection plays in this context since Africa is responsible for more than 80% of global malaria burden. Therefore, the current study was undertaken to investigate the effects of *Plasmodium falciparum* infection on circulating levels of leptin and adiponectin in T2DM and non-diabetic controls in relation to measures of adiposity in a two-year prospective study.

Materials and methods

Study site, participants' selection, anthropometry and laboratory analyses

The study was carried out at Cape Coast Teaching Hospital (CCTH). CCTH is a referral hospital for the various health facilities in the Central region with a recognized Diabetic Clinic. Cape Coast, the capital of the Central region has an estimated population of 169,894 according to the 2010 Population and Housing Census. The inhabitants are mainly farmers and fishermen in the informal sector with a relatively small proportion of the working population in the formal sector. The metropolis is christened the educational hub of Ghana. Due to its strategic location, characteristics of individuals who patronize the services of CCTH reflect those of the entire region.

One hundred diabetic participants aged 40–80 years were randomly selected from database of diabetics receiving appropriate treatments at the CCTH. Controls were age-matched with the diabetics and were selected from the general inhabitants of the metropolis. In all, 200 respondents who met the inclusion criteria were enrolled for the study. Both groups of participants were followed over a period of two years for symptomatic *P. falciparum* infection. Anthropometric indices, fasting serum leptin and adiponectin levels were measured before and during *P. falciparum* malaria. Details of sample preparation and storage have been described elsewhere [21].

Anthropometric measurements

Weight was measured to the nearest 0.1 kg with height to the nearest 0.1 cm. Body mass index was computed as the ratio of weight in kilogramme to the square of the height in metre (kg/m^2). Weight and height were measured in light clothing without footwear.