THE RELATIONSHIP BETWEEN TRADITIONAL CARDIOVASCULAR RISK FACTORS, BODY COMPOSITION AND C-REACTIVE PROTEIN AMONGST 19 to 60 YEAR OLD BLACK WOMEN

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Dissertation submitted in partial fulfilment of the requirements for the M.Sc. degree in the School of Biokinetics, Recreation and Sport Science in the Faculty of Health Sciences at the North-West University, Potchefstroom Campus

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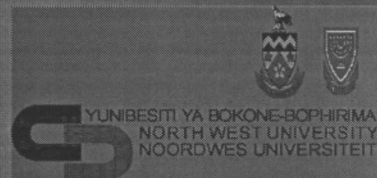

FOREWORD

The great thing in this world is not so much where we stand, as in what direction we are going... - Oliver Wendell Holmes

Without the guidance, grace and mercy of my Heavenly Father, the completion of this study would not have been possible. I am truly grateful for all of the talents and opportunities He has blessed me with, and I pray that He will grant me the wisdom and strength to always keep my eyes fixed on Him, the true Compass on my journey through life.

I would also like to express my sincere thanks and appreciation to the following people for their love, patience, understanding and unselfish contribution to the completion of this study:

- My parents and brother, who have always been supportive of my studies. Without your help, support and faith in my abilities, this dissertation would never have become a reality.
- My grandparents, for your continuous support and interest in my studies.
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The author

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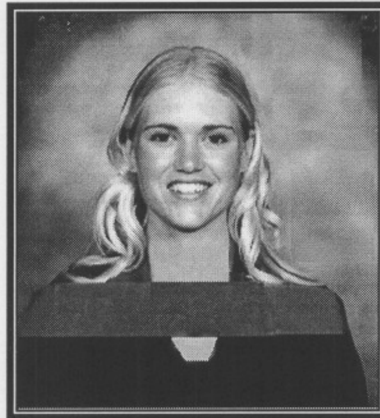
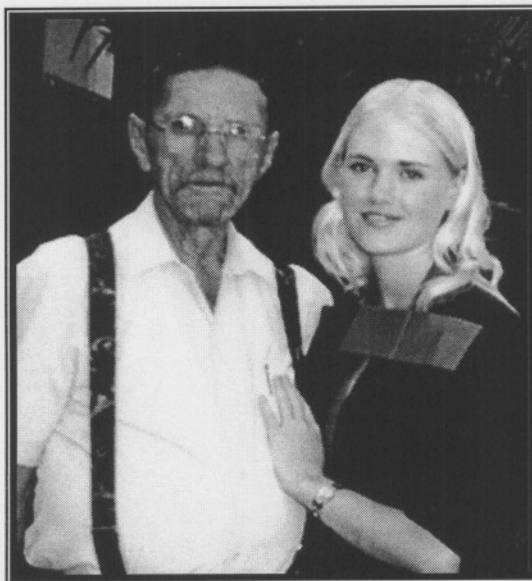


Opinions expressed and conclusions arrived at are those of the author(s) and are not necessarily to be attributed to any organisation or institution.

This dissertation is dedicated in loving memory to
my grandfather,
Gabriël Cornelius Johannes Slabbert
(12/10/1930 – 18/10/2003)



"So pluk Ek dan elke blom net op die regte tyd, want'k
plant hul nie vir hierdie aarde nie,
maar vir My ewigheid "

DECLARATION

The co-authors of the articles which form part of this dissertation, Prof. J. Hans De Ridder (supervisor), Prof. H. Salome Kruger, (co-supervisor), Dr. Colette Underhay (help-supervisor), Dr. Alta Schutte and Dr. Machteld van Lieshout, hereby give permission to the candidate, Ms Sonja Slabbert to include the two articles as part of a Masters dissertation. The contribution (advisory and supportive) of these co-authors was kept within reasonable limits, thereby enabling the candidate to submit this dissertation for examination purposes. This dissertation, therefore, serves as partial fulfilment of the requirements for the M.Sc. degree within the School of Biokinetics, Recreation and Sport Science in the Faculty of Health Sciences at the North-West University, Potchefstroom campus.

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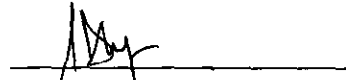

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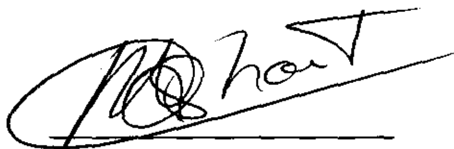

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SUMMARY

The prevalence of obesity has increased dramatically in the past decade. This foreshadows an increase in the rates of morbidity and mortality from obesity related diseases. The high prevalence of coronary heart disease (CHD) is a problem throughout the world as well as in South Africa. The process of urbanisation of Africans from rural to urban areas is exposing the African population to Western lifestyles, with an increase in the incidence of CHD being reported. Research is more frequently proposing that obesity may be seen as a factor linking elevated C-reactive protein (CRP) concentrations and atherosclerosis. CRP is an acute phase reactant and a sensitive marker for acute and chronic inflammation of diverse causes. This poses the question of whether the increased risk of diabetes, CHD and many other chronic diseases in the obese might be explained by a state of chronic systemic inflammation.

The purpose of this study was, therefore, firstly to determine whether there is an association between CRP concentrations and body composition in 19 to 60 year old black women. Partial Pearson correlations coefficients were used to determine associations between CRP and several body composition variables. Body mass index (BMI), waist circumference, percentage body fat and waist-hip-ratio (WHR) were all significantly correlated with CRP throughout the anthropometric spectrum. An analysis of variance (ANOVA) with a Games-Howell *post hoc* test was done to determine statistically significant differences among the different categories within each of the body composition variables. Significant differences ($p < 0.05$) were found within the categories of all the measured body composition variables, except for the various WHR categories. During a signal detection analysis, BMI was identified as the best predictor of increased CRP concentrations at a cut-off point of 27.68 kg/m^2.

The second purpose of this study was to assess the relationship of CRP to traditional cardiovascular risk factors in the study's population sample of 19 to 60 year old black women. Pearson correlation coefficients were used to analyze log-normalized CRP

concentrations as the dependent variable in relation to several variables which form part of the traditional risk factors for CHD. All of the variables were significantly correlated with CRP at the level of $p \leq 0.05$, except for total cholesterol and low-density lipoprotein cholesterol. BMI, percentage body fat and fibrinogen levels were associated with lnCRP at a practically significant level of $r \geq 0.5$. BMI and fibrinogen were also found to be independently associated with lnCRP with $p \leq 0.05$ during a forward stepwise multiple linear regression analysis. Within this study's population sample, it was found that those women who presented with six traditional risk factors had a three to five-fold increase in CRP concentrations compared to women with three or less risk factors. Further research is required to determine appropriate intervention programmes which could prevent or reduce the incidence of CHD among the obese by means of weight-loss, therefore, potentially lowering elevated CRP concentrations.

Key words: **Obesity, C-reactive protein, coronary heart disease, risk factors, physical activity, black women**

OPSOMMING

Die voorkoms van obesiteit het oor die afgelope dekade dramaties gestyg en daarmee saam die voorspelling van 'n toename in morbiditeit sowel as mortaliteit as gevolg van obesiteits verwante siektetoestande. In Suid-Afrika, sowel as wêreldwyd, is die hoë voorkoms van koronêre hartsiektes (KHS) 'n probleem. Met die proses van verstedeliking van Swart Suid-Afrikaners vanaf die landelike gebiede na stedelike areas, is diè populasie blootgestel aan Westerse lewenstyle, en daarmee saam word 'n toename in die voorkoms van KHS geraporteer. Navorsing dui al hoe meer daarop dat obesiteit moontlik as die skakel kan dien tussen kroniese sistemiese inflammasie en arteriosklerose. C-reaktiewe proteïen (CRP) is 'n akute fase reaktant en is 'n sensitiewe merker vir akute sowel as kroniese inflammasie toestande. Die vraag ontstaan dus of diè verskynsel moontlik die verhoogde risiko vir diabetes mellitus, KHS en al die ander kroniese toestande wat voorkom by obesiteit verduidelik.

Die doel van hierdie studie was eerstens om die verband te bepaal tussen CRP konsentrasies en liggaamsamestelling by 19 tot 60 jarige swart vroue. Parsiële Pearson korrelasies was gebruik om die verband tussen CRP en die liggaamsamestelling veranderlikes te bepaal. Die liggaamsmassa indeks (LMI), minimum abdominale omtrek, persentasie liggaamsvet en maag-heup-ratio (MHR) waardes het almal statisties betekenisvol gekorreleer met die CRP konsentrasies. 'n Eenrigting variansie analise (ANOVA) tesame met 'n Games-Howell *post hoc* toets was gebruik om statisties betekenisvolle verskille binne die verskillende kategorieë van elk van die liggaamsamestelling veranderlikes te bepaal. Betekenisvolle verskille ($p \leq 0.05$) was gevind binne die verkillende kategorieë van al die veranderlikes behalwe die MHR kategorieë. Tydens 'n sein waarnemings analise was LMI geïdentifiseer as die beste aanduider vir verhoogde CRP konsentrasies met 'n afsny punt van 27.68 kg/m^2.

Die tweede doel van die studie was om die verband tussen CRP en tradisionele risiko faktore vir KHS te bepaal by die studie se steekproef van 19 tot 60 jarige swart vroue.

Pearson korrelasies was gebruik om die log-normaliseerde CRP (lnCRP) konsentrasies se verband te bepaal met verskeie veranderlikes wat deel vorm van die tradisionele kardiovaskulêre risiko faktore. Statisties betekenisvolle korrelasies ($p \leq 0.05$) is gevind vir al die veranderlikes, behalwe vir totale cholesterol en lae-digtheid lipoproteïen cholesterol. Daar is ook gevind dat LMI, persentasie liggaamsvet en fibrinogeen praktiese betekenisvolle verbande toon ($r \geq 0.5$) met CRP konsentrasies. LMI en fibrinogeen was ook onafhanklik geassosieer met lnCRP ($p \leq 0.05$) tydens 'n vorentoe stapsgewyse meervoudige regressie analise. Binne die studie se populasie groep is gevind dat vroue met 6 tradisionele risiko faktore teenwoordig binne hul profiel, vyf keer hoër CRP konsentrasies vertoon het in vergelyking met vroue met drie of minder risiko faktore. Verdere navorsing word benodig om gepaste intervensie programme te ontwerp wat deur middel van gewigsverlies die voorkoms van verhoogde CRP konsentrasies te verhoed en so dan ook KHS by obese persone te verminder of te voorkom.

Sleutel terme: Obesiteit, C-reaktiewe proteïen, koronêre hart siektes, risiko faktore, Interleukien-6, fisieke aktiwiteit, swart vroue

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Table 6 CRP means for each of the risk groups in a 101 apparently healthy African women 64

LIST OF ABBREVIATIONS

ACSM	American College of Sports Medicine
ANOVA	Analysis of variance
ARIC	Atherosclerotic Risk in Communities
BF	Body fat
BMI	Body mass index
°C	Degrees Celsius
CARDIA	Coronary Artery Risk Development in Young Adults
CHD	Coronary heart disease
cm	centimeter
CRP	C-reactive protein
CVD	Cardiovascular disease
Db	Body density
ECG	Electrocardiogram
g/mm^2	grams per millimeter squared
HDL-C	High-density lipoprotein cholesterol
HIV	Human immunodeficiency virus
hsCRP	high-sensitivity C-reactive protein
IL-6	Interleukin-6
Inc	Incorporated
kg/m^2	kilogram per meter squared
LDL-C	Low-density lipoprotein cholesterol
max	maximum
min	minimum
ml	milliliter

mm	millimeter
mg/dL	milligram per deciliter
mg/L	milligram per liter
MRC	Medical Research council
NCD	Non-communicable diseases
NHANES	National Health and Nutrition Examination Surveys
NRF	National research foundation
POWIRS	Profiles of Obese Women with Insulin Resistance Syndrome
rpm	revolutions per minute
SD	Standard deviation
SE	Standard error
SF	Skinfolds
TC	Total cholesterol
TNF-α	Tumour necrosis factor-alpha
UK	United Kingdom
US	United States
WC	Waist circumference
WHO	World Health Organization
WHR	Waist-hip-ratio
x^2	chi squared

1 Problem statement and aim of study

1.1 INTRODUCTION
1.2 PROBLEM STATEMENT
1.3 OBJECTIVES
1.4 HYPOTHESES
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1.1 INTRODUCTION

In all populations, developed and developing, rural and urban, obesity is increasing. In Africa, when rural populations lived traditionally, there was very little gain in weight with age. However, with transitional changes occurring, as in South Africa, especially in urban dwellers, obesity has become common, affecting approximately half of African women (Walker, 1998:22). In the South African Demographic and Health Survey it was found that 56.6% of women were overweight or obese and 42% had abdominal obesity with a waist-hip-ratio (WHR) > 0.85. It was also found that obesity increased with age and higher levels of obesity were found in urban African women (Puoane *et al.*, 2002:1041).

Although the prevalence of obesity in South African populations is higher in black than in white women (Puoane *et al.*, 2002:1047), it is not yet clear why obesity is more common in African women. It might be because obese black South African women are culturally and aesthetically looked upon with far less disfavour than obese white women (Kruger *et al.*, 1994:105). Although obesity in black women has been regarded as "healthy obesity" by some research groups (Walker *et al.*, 1989:228), a South African study showed an unexpectedly high prevalence of hypertension and moderate-risk hypercholesterolemia in a black population in which a high prevalence of obesity was also found (Mollentze *et al.*, 1995:93). In the CARDIA and ARIC studies the

association between indices of obesity and cardiovascular risk factors for blacks was of the same strength as the association for whites and it was recommended by Folsom *et al.* (1991:1604S-1611S) that both blacks and whites should avoid excess adiposity.

While much of the cardiovascular risk attributable to obesity may be mediated through effects on blood pressure, lipids and glucose tolerance, some of this risk may be mediated by inflammatory pathways. Adipocytes secrete interleukin-6 (IL-6), one of the chief determinants of hepatic C-reactive protein (CRP) production (Bataille & Klein, 1992:982; Heinrich *et al.*, 1990:623; Mohamed-Ali *et al.*, 1997:4199). CRP, an acute phase reactant, is a sensitive marker of inflammation and while CRP is associated with an increased risk of coronary heart disease (CHD) (Danesh *et al.*, 2000:199-203; Ridker *et al.*, 1998:731-733), it has also shown to be positively correlated with measures of obesity (Visser *et al.*, 1999:2133). Obesity may, therefore, be regarded as a low-grade systemic inflammatory disease, which may explain the increased risk of diabetes, heart disease, and many other chronic diseases in the obese (Das, 2001:953-954).

To prevent and treat obesity, especially in black women, more should be known about the underlying causes of obesity among these women to develop appropriate and culturally accepted interventions.

1.2 PROBLEM STATEMENT

The connection between body composition and state of health is a subject that has been in the spotlight from the time of Hippocrates (Walker, 1998:22). From studies of art and literature, obesity appears to have been uncommon in Western populations until the time of the Industrial Revolution, when there were increases in urbanisation and a decrease in physical activity (Walker, 1995:1070). Obesity has become a serious and common public health problem, with research showing that the appearance of obesity is as high as 54.3% among black South African women. With the rise in socio-economic status, urbanisation and diminishing physical activity, the proportion affected has increased (Walker *et al.*, 2001:369). Obesity levels for African men is as low, or lower in some studies than that in white men; but prevalences in African women far exceed those in white women and are reaching those of African-American women (Mollentze

et al., 1995:93; Walker *et al.*, 2001:369).

Obesity may be classified as a body mass index (BMI) of 30 kg/m² or more and it is functionally defined as the percentage body fat at which disease risk increases. Obesity can also be defined as a disease in which excess body fat has accumulated to an extent that health may be adversely affected (ACSM, 2000:214, Forbes, 1995:46; WHO, 1998:7). It could also for a greater part be the result of a positive energy balance (Bray, 1990:497).

Obesity is a chronic disease which is associated with many other diseases and risk factors such as hypertension, diabetes mellitus, certain types of cancers, orthopaedic problems, dyslipidemia and CHD (Hanusch-Enserer *et al.*, 2003:355; McArdle *et al.*, 1994:482). Obesity is also associated with long-term morbidity and mortality which is the result of an unhealthy lifestyle that includes unhealthy eating habits, smoking, a sedentary lifestyle and high stress environments (WHO, 1998:50).

CRP is an acute phase reactant expressed principally by the liver. In healthy, lean individuals CRP circulates at low concentrations in plasma (< 2mg/L) (Gabay & Kushner, 1999:452). These levels rise dramatically in response to injury, infection and inflammation (Steel & Whitehead, 1994:83). Research has shown that low-grade, systemic inflammation occurs in obesity (Das 2001:960). Therefore CRP concentrations serve as a marker for inflammation and are also associated with cardiovascular risk factors and cardiovascular and non-cardiovascular causes of death (Das, 2001:960). Adiposity has been consistently related to CRP concentrations in adults and a strong correlation was also found between levels of CRP and BMI (Cook *et al.*, 2000:145).

The reason for raised levels of CRP in the obese can possibly be attributed to interleukin-6 (IL-6). IL-6 is a cytokine that activates the production of CRP in the liver and CRP concentrations have shown to be a direct indicator of IL-6 levels *in vivo* in humans (Fried *et al.*, 1998:849). Approximately 25-30 % of serum IL-6 is released by adipose tissue and the secretion of IL-6 by subcutaneous adipose tissue is in proportion to adipose mass (Mohamed-Ali *et al.*, 1997:4199). CRP concentrations are also independently associated with BMI and a higher risk for coronary heart disease (Ridker

et al., 1998:732, Visser *et al.*, 1999:2133). Omental adipose tissue produces three-fold more IL-6 than subcutaneous adipose tissue (Fried *et al.*, 1998:848), which could partially account for increased mortality rates in abdominally obese subjects if IL-6 or CRP contributed to disease promotion.

It is well known that CHD is a multifactorial phenomenon, with no one factor being essential or sufficient to produce the disease. Invariably, the risk associated with any particular factor is markedly influenced by others (Kannel, 1990:208) and multivariate risk assessments are required to ascertain the net and joint effect of risk factors. Traditional CHD risk factors include aging, hypertension, dyslipidemia, smoking and diabetes mellitus. Fibrinogen and CRP too have also been proposed as major independent risk factors for CHD, which should be screened for in an effort to better identify patients at high risk of cardiovascular events (Kannel *et al.*, 1987:1183, Ridker, 1999:934). With the development of atherosclerosis now being considered to be due, in part, to an inflammatory response (Ross, 1999:115), the screening of a marker such as CRP has shown to improve cardiovascular risk prediction adjunctive to the assessment of traditional risk factors (Danesh *et al.*, 2000:202, Ridker *et al.*, 2000:842). The relationship of CRP to CHD raises the question of how other risk factors relate to this marker and whether CRP may be the missing link between obesity in particular and CHD. Few studies, however, have explored the relationship between CRP and other determinants of cardiovascular risk.

The questions to be answered in this study were firstly if CRP has any association with body composition in 19 to 60 year old black women and secondly, which of the traditional cardiovascular risk factors could best be used as an indicator of plasma CRP concentrations in 19 to 60 year old black women (Figure 1). These questions could possibly help to describe the role that body composition and traditional cardiovascular risk factors play in predicting CRP concentrations. It would also highlight the role of CRP in predicting future cardiovascular risk as part of preventive and treatment intervention programs.

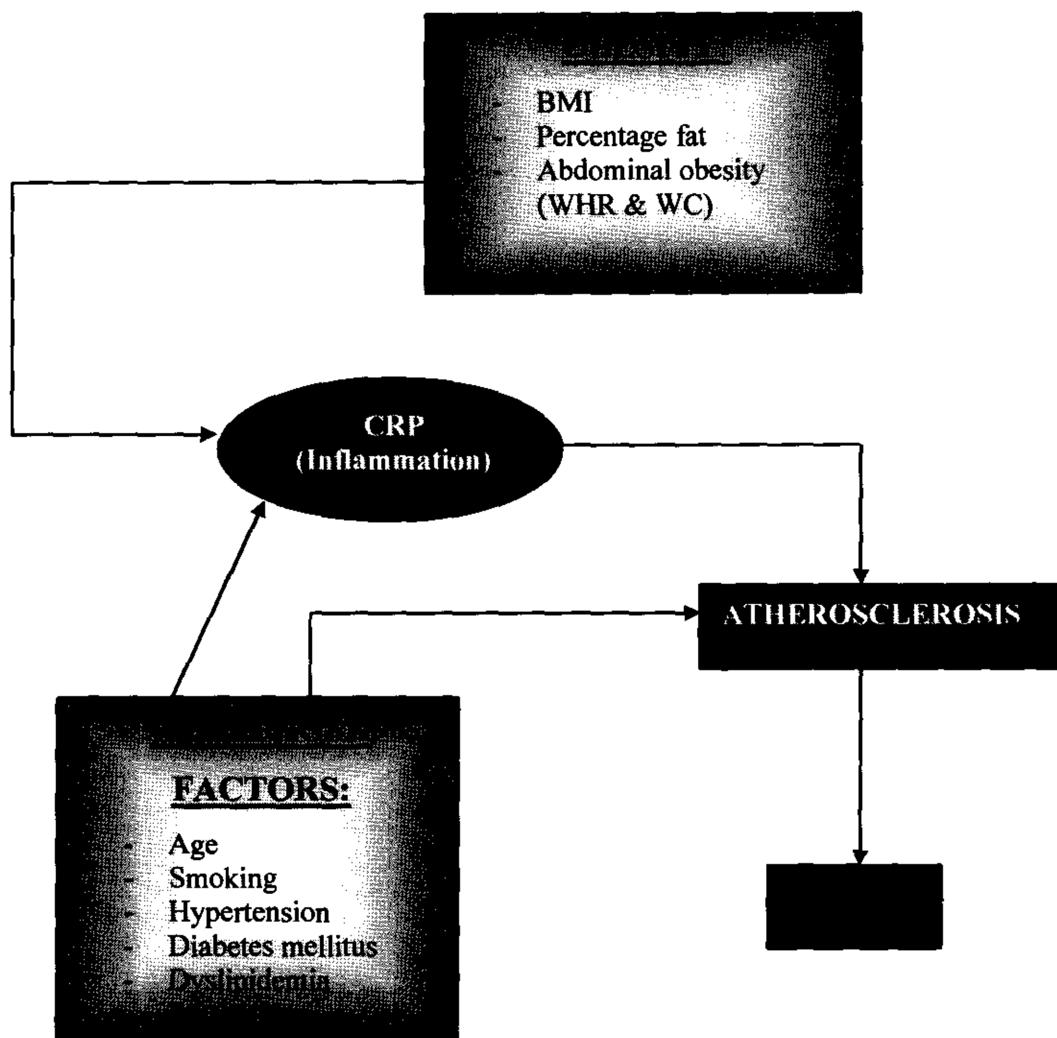

Figure 1: Associations between body composition, risk factors and C-reactive protein.

1.3 OBJECTIVES

The aims of this study were:

- To determine if there is a relationship between CRP concentrations and body composition (BMI, percentage body fat, waist circumference and WHR) in 19 to 60 year old black women.
- To determine the relationship of CRP concentrations to traditional cardiovascular risk factors in 19 to 60 year old black women.

1.4 HYPOTHESES

This study is based on the following hypotheses:

- CRP concentrations show a relationship with body composition (BMI, percentage body fat, waist circumference and WHR) in 19 to 60 year old black women.
- Certain traditional cardiovascular risk factors can be used as indicators of CRP concentrations in 19 to 60 year old black women.

1.5 STRUCTURE OF THE DISSERTATION

This dissertation is presented in four main parts, namely an introduction (Chapter 1), a review article (Chapter 2) and two research articles (Chapter 3 & 4). A summary with conclusions and recommendations will follow (Chapter 5). In the introduction, a problem statement, objectives and hypotheses are presented. The articles were each written according to the instructions to authors of the journal to which the article will be submitted. The review article is based on obesity as an inflammatory condition. The research article (Chapter 3), investigates the association between serum levels of CRP and body composition amongst 19 to 60 year old black women. Chapter 4 investigates the relationship of plasma CRP to traditional cardiovascular risk factors in 19 to 60 year old black women. The results of the studies in Chapter 3 and 4 are presented and interpreted in each chapter respectively and then summarised in Chapter 5, together with conclusions and recommendations. Chapter 5 is followed by a list of appendices.

When the literature was studied it became clear that more information on obesity in black South African women and the health risks associated with obesity in these women is needed.

The structure of the dissertation is shown in Figure 2.

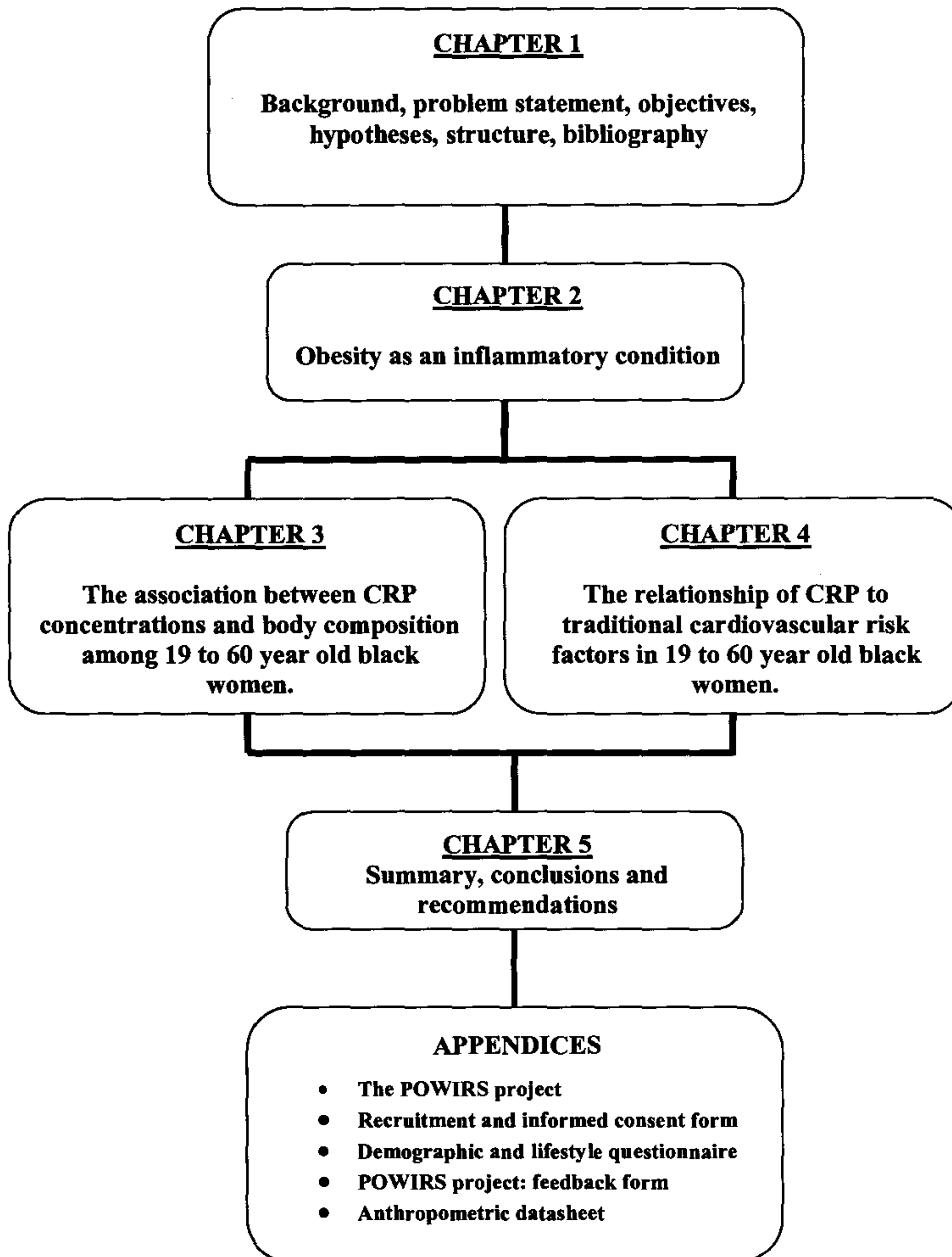

Figure 2: Structure of dissertation

1.6 REFERENCES

ACSM
see
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2 Obesity as an inflammatory condition (Review article)

Authors: S. Slabbert, J.H. de Ridder, H.S. Kruger and C. Underhay.

Key words: obesity; C-reactive protein; Interleukin-6; inflammation; physical activity

ABSTRACT

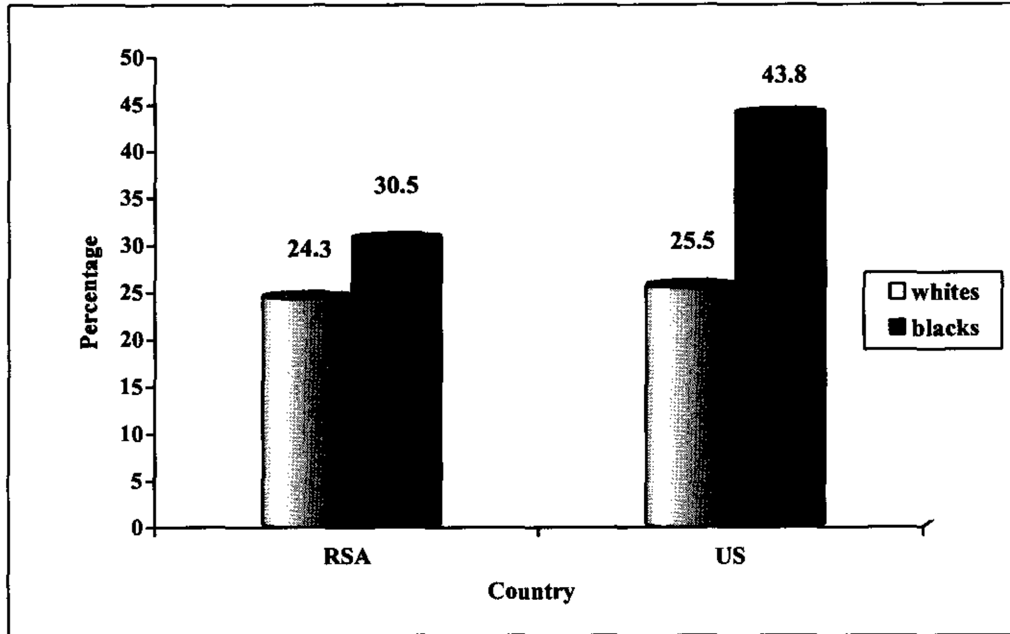
The prevalence of obesity has increased dramatically in the past decade. This foreshadows an increase in the rates of morbidity and mortality from obesity-related diseases. Research is more frequently proposing that obesity may be seen as a factor linking chronic, systemic inflammation and atherosclerosis. C-reactive protein is an acute phase reactant and a sensitive marker for acute and chronic inflammation of diverse causes. Human adipose tissue expresses interleukin-6, a cytokine that activates the production of C-reactive protein from the liver, potentially inducing low-grade systemic inflammation in persons with excess body fat. This could explain the increased risk of diabetes, heart disease and many other chronic diseases in the obese. This paper aims to provide a review on obesity as an ever-growing epidemic and the possible role that chronic systemic inflammation might play in contributing to the risks associated with one of the most common public health problems.

OPSOMMING

Die voorkoms van obesiteit het oor die afgelope dekade dramaties gestyg en daarmee saam die voorspelling van 'n toename in morbiditeit sowel as mortaliteit as gevolg van obesiteit verwante siektetoestande. Navorsing dui al hoe meer daarop dat obesiteit moontlik as die skakel kan dien tussen kroniese sistemiese inflammasie en arteriosklerose. C-reaktiewe proteïen is 'n akute fase reaktant en is 'n sensitiewe merker vir akute sowel as kroniese inflammasie toestande. Interleukien–6 is 'n sitokinien wat hoofsaaklik in vetweefsel geproduseer word. Dit aktiveer die produksie van C-reaktiewe proteïen deur die lewer, met die potensiële gevolg van laegraadse sistemiese inflammasie by persone met oormatige liggaamsvet. Die verskynsel kan moontlik die verhoogde risiko vir diabetes mellitus, koronêre hartsiektes en al die ander kroniese toestande wat voorkom by obesiteit verduidelik. Die doel van hierdie artikel is om 'n oorsig te bied op die groeiende epidemie van obesiteit en die moontlike rol wat kroniese sistemiese inflammasie speel in die bydrae tot die risiko's wat geassosieer word met een van ons mees algemene publieke gesondheidsprobleme.

INTRODUCTION

In all populations, developed and developing, rural and urban, obesity is increasing. From 1976 to 1980, 43.8% of black women and 25.2% of white women were reported to be overweight or obese in the United States (Dustan, 1990:396) (Figure 1). According to the third National Health and Nutrition Examination Survey, more than 55% of Americans are overweight or obese and obesity has increased by 30% during the last 50 years, while most of Europe has seen a 10 – 40% increase in obesity during the last ten years (Willett, Dietz & Colditz, 1999:427; Field, Coakley, Must, Spadano, Laird, Dietz, Rimm & Colditz, 2001:1581). In the South African Demographic and Health Survey, it was found that 56.6% of women were overweight or obese (Puoane, Steyn, Bradshaw, Laubscher, Fourie, Lambert & Mbananga, 2002:1041) and Mollentze, Moore, Steyn, Joubert, Steyn, Oosthuizen and Weich (1995:93) found that the prevalence of obesity is as high as 54.3% among 45-54 year old black South African women.



• Overweight is defined as a body mass index (kg/m²) = 27.3 for women
National Health and Nutrition Examination Survey 1976-1980, Vital and Health Statistics Series II, Number 238, National Center for Health Statistics.

Figure 1: Percentage of overweight or obese females in South Africa and the US, according to NHANESS II and the South African Demographic and Health Survey. Adapted from Dustan (1990:396) and Puoane *et al.* (2002:1047).

Obesity appears to have been uncommon in Western populations until the time of the Industrial Revolution, when there were increases in urbanization and a decrease in physical activity (Walker, 1995:1070). Among sub-Saharan Africans in general, a generation or so ago there was very little gain in weight or in blood pressure, with age. Even at present, in most populations, especially in the indigent masses, obesity prevalence remains very low at 1-5%. However, in South Africa and some neighbouring countries like Botswana, Namibia and Zimbabwe (Table 1), with the rise in socio-economic status, urbanization, and diminishing physical activity, the proportion affected has increased (Walker, Adam & Walker, 2001:368). In numerous countries worldwide, such have been the increases, especially in Western populations and especially in women, that according to the World Health Organization (WHO), by the year 2025 300 million people are likely to be obese (WHO, 1998:132).

Table 1: Body mass index and percentages of obese African women

Country	BMI*	Obese (%)
Namibia	22.5 ± 4.4	7.1
Zimbabwe	23.1 ± 3.7	5.7
Tanzania	21.7 ± 3.0	1.9
South Africa	*28.0 ± 6.2*	*32.0*
Rural Zulu	-	31.6
Rural Venda	25.4 ● 4.2	19.9
Jhb. Squatters	29.8 ± 7.2	33.3
Cape Town	27.8 ± 6.2	34.4
Durban	26.6 ± 5.0	22.6
Qwa Qwa Africans	28.9 ± 7.0	38.4
Mangaung Africans	29.6 ± 7.4	43.5
North West Africans	26.9 ± 6.8	28.6

* BMI = body mass index

Adapted from Walker *et al.* (2001:369), Mollentze *et al.* (1995:93) and Kruger, Venter & Vorster (2001:735).

According to Hanusch-Enserer, Cauza, Spak, Dunky, Rosen, Wolf, Prager and Eibl (2003:355) and McArdle, Katch and Katch (1994:482), obesity is a chronic disease which is associated with many other diseases and risk factors such as hypertension, diabetes mellitus, certain types of cancers, orthopedic problems, dyslipidemia and coronary heart disease (CHD). The detrimental effects of obesity can be observed from childhood into adulthood (WHO, 1998:58; Must & Strauss, 1999:S3) and obesity is also associated with increased long term morbidity and mortality in both genders (Stevens, Cai, Pamuk, Williamson, Thun & Wood, 1998:6; National Task Force on the Prevention and Treatment of Obesity, 2000:901), which is the result of an unhealthy lifestyle that includes unhealthy eating habits, smoking, a sedentary lifestyle and high stress environments (WHO, 1998:101-142). It has also been proven to be a major independent risk factor for CHD (Eckel & Krauss, 1998:2099; Hubert, Feinleib, McNamara & Castelli, 1983:973).

The aim of this review article is to point out how obesity can be described as an inflammatory condition, which may partly be the mechanism for the development of non-communicable diseases.

OBESITY AS A PUBLIC HEALTH PROBLEM

It is clear from the literature that obesity is a critical public health problem. It may be classified as a body mass index (BMI) of 30 kg/m² or more and it is functionally defined as the percent body fat (32%) (Lohman 1992:80) at which disease risk increases (Figure 2) (Kumanyika & Adams-Campbell 1991:48). Obesity can also be defined as a disease in which excess body fat has accumulated to an extent that health may be adversely affected (ACSM, 2000:214; WHO, 1998:6). It could also, for a greater part, be the result of a positive energy balance (Bray, 1990:497).

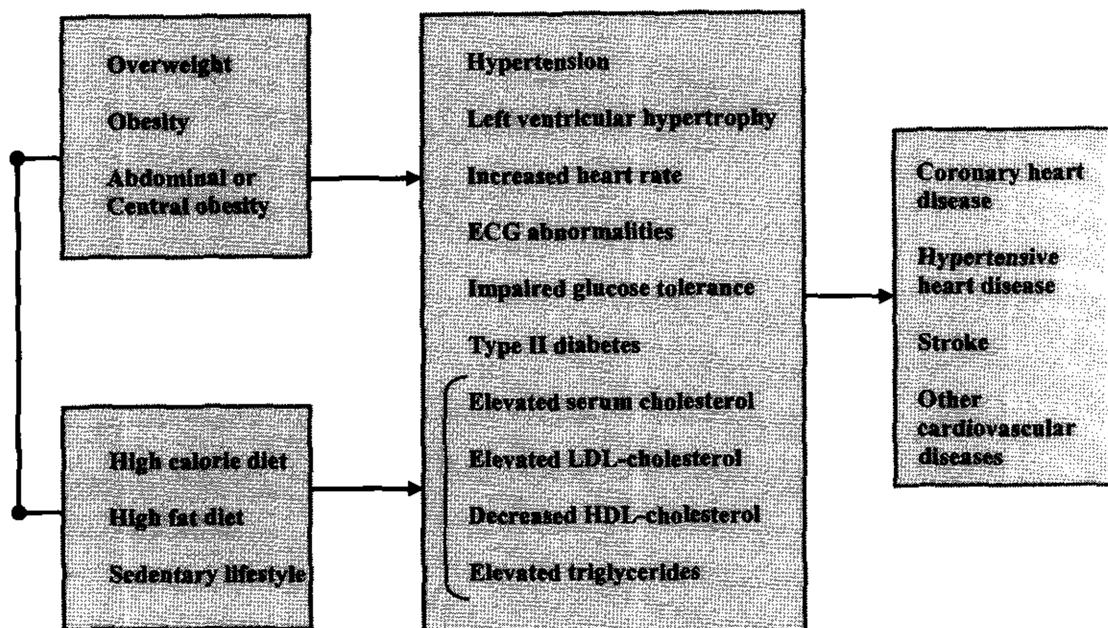


Figure 2. Weight-related variables with established relations to cardiovascular disease risk factors, morbidity or mortality.

**ECG = Electrocardiogram
Low density lipoprotein
† High density lipoprotein

Adapted from Kumanyika & Adams-Campbell (1991:48).

In the context of the consensus that obesity is a critical health problem, the apparent marked excess of obesity among black women (Van Italie, 1985:983) is of particular interest because it parallels the marked black female excess of several obesity-related risk factors and health outcomes (Kumanyika, 1987:45). African obese women are culturally and esthetically looked upon with far less disfavour than obese white women (Kruger, Van Aardt, Walker & Bosman, 1994:106) and it has been speculated that even severe obesity in black women may be far less detrimental than in white women (Walker & Segal, 1980:263; Walker, Walker, Walker & Vorster, 1989:227). Although some research groups (Walker *et al.*, 1989:228) have regarded obesity in black women as "healthy obesity", a South African study showed an unexpectedly high prevalence of hypertension and moderate-risk hypercholesterolaemia in a black population, in which a high prevalence of obesity was also found (Mollentze *et al.*, 1995:95). In the CARDIA and ARIC studies, the association between indices of obesity and cardiovascular risk factors for blacks was of the same strength as the association for whites. The investigators (Folsom, Burke, Byers, Hutchinson, Heiss, Flack, Jacobs & Caan, 1991:1610S) recommended that both blacks and whites should avoid excess adiposity.

Obesity appears to have qualitatively similar health consequences for black and white women, but may be less strongly related to some disease risks in black women than in white women. Obesity risks of black women may, however, be enhanced by the presence of multiple risk factors (Kumanyika, 1987:45). Along with obesity, elevated blood pressure and mortality due to heart disease, stroke, and diabetes occur in black women at rates that are 1.5 to 2.5 times the rates in white women. Across the board, black women are more frequently classified as overweight than white women in a ratio approaching or exceeding 2:1 (Kumanyika, 1987:32).

Diabetes is more common in blacks than it is in whites (Dustan, 1990:398) and this may explain part of the difference in the prevalence of hypertension between blacks and whites. Race differences in mortality, from selected diseases including diabetes are of interest. As seen from Table 2, mortality among blacks is greater than among whites for all of the listed diseases. It would be of interest to focus on diabetes mellitus for which death rates of black women are highest of all. This may relate to the increased prevalence of obesity among black women (Dustan, 1990:398).

Table 2: Race differences in mortality from cardiovascular diseases in women in the US*

	Black women	White women
All causes	589.1	390.6
Major cardiovascular diseases	250.5	157.4
Ischemic heart disease	100.8	82.9
Stroke	50.3	27.9
Hypertension	5.2	1.2
Diabetes mellitus	21	8.1

* The figures are age-adjusted deaths/100,000

Adapted from Dustan, (1990:398).

Some of the differences between and within black and white women may be accounted for by the high levels of high-density lipoprotein cholesterol (HDL-C) among obese and non-obese black women (Nelson, Hunt, Rosamond, Ammerman, Keyserling, Mokdad & Will, 2002:5). Similarly, one of the reasons for the low incidence of CHD in black South Africans (Gilpin, Walker, Walker & Evans, 1989:13) may be the high prevalence of a favourable HDL-C:TC ratio, but a reason for concern is a similar tendency of this ratio to decrease with age (Kruger *et al.*, 2001:738; Mollentze *et al.*, 1995:95; Steyn, Jooste, Bourne, Fourie, Badenhorst, Bourne, Langenhoven, Lombard, Truter, Katzenellenbogen, Marais & Oelofse, 1991:484).

Although most black South African subjects have favourably high HDL-C levels, HDL-C correlates negatively with BMI, waist-to-hip ratio (WHR) and waist circumference (WC), which indicates lower levels of protective HDL-C among the most obese subjects (Mollentze *et al.*, 1995:95; Steyn *et al.*, 1991:484). The literature suggests that obesity may compromise the protective cholesterol component in black women (Gartside, Khoury & Glueck, 1984:641). Among males and young females, HDL-C levels of blacks are notably higher than those of whites, but this difference is not seen in adult females (Glueck, Gartside, Laskarzewski, Khoury & Tyroler, 1984:818; Tyroler, Glueck, Christensen, Kwiterovich, 1980:105). High levels of obesity in black women have been considered a plausible explanation for this apparent loss of the HDL-C advantage (Gartside *et al.*, 1984:641). It can, therefore, be concluded that obesity in

African women is, as in other populations, associated with an increased risk of non-communicable diseases (Kruger *et al.*, 2001:739).

On the question of causes, no clear mechanism for the excess obesity in black women can be identified. To prevent and treat obesity, especially in black women, more should be known about the underlying causes of obesity among these women to develop appropriate and culturally accepted interventions.

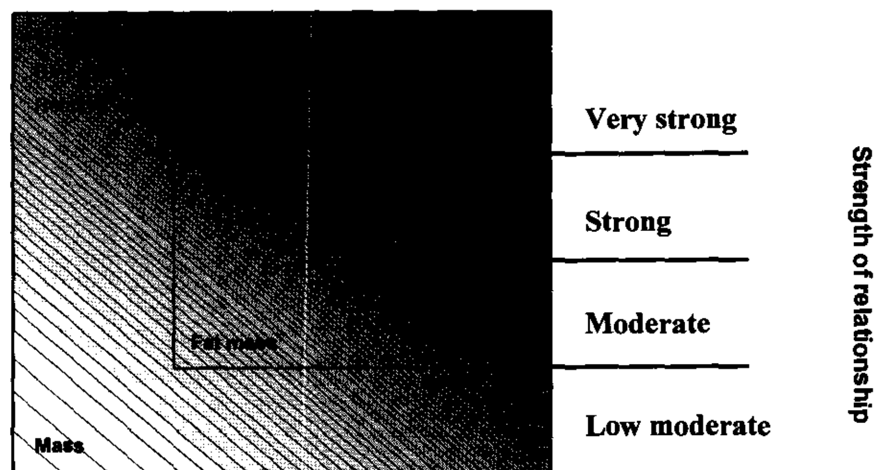
Abdominal obesity

Abdominal obesity is identified as an independent risk factor for CHD in both men and women (Lapidus, Bengtsson, Larsson, Pennert, Rybo & Sjostrom 1984:1260) and in both black and white subjects (Folsom *et al.*, 1991:1610S). While BMI reflects general obesity, WC and WHR are related to central-type obesity, where body fat is primarily located in the abdomen. Prospective epidemiological studies have revealed that central obesity (determined by WC and WHR) conveys an independent prediction of coronary artery disease risk and is more relevant compared to general obesity (determined by BMI) (Folsom, Kaye, Sellers, Hong, Cerhan, Potter & Prineas, 1993:486).

High levels of deep abdominal fat have been correlated with glucose intolerance, hyperinsulinaemia, hypertension, increases in plasma triglyceride levels and decrements in HDL levels (Zamboni, Armellini, Milani, Demarchi, Todesco, Robbi, Bergamo-Andreis & Bosello, 1992:497-501). This metabolic profile is consistent with CHD, Type II diabetes and stroke morbidity. Bergstrom, Leonetti, Newel-Morris, Shuman, Wahl & Fujimoto (1990:491-493) reported that even when the effects of glucose tolerance and BMI were accounted for, males with clinical CHD had more deep abdominal fat than their sub-clinical counterparts (Figure 3).

Cox, Whichelow, Ashwell, Prevost and Lejeune (1997:677) and Guagnano, Ballone, Merlitti, Murri, Pace-Palitti, Pilotti and Sensi (1997:634), who reported that indices of abdominal obesity were more strongly associated with blood pressure than BMI, found a positive correlation of both WC and WHR with blood pressure. More evidence for the harmful effects of abdominal obesity became available from the Nurses' Health Study in which it was found that a higher WC was associated with an increased risk of CHD,

even after controlling for BMI (Rexrode, Carey, Hennekens, Walter, Colditz, Stampfer, Willet & Manson, 1998:1846).



* BF = body fat; # SF = skinfold; † WHR = waist-hip-ratio.

Figure 3: Relationship of anthropometric measures to risk factors for major pathologies as illustrated by Norton and Olds (1996:367).

Accumulation of trunk fat is characteristic of adult-onset obesity and has been associated with diabetes, hyperlipidemia, hypertension, heart disease, stroke and other diseases in several populations (Lemieux, Pascot, Prud'Homme, Alméras, Bogaty, Nadeay, Bergeron & Després, 2001:965; Okosun, Rotimi, Forrester, Fraser, Osotimehin, Muna & Cooper, 2000:180).

MARKERS OF INFLAMMATION

C-reactive protein

C-reactive protein (CRP) is an acute phase reactant, synthesized primarily in hepatocytes and secreted by the liver. It is regulated by a variety of inflammatory cytokines of which interleukin-6 (IL-6) and tumour necrosis factor-alpha (TNF-α) are mainly involved (Heilbronn & Clifton, 2002:316-319). The synthesis of adipose tissue TNF-α could induce the production of IL-6, CRP and other acute-phase reactants (Yudkin, Stehouwer, Emeis & Coppack, 1999:976), therefore contributing to the

maintenance of a chronic low-grade inflammation state involved in the progression of obesity and its associated co-morbidities.

CRP has a normal range of < 2 mg/l in populations without evidence of acute illness (Gabay & Kushner, 1999:452), but concentrations may rise a hundred-fold in response to trauma, inflammation and infection and decreases just as rapidly with the resolution of the condition (Das, 2001:954; Macy, Hayes & Tracy 1997:52). Therefore, enhanced levels of CRP can be used as a sensitive marker of systemic inflammation (Das, 2001:954). Pannacciulli, Cantatore, Minenna, Bellacicco, Giorgino and De Pergola (2001:1418) found four factors - age, insulin resistance, central fat accumulation and the amount of total body fat to be the most powerful predictors of CRP concentrations in apparently healthy adult women. Recently CRP concentrations have been shown to be significantly associated with several cardiovascular risk factors, such as age, smoking, hypertension, exercise, plasma lipids, homocysteine and BMI (Rohde, Hennekens & Ridker, 1999:1021).

Concerning the relationship between CRP concentration and BMI level, it was found that the prevalence of elevated CRP levels (concentrations ≥ 0.22 mg/dl) is higher in both overweight (BMI 25-29.9 kg/m^2) and obese (BMI ≥ 30 kg/m^2) patients than in normal weight (BMI < 25 kg/m) subjects (Visser, Bouter, McQuillan, Wener & Harris, 1999:2133). Even moderately elevated CRP plasma concentrations have been associated with a significant increase in risk of future myocardial infarction, stroke and peripheral atherosclerosis among apparently healthy middle-aged men and women (Ridker, Cushman, Stampfer, Tracy & Hennekens, 1998:427; Ridker, Buring, Shih, Matias & Hennekens, 1998:732) even after adjustment for known cardiovascular risk factors (Rohde, *et al.*, 1999:1021).

In particular, CRP concentrations have been recently demonstrated to be as strong as apolipoprotein B-100 levels and TC/HDL-C ratio in predicting the risk of cardiovascular events in women and even stronger than concentrations of TC, HDL-C, lipoprotein(a) and homocysteine (Ridker, Hennekens, Buring & Rifai, 2000:842). Several studies (Visser *et al.*, 1999:2133; Cook, Mendall, Whincup, Carey, Ballam, Morris, Miller & Strachan, 2000:149) have recorded similar results in which they observed that overweight and obese children and adults have elevated serum levels of

CRP, IL-6 and TNF-α. Visser, Bouter, McQuillan, Wener and Harris (2001:15) observed an increase in CRP concentration in overweight children compared with normal weight children, even after carefully controlling for disease and other factors known to influence CRP concentrations, therefore confirming a state of low-grade systemic inflammation in overweight and obese persons. This may explain the increased risk of diabetes, heart disease and many other chronic diseases in the obese.

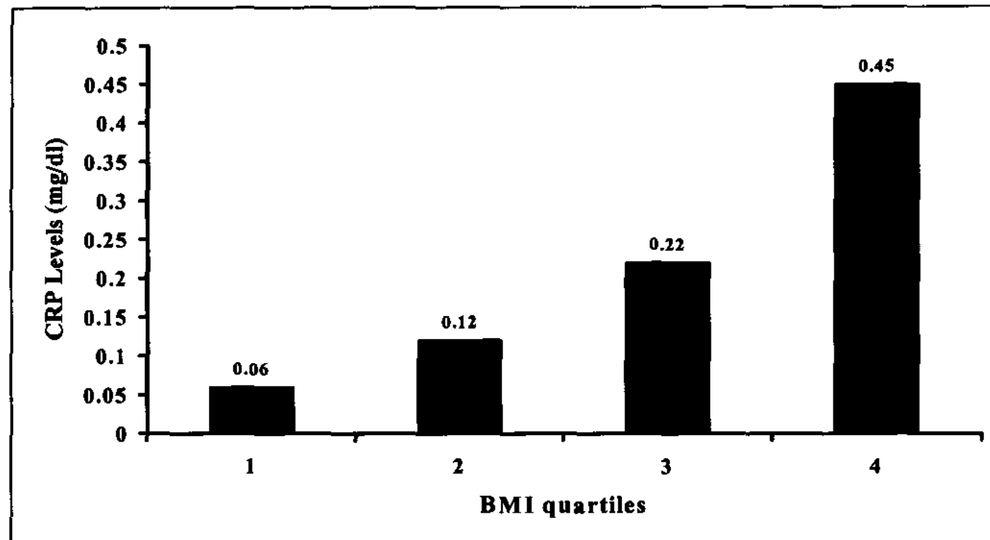
Interleukin-6

Adipose tissue was previously considered a passive storage depot for fat but is now known to play an active role in metabolism (Flier, 1995:15). The reason for increased production of CRP in obesity is most likely due to IL-6. IL-6 is a cytokine produced in the adipose tissue of healthy humans. It is released into the circulation and activates the production of CRP from the liver and CRP levels are a direct indicator of IL-6 levels *in vivo* (Fried, Bunkin & Greenberg, 1998:849; Mohamed-Ali, Coodrick, Rawesh, Katz, Miles, Yudkin, Klein & Coppack, 1997:4199). IL-6 is believed to represent the major regulator of the hepatic acute phase response (Bataille & Klein, 1992:982-983; Heinrich, Castell & Andus, 1990:623) so that a substantial contribution to circulating levels from adipose tissue may mean that obesity can resemble a low-grade inflammatory state (Yudkin, Kumari, Humphries & Mohamed-Ali, 2000:211).

Approximately 25-30% of serum IL-6 originates from adipose tissue and the secretion of IL-6 from subcutaneous fat is in proportion to fat mass (Mohamed-Ali *et al.*, 1997:4199). Omental fat cells secrete approximately two to three times more IL-6 compared to subcutaneous adipocytes (Fried *et al.*, 1998:848). Therefore, subjects with more abdominal fat may have increased IL-6 and CRP, which could partially account for increased mortality rates in abdominally obese subjects if IL-6 or CRP contributed to disease promotion (Heilbronn & Clifton, 2002:317).

The synthesis of adipose tissue TNF-α could induce the production of IL-6, CRP and other acute-phase reactants, thereby contributing to the maintenance of a chronic low-grade inflammation state involved in the progression of obesity and its associated co-morbidities (Bulló, Garcia-Lord, Megias & Salas-Salvadó, 2003:528).

Although little is known about the effects of IL-6 on adipose tissue, one possible action is a down-regulation of adipose tissue lipoprotein lipase (Greenberg, Nordan, McIntosh, Calvo, Scow & Jablons, 1992:4115). The regulated production of this multifunctional cytokine may modulate regional adipose tissue metabolism and may contribute to the recently reported correlation between serum IL-6 and the level of obesity. (Fried *et al.*, 1998:850)



* quartile 1 (< 22.4); quartile 2 (22.4- < 24.6); quartile 3 (24.6- < 28.3); quartile 4 (≥ 28.3)
Adapted from Rexrode, Pradhan, Manson, Buring & Ridker (2003:5).

Figure 4: Median CRP levels by BMI quartiles* in women

Adipose tissue and inflammatory markers

In a study by (Rexrode *et al.*, 2003:7), BMI was the strongest predictor of elevated inflammatory markers (Figure 3). The associations with BMI were dramatic; women in the highest BMI quartile (BMI ≥ 28.3 kg/m²) had a more than twelve-fold increased risk of having elevated CRP levels and a more than four-fold increased risk of elevated IL-6 levels and higher CRP and IL-6 levels were observed with each increment in BMI (Rexrode *et al.,* 2003:7) (Figure 4).

Pannacciulli *et al.* (2001:1419) hypothesized that adipose tissue is responsible for a mild, chronic inflammatory state, as expressed by levels of CRP, IL-6 and TNF-α, which may induce insulin resistance and endothelial dysfunction, therefore leading to

atherosclerosis as proposed by Yudkin *et al.* (1999:977). Human abdominal visceral adipose tissue has been reported to release more IL-6 compared to subcutaneous adipose tissue (Fried *et al.*, 1998:849) thereby explaining the results of Pannacciulli *et al.* (2001:1419) that WC is a stronger predictor of CRP concentrations than total fatness, expressed as BMI or fat mass.

These findings fit well with a growing body of evidence implicating adipose tissue in general and visceral adiposity in particular as key regulators of inflammation. Although subcutaneous fat clearly plays an important role, Tracy (2001:881) found the identification of visceral adiposity to be a key correlate of CRP in men, which is consistent not only with the emerging role of abdominal fat in the metabolic syndrome (Montague & O'Rahilly, 2000:886) but also with the concept of "non-overweight obesity" as proffered by Dvorak and colleagues (Dvorak, Denino, Ades & Poehlman, 1999:2213). They suggested that the role of visceral fat may be more complex than suspected, because even people who are not obviously overweight may still have disproportionately too much visceral fat, with the result of a predisposition toward insulin resistance and atherosclerotic disease, possibly through inappropriate cytokine secretion (Tracy 2001:882).

If true, this concept begs the question of whether the key variable might not be disproportionate visceral adiposity rather than what has traditionally been considered obesity as characterized by weight, WC, or BMI (Tracy 2001:882). It is suggested that adiposity and in particular visceral adipose tissue is a key promoter of low-grade chronic inflammation (Forouhi, Sattar & McKeigue, 2001:1331).

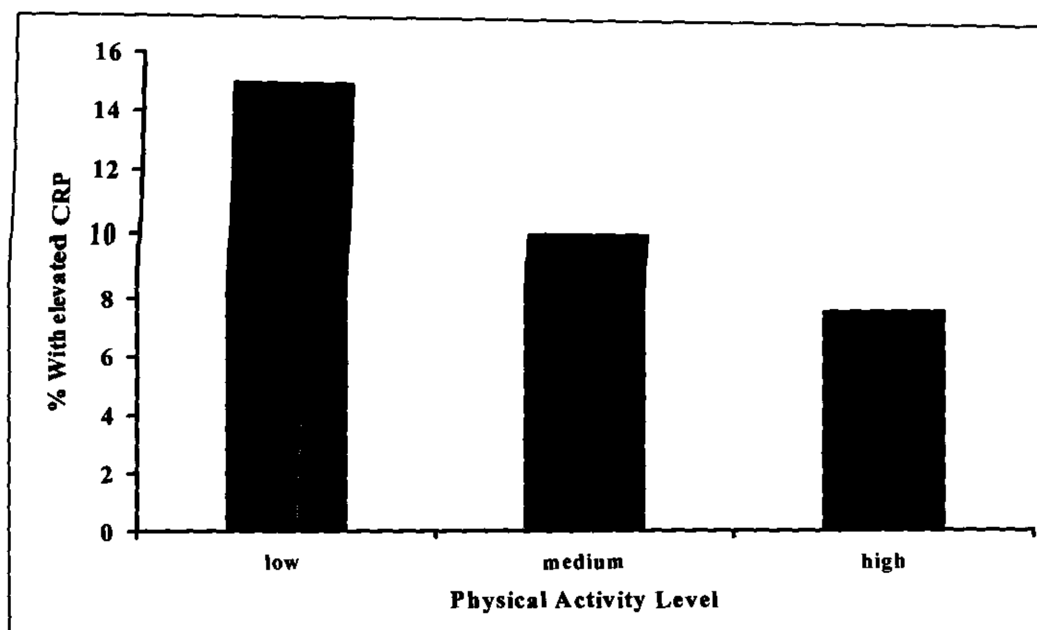
WEIGHT LOSS AND PHYSICAL ACTIVITY

Lemieux *et al.* (2001:966) suggest that because of the powerful association with obesity, weight loss may be another method for down regulating an individual's inflammatory status. Heilbronn, Noakes and Clifton (2001:969) studied a group of healthy obese women, characterized by an average BMI of 34 kg/m^2, with a range of 28 to 44 kg/m^2. These subjects were placed on a very low fat diet for twelve weeks and an average weight loss of 8 kg was achieved. CRP decreased by 26% and the authors observed a strong correlation between weight loss and change in CRP.

It is suggested by Saito, Ishimitsu, Minami, Ono, Ohrui and Matsuoka (2003:78) that correction of overweight may be effective in reducing plasma CRP. Indeed, in a recent study, Tchernof, Molan, Sites, Ades and Poehlman (2002:567) reported that adiposity was a significant predictor of plasma CRP and that caloric restriction-induced weight loss markedly reduced plasma CRP in obese postmenopausal women. It has also been reported by Smith, Dykes, Douglas, Krishnaswamy and Berk (1999:1725) that moderate exercise reduces inflammation markers. In their study, they reported CRP levels as measured before an exercise programme which ranged from 0 to 0.9 mg/dL in the lower quartile to 5.8 to 37.5 mg/dL in the upper quartile, with a mean value of 4.81 (1.09) mg/dL. Values taken after the exercise programme decreased by 35% to 3.13 (0.64) mg/dL ($P = 0.12$) (2-sided t-test). The frequency of values in the upper quartile dropped by 50% after following the exercise programme ($P= 0.01$).

Tisi, Hulse, Chulakadabba, Gosling and Shearman (1997:347) evaluated several markers of disease severity in a randomized trial of therapeutic exercise training in 49 patients with intermittent claudication. In their findings, serum CRP levels were significantly reduced after 3 to 6 months of regular physical activity. The observation by Rohde *et al.* (1999:1021) that men who exercise regularly were more likely to have lower CRP levels is consistent with the findings of Tisi *et al.* (1997:347), as well as with the known beneficial effects of regular physical activity.

Abramson and Vaccarino (2002:1288-1289) also found that more frequent physical activity is independently associated with lower odds of having elevated inflammation levels among apparently healthy US adults 40 years and older, independent of several confounding factors. They found that among those engaging in low, medium and high physical activity levels, the percentages of persons with elevated CRP levels were 15.1%, 9.7%, and 6.5% respectively. As physical activity levels increased, the odds of having an elevated CRP level significantly decreased independent of other factors (Figure 5).



As reported by Abramson and Vaccarino (2002:1289).

Figure 5: Unadjusted percentages of persons with elevated CRP levels according to frequency of physical activity

In another study, Ford (2002:567) found that physical activity is inversely associated with CRP concentrations, suggesting that physical activity may mitigate inflammation. These results add to mounting evidence that physical activity may reduce inflammation, which is a critical process in the pathogenesis of cardiovascular disease. Taken together, these physical and dietary approaches to correct obesity may be promising in inhibiting cardiovascular inflammation and future risk of developing cardiovascular diseases (Saito *et al.*, 2003:78).

More and more reports are indicating that markers of inflammation are predictive of increased CHD incidence and mortality, (Danesh, Whincup & Walker, 2000:199-204; Rohde *et al.*, 1999:1021; Ridker *et al.*, 1998:427) and the development of CHD is increasingly being viewed as an inflammatory process (Ridker *et al.*, 1998:733). As such, it might be reasonable to hypothesize that if physical activity lowers CHD risk, it may do so in part by preventing or reducing inflammation. It is not clear how physical activity could influence the specific inflammatory activity associated with cardiovascular disease or other diseases. By reducing adipose mass, physical activity

activity in the study done by Ford (2002:566), suggesting that physical activity influences the inflammatory process through other mechanisms. Geffken, Cushman, Burke, Polak, Sakkinen and Tracy (2001:248) suggest that physical activity can reduce inflammation by improving insulin resistance because concentrations of several inflammatory markers were raised in insulin-resistant subjects.

Assuming physical activity does indeed help prevent or reduce inflammation, what is the mechanism by which it would accomplish this effect? Strenuous physical activity can lead to muscle damage and thereby increase inflammation (Pyne, 1994:55). In contrast, however, there are plausible mechanisms by which physical activity could also reduce inflammation. For example, obesity is a factor that is strongly related to higher levels of inflammation (Visser *et al.*, 1999:2135) and it has been suggested that physical activity may reduce inflammation by reducing obesity levels (Geffken *et al.*, 2001:248). However, in the study done by Abramson and Vaccarino (2002:1289), it was observed that physical activity was associated with lower levels of inflammation even after adjustment for measures of general obesity (BMI) and central obesity (WHR). Therefore, they found it unlikely that the association between activity and inflammation is mediated entirely by reductions in obesity.

Other mechanisms linking exercise to lower inflammation levels may involve antioxidant effects of exercise. Although exercise increases oxidative metabolism and thereby induces oxidative stress, there is also evidence from several studies that adapting to long-term exercise or physical training can significantly elevate antioxidant defences (Alessio & Blasi, 1997:299; Leeuwenburgh & Heinecke, 2001:836). Since elevated levels of CRP and other markers of inflammation have been shown to be important predictors of increased CHD risk (Ridker *et al.*, 1998:733), the study by Abramson and Vaccarino (2002:1291) implies, although it does not prove, that physical activity may lower CHD risk by reducing inflammation. Their results suggest that the anti-inflammatory effects of regular physical activity may mediate the association between physical activity and reduced coronary heart disease risk (Abramson & Vaccarino 2002:1291).

CONCLUSION

The etiology of obesity represents a complex interaction of genetics, diet, metabolism and physical activity levels. Clearly, diet and physical activity play significant roles in the prevalence of obesity. A positive association has been observed between BMI and CRP levels, a sensitive marker for systemic inflammation in healthy adults and children. The reason for the apparent association between CRP and BMI are not clear, but several explanations are possible.

Obesity has been positively associated with increased serum concentrations of vascular inflammatory markers, and adipose tissue has been proposed as a factor directly modulating pro-inflammatory cytokine levels. Individuals with obesity are also at an increased risk for various chronic diseases, several of which are also characterized by elevated CRP concentrations. Elevated CRP levels have also been independently associated with increased risk of myocardial infarction, ischemic heart disease and peripheral arterial disease.

This is interesting because more frequent physical activity is associated with lower odds of having elevated inflammation levels. Research suggests that the anti-inflammatory effects of regular physical activity may mediate the association between physical activity and reduced coronary heart disease risk.

From the preceding discussion it is evident that low-grade, systemic inflammation occurs in obesity and that weight loss after dietary treatment, as well as regular physical activity may lower CHD risk by reducing inflammation. Studies that examine physical activity as a prospective predictor of inflammation in general population samples are needed to establish whether physical activity truly prevents or reduces inflammation and whether this reduction accounts for the association between increased physical activity and lower CHD risk.

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3 The association between C-reactive protein concentrations and body composition in 19 to 60 year old black women

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Objective: To investigate the association between circulating C-reactive protein (CRP) concentrations and indices of body composition among 19 to 60 year old black women.

Research Methods and Procedures: A cross-sectional study of 102 urban African women. Measurements of high sensitivity CRP concentrations. Body composition as measured by body mass index (BMI), percentage body fat, waist circumference (WC) and waist-to-hip ratio (WHR).

Results: BMI, WC, percentage body fat and WHR were all significantly correlated with CRP throughout the anthropometric spectrum. BMI was found to be the strongest predictor of elevated CRP concentrations among these women.

Discussion: Indices of both total and abdominal adiposity were strongly associated with significantly increased concentrations of CRP. It is suggested that adiposity may also be a key promoter of low-grade chronic inflammation in these African women. Further studies should be performed to determine whether losing weight by exercise or diet is associated with reductions in plasma CRP concentrations.

Key words: body mass index, percentage body fat, waist circumference,
waist-to-hip ratio, inflammation

Introduction

Today, as standards of living continue to rise, weight gain and obesity are posing a growing threat to health in countries all over the world. Obesity is a chronic disease, prevalent in both developed and developing countries and affecting children as well as adults (1). Indeed, obesity is now so common that it is replacing the more traditional public health concerns, including under nutrition and infectious disease as one of the most significant contributors to ill health (1). Furthermore, as obesity is a key risk factor in the natural history of other chronic and non-communicable diseases (NCDs) in developed countries, it is only a matter of time before the same high mortality rates for such diseases will be seen in developing countries with well established market economies (1).

The underlying cause of obesity is the undesirable positive energy balance which is associated with weight gain (2). Obese individuals differ not only in the amount of excess fat they store, but also in the regional distribution of fat within the body. The distribution of fat induced by weight gain affects the risks associated with obesity and the kind of disease that results (1, 3).

Body mass index (BMI) provides the most useful, albeit crude, population-level measure of obesity (1) and can be used to estimate obesity associated risks within a population. BMI, however, does not account for the wide variation in body fat distribution and may not correspond to the same degree of fatness or associated health risk in different individuals and populations (1).

BMI does not take into account the composition of the individual's body weight, therefore, individuals with a high BMI value may have either excess fat or a large lean body mass. Obesity, therefore, may be better defined as an excessive amount of body fat relative to body weight (4). To classify levels of body fatness, relative body fat, also called percentage body fat, is used and is expressed as a percentage of total body weight.

During the past ten years or so, it has become accepted that waist-to-hip ratio (WHR) (WHR > 1.0 in men and > 0.85 in women) indicates abdominal fat accumulation (5, 6)

and some experts consider the hip circumference to provide additional valuable information related to gluteofemoral muscle mass and bone structure (6). However, recent evidence suggests that waist circumference (WC) alone may provide a more practical correlate of abdominal fat distribution and associated ill health (7).

WC is a convenient and simple measurement that is unrelated to height, correlates closely with BMI and WHR (7) and is an approximate index of intra-abdominal fat mass and total body fat (8). Furthermore, changes in WC reflect changes in risk factors for cardiovascular disease (CVD) (3) and other forms of chronic diseases, even though different ethnic populations differ in the level of risk associated with a particular waist circumference. A globally applicable grading system of waist circumference has to date, not yet been developed (1).

C-reactive protein (CRP) is an acute phase reactant produced by hepatocytes in response to a wide range of stimuli. Circulating at low concentrations in healthy individuals, CRP rises dramatically in response to infection, inflammation and injury (9). Plasma CRP concentrations have long been a widely used marker of disease activity in inflammatory conditions, but more recently, there has been increased interest in the possible relevance of low-grade inflammatory processes to obesity and cardiovascular disease (10, 11, 12). CRP plasma concentrations are determined mainly by the synthesis rate in the liver which is regulated by a variety of inflammatory cytokines of which Interleukin-6 (IL-6) is mainly involved (30). Approximately 20-30% of serum IL-6 originates from adipose tissue (13) and omental fat cells secrete approximately two to three times more IL-6 than subcutaneous adipocytes (14). Therefore, people with more abdominal fat may have increased IL-6 and CRP, which could partially account for the increased mortality rates in abdominally obese subjects. Despite the sharp increases that occur during the acute-phase response, longer-term plasma CRP concentrations show about the same degree of year-to year consistency within individuals as some more extensively studied risk factors such as blood cholesterol concentrations and blood pressure (15). Visser *et al.* (16) have also raised broader questions about low-grade inflammation and coronary heart disease (CHD) by suggesting that plasma CRP might at least partly mediate the effects of obesity on CHD.

The aim of this study was to investigate the association between serum concentrations of CRP and indices of body composition among 19 to 60 year old urban African women and to determine which indices could best be used to predict the risk of having elevated concentrations of plasma CRP. The study's subject sample was chosen because the emergence of NCD in Africans in South Africa is characterised by high rates of female obesity and the prevalence of obesity in African women is now double that of Caucasian women (17, 18). To our knowledge, such a study has not yet been performed on African women.

Research Methods and Procedures

The study is a cross-sectional design and formed part of the POWIRS-project (Profiles of Obese Women suffering from the Insulin Resistance Syndrome), which was approved by the Ethics Committee of the North-West University (project number: 03M03). The study was conducted during January and February 2003. It was set in the North West province of South-Africa and consisted of 102 African women volunteers working at a governmental institution. Subjects were recruited by a dietician employed at the institution and the inclusion criteria were apparently healthy African women aged between 19 and 60 years. The dietician attempted to recruit only HIV negative subjects (according to their status as determined three months before the study) as a HIV positive status could result in higher CRP concentrations due to the presence of infections. The negative status of all subjects however cannot be guaranteed. Pregnant and lactating women and those with oral temperatures above 37°C were excluded. Subjects were recruited based on their BMI as measured at the worksite Medical Station. Three groups of subjects were selected based on BMI guidelines of the Report of a World Health Organization Consultation on Obesity (1).

All subjects were fully informed about the objectives and procedures of the study prior to their inclusion and assistance was available to provide information in their home language. All subjects signed an informed consent form. Subjects identified with hypertension, diabetes or other abnormalities were referred to local clinics, hospitals or their physicians. All subjects received a short report of their health information.

Each day a group of eight to ten women were invited to stay in a metabolic unit. Upon their arrival, each participant received her own room, subject number and participant data sheet. The participants received supper at 19:00 and were requested not to eat anything else during the night in order for them to be fasted during the following morning's measurements. The next morning the first participant was woken at 6:00. Body weight was measured and the subject then returned to her room for blood sampling. The next subject was then woken and the same procedures were followed.

The fasted blood sampling was done by a registered nurse and blood was taken from the *vena cephalica* using a sterile butterfly infusion set and syringes. For preparation of serum, blood was allowed to clot in glass tubes, centrifuged at 3500 rpm for 10 minutes (Universal 16™, Hettich), and transferred to 1.5ml Eppedorff tubes. Plasma was collected in EDTA tubes and centrifuged at 3700 rpm for 10 to 15 minutes at 4°C (Universal 32R, Hettich) The serum was then immediately removed and stored at -84°C for analysis. CRP was measured using a high-sensitivity, near infrared particle immunoassay by rate turbidimetry with a high sensitivity CRPH reagent (Beckman Coulter Inc., Nyon, Switzerland) in conjunction with an IMMAGE® Immunochemistry System (Cat. No. 474630) and Calibrator 5 Plus.

Anthropometric measurements: Body weight was measured by a Precision (A & D Company, Japan) electronic scale, stature was measured using an Invicta stadiometer (IP 1465, UK) and waist circumference, hip circumference and skin folds were taken by a qualified level II anthropometrist according to standardized methods as described by Norton and Olds (19). Circumferences were measured by a Lufkin (Cooper Tools, Apex, NC) unstretchable metal measuring tape to the nearest 0.1 cm and a Harpenden (British Indicators, UK) skin fold calliper with a constant pressure of 10 g/mm^2 was used for the measurements of the skin folds to the nearest 0.2 mm.

Statistical Analysis: Statistical analysis was performed using SPSS for Windows (version 11.0.1; SPSS Inc., Chicago). Results are presented as mean ± standard deviation for all of the variables within the whole group and as mean ± standard error in all categories within each of the measured variables of the group. Two-tailed partial Pearson correlation coefficients were used to quantify the associations among variables for the total group and per body composition category. Data were adjusted for age and

smoking. If no smokers were present within categories of the variables, correlations were only adjusted for age.

To examine the contribution of overall adiposity to the variation of CRP concentrations, the anthropometric indices of the entire sample were divided on the basis of the following values (see also first two columns of Table 3): BMI as weight in kilograms divided by height in metre squared; underweight was defined as BMI < 18.5 kg/m^2; normal range was defined as 18.5-24.99 kg/m^2; overweight was defined as BMI 25-29.9 kg/m^2; and obesity was defined as BMI ≥ 30 kg/m^2 for all subjects (1). Waist circumference was categorized as: low or normal risk (< 80cm); increased risk (80-88cm) and substantially increased risk (> 88cm) (1). The cut off point for central obesity was a waist circumference ≥ 88 cm (1). The WHR was computed as the waist circumference divided by hip circumference and was categorized as: low (< 0.73); moderate (0.73-0.79); high (0.80-0.87) and very high (> 0.87) (20), with a cut off point of ≥ 0.85 to define abdominal obesity (1). Percentage body fat was determined using the appropriate equations necessary when measuring obese as well as non-obese African women respectively (21, 22) and was categorized as: very low (< 11); low (11-22.99); average (23-23.99); high (24-31.99) and very high (> 32), adapted from the percent body fat standards for women in relation to health according to Lohman (23). The prediction equations used were the following:

Obese women (22): 0.11077 (AB C) – 0.17666 (HT) + 0.14354 (BW) + 51.03301, *with* AB C = [($AB_1 + AB_2$)/2], HT = height (cm); BW = body weight (kg); ABC (cm) = average abdominal circumference; AB_1 (cm)= abdominal circumference anteriorly midway between the xyphoid process of the sternum and the umbilicus and laterally between the lower end of the rib cage and iliac crests and AB_2 (cm) = abdominal circumference at the umbilicus level.

Non-obese African women (21):

Sum of 7 skinfolds (mm): chest, abdomen, thigh, triceps, subscapular, suprailiac and midaxillary.

Equation: Db (g/cc) = 1.0970 - 0.00046971 (Σ 7 skinfolds) + 0.00000056 (Σ 7skinfolds)^2 - 0.00012828 (age), converting Db to percentage body fat: [(4.85/Db) – 4.39] x 100

HsCRP was categorized as: low (< 0.1 mg/dL); average (≥ 0.1 and < 0.3 mg/dL); high (≥ 0.3 and <1.0 mg/dL) and very high relative risk (≥ 1.0 mg/dL) respectively (24). An analysis of variance (ANOVA) was done to determine whether there were statistically significant differences among the categories within each of the body composition variables and the minimal statistical significance was defined as $p < 0.05$. The ANOVA was followed by a Games-Howell *post hoc* test for all variables except WHR, for which the ANOVA was not significant. A signal detection analysis was done to identify risk predictors of elevated CRP concentrations (defined as > 0.2 mg/dL). The test was used because of its ability to identify individuals that are homogeneous in both outcome and risk predictors (25).

Results

All the volunteers completed the study. Data from one of the subjects were excluded from the data analysis because of the presence of infection, accompanied by an unusually high CRP concentration. General, anthropometric and metabolic characteristics of the population are shown in Table 1.

Table 1. Descriptive data for CRP and anthropometrical variables in the group (n = 101)

Variable	Mean ± SD	Min	Max
Age (years)	31.2 ± 8.7	19	56.0
Body mass index (kg/m^2)	28 ± 6.4	18.2	50.0
Percentage body fat*	33.6 ± 11.4	15.4	56.1
Circumferences:			
Waist Minimum† (cm)	81.7 ± 13.3	61.8	118.5
Mid-xiphoied-umbilicus (cm)	84.1 ± 14.8	62.2	133.1
Hip (cm)	106.6 ± 12.3	75.8	150.3
Waist-to-hip ratio	0.77 ± 0.07	0.63	1.0
C-reactive protein (mg/dL)	0.4 ± 0.46	0.02	2.1

* Percentage body fat calculated using prediction equations (21, 22)
† Waist circumference

Table 2. Correlation of CRP concentrations with anthropometrical indices in a sample of 101 women

Anthropometric variables	CRP	
	correlation *	p-value
Body mass index	0.6105	<0.01
Percentage body fat	0.5068	<0.01
Waist circumference (cm)	0.5559	<0.01
Waist-hip ratio	0.615	<0.05

* Partial correlation coefficients for the total group (controlled for smoking and age)
Coefficient / 2-tailed significance

The sample of women in the present study was characterized by a waist circumference average which falls between the normal and increased risk categories. The WHR average, however, fell into the moderate category. Table 2 displays the correlation coefficients between CRP plasma concentrations and all the body composition variables investigated. CRP was positively correlated with BMI ($p < 0.01$), percentage body fat ($p < 0.01$), WC ($p < 0.01$) and WHR ($p < 0.05$). CRP concentrations were also examined according to BMI (Figure 1), percentage body fat (Figure 2), WC (Figure 3) and WHR (figure 4) categories and progressive increases in serum CRP were especially observed for BMI and WC. The *post hoc* test revealed that the CRP concentrations in the obese category of BMI were significantly higher than both the overweight as well as the normal weight categories. CRP concentrations in the very high percentage body fat category were also significantly higher than those in the high, average and low categories. Significantly higher CRP concentrations were also found in the substantially increased risk group compared with subjects in the increased and low risk WC categories. The ANOVA for WHR revealed that CRP concentrations were not significantly different among the various WHR categories. The signal detection analysis identified BMI to be the best predictor of increased CRP concentrations at a cut-off point of 27.68 kg/m^2; χ^2 (N = 100) = 28.66, $p < 0.001$.

Table 3. Associations between CRP concentrations and anthropometrical indices

Variables	Range	Mean *	n	CRP (mg/dL)		
				Mean ± SE	Correlation†	p-value
Body mass index (1)						
Underweight‡	<18.5 kg/m²		1			
Normal§	18.5-24.99 kg/m²	21.92	37	0.18 ± 0.04	0.0048	0.978
Overweight	25-29.9 kg/m²	27.17	25	0.35 ± 0.05	0.0524	0.808
Obese	≥ 30 kg/m²	34.78	37	0.67 ± 0.10	0.6275	0.000 ‖
Percentage body fat (23)						
Low	<11	19.92	24	0.17 ± 0.05	0.2561	0.250
Average§	11-22.99	23.73	4	0.16 ± 0.04	0.9763	0.139
High	23-23.99	27.36	24	0.28 ± 0.06	0.1479	0.511
Very high	24-31.99	44.07	48	0.61 ± 0.08	0.4022	0.006 ‖
Waist circumference (cm) (1)						
Low/normal risk	<80	71.18	51	0.24 ± 0.04	0.3061	0.032 ‖
Increased risk§	80-88	84.45	20	0.31 ± 0.06	0.3850	0.104
Substantially increased risk	>88	98.76	29	0.75 ± 0.11	0.4650	0.015 ‖
Waist-hip ratio (20)						
Low	<0.73	0.69	32	0.32 ± 0.07	-0.2330	0.215
Moderate	0.73-0.79	0.76	39	0.33 ± 0.07	0.0394	0.933
High	>0.87	0.92	8	0.56 ± 0.14	0.3869	0.102
Very high§	0.80-0.87	0.82	21	0.60 ± 0.13	0.2051	0.223

* Mean in each category of the variables
† Pearson correlation between CRP and body composition variables
‡ No data is reported because there is only 1 subject in category 1 of BMI
§ No smokers in the category
‖ $p < 0.05$
** no subjects present in category 1 of percentage body fat

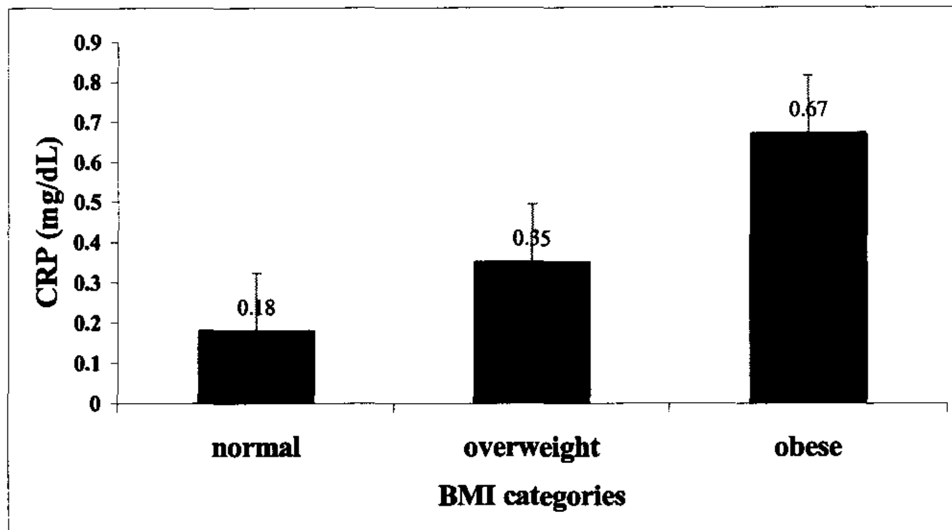

Figure 1. Mean ± SE for CRP concentrations in relation to BMI categories

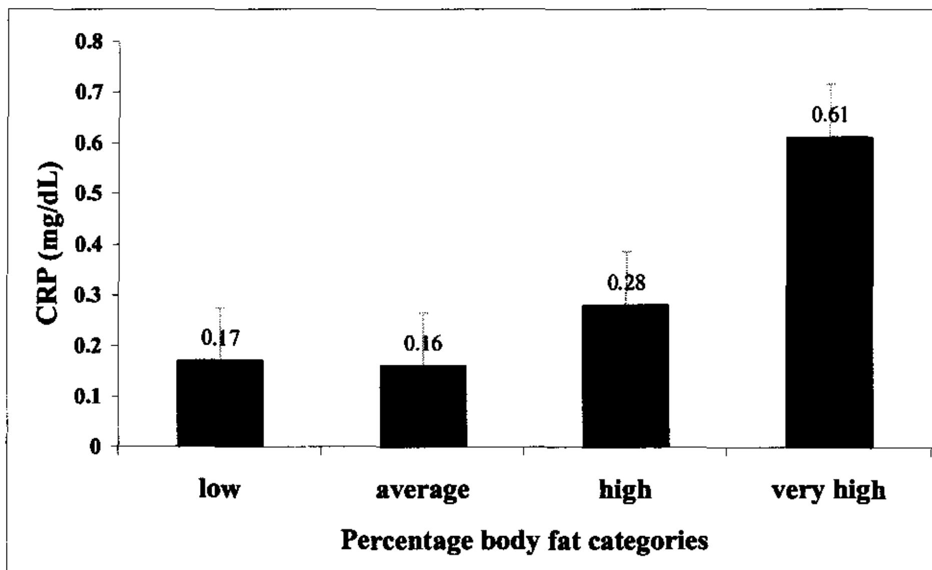

Figure 2. Mean ± SE for CRP concentrations in relation to percentage body fat categories

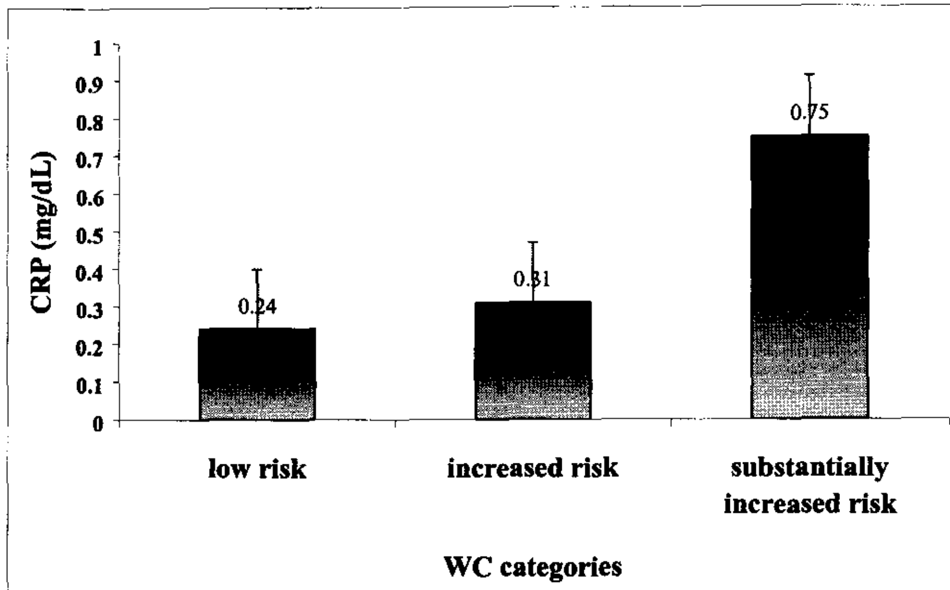

Figure 3. Mean ±SE for CRP concentrations in relation to WC categories

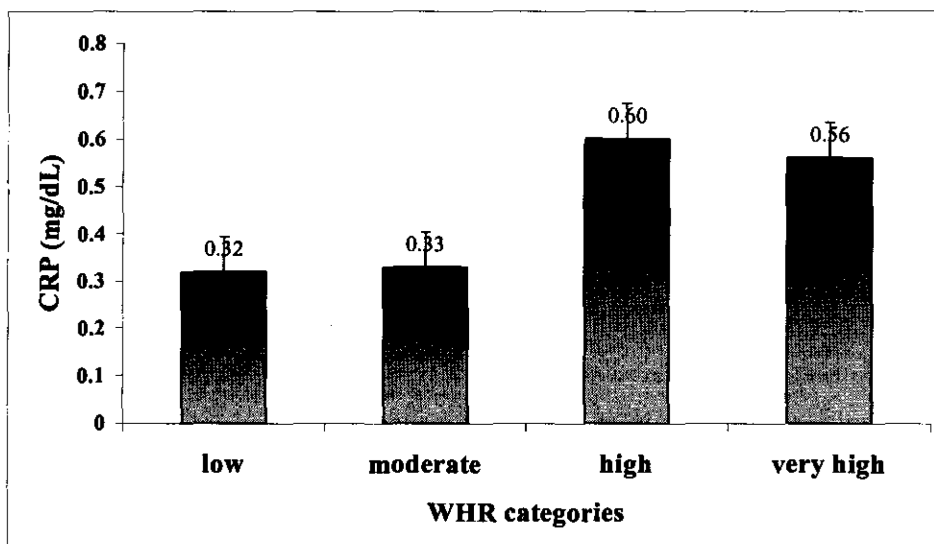

Figure 4. Mean ± SE for CRP concentrations in relation to WHR categories

Discussion

CRP is a major acute-phase protein (9) and falls among putative new markers of CHD risk (26). It has been associated with chronic systemic inflammation and has been suggested to predict CHD risk beyond traditional risk factors (10, 11).

It was found that significant relationships between plasma CRP concentrations and measures of adiposity among indices of body composition, such as BMI, total percentage body fat, WC and WHR exist. Similar results were found by Pannacciulli *et al.* (27) and Forouhi *et al.* (28) which reported positive and significant relationships of CRP with BMI, percentage body fat and WC. The reasons for associations between plasma CRP and indices of adiposity are not clear, but several mechanisms may link adipose tissue to elevated CRP concentrations. Concentrations of IL-6, which also induces the production of CRP (29), were found by Vgontzas and colleagues (30) to be elevated in obese individuals. Because the synthesis of CRP by the liver is largely regulated by IL-6 (31) and because approximately 30% of total circulation concentrations of IL-6 originate from adipose tissue in healthy subjects (13), these relationships are compatible with an adipose tissue origin of IL-6. Therefore, this biological feature of adipocytes may explain the statistically significant relationship between fat mass and CRP, observed in this study. Serum concentrations of Il-6 were not measured in the present study. Although the results support the hypothesis that IL-6 produced by the adipocytes increase CRP concentration, direct assessment of IL-6 concentration is needed in future studies.

Visser *et al.* (16) found that a higher BMI is associated with higher CRP concentrations that could not be explained by inflammatory disease or other factors or diseases known to increase CRP concentrations. In this study, it was also found that BMI was the strongest predictor of elevated concentrations of CRP and the correlation of BMI with CRP concentrations remained statistically significant even after adjusting for age, WC, percentage body fat and WHR. During this study, it was also found that the cut-off point for prediction of elevated CRP was at a BMI of 28 kg/m^2, which is lower than the cut-off point used to indicate obesity and, therefore, it may be hypothesized that the increased risk for CHD may well start before people are classified as obese. This study cannot determine whether obesity causes elevated CRP concentrations directly, or

whether higher CRP concentrations are a marker of other intermediate conditions such as atherosclerosis or insulin resistance which influence the underlying burden of inflammation among overweight and obese individuals. However, it is important to be aware that obese individuals are at a substantially increased risk of having an elevated CRP.

It is suggested that because of the powerful association with obesity, weight loss may be another method for down regulating an individual's inflammatory status (32). This could be expected, since body composition is mainly determined by the balance of diet and physical activity. In a group of obese postmenopausal women it was found that caloric restriction-induced weight loss markedly reduced plasma CRP (33) and Ford (34) found that physical activity is inversely associated with CRP concentrations, suggesting that physical activity may mitigate inflammation. These results add to mounting evidence that weight loss through diet and exercise may reduce inflammation, which is a critical process in the pathogenesis of cardiovascular disease. Therefore, it may be that the deleterious health effects of obesity associated with CHD are partly due to poor dietary habits and physical inactivity underlying the development and maintenance of obesity.

Future studies are needed to investigate further the association between CRP concentrations and weight loss through diet and excercise and to determine whether these associations between body composition and CRP concentrations are similar among Caucasion and African women in particular.

Acknowledgements

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4 The relationship of C-reactive protein to traditional cardiovascular risk factors in 19 to 60 year old black women

S. Slabbert, J.H. de Ridder, H.S. Kruger, C. Underhay and A. Schutte

Objective: To assess the relationship of C-reactive protein (CRP) to traditional cardiovascular risk factors in 19 to 60 year old black women.

Design: A cross-sectional study.

Measurements: Demographic questionnaires, anthropometric measurements, systolic and diastolic blood pressure, fasting glucose, blood lipids, fibrinogen and high sensitivity CRP (hsCRP).

Subjects: 102 urban African women

Results: All of the variables were significantly correlated with CRP at the level of $p \leq 0.05$ except for total cholesterol and low-density lipoprotein cholesterol. Body mass index (BMI), percentage body fat and fibrinogen levels were associated with log-normalized CRP (lnCRP) at a practically significant level with correlations ≥ 0.5. BMI and fibrinogen were also found to be independently associated with lnCRP with $p \leq 0.05$ during a forward stepwise multiple linear regression analysis. Women with six traditional risk factors had a three to five-fold increase in CRP concentrations compared to women with three or less risk factors.

Conclusions: CRP concentrations were associated with several cardiovascular risk factors which are involved in the promotion of an inflammatory state of atherosclerosis that may ultimately lead to coronary heart disease.

Keywords: C-reactive protein, cardiovascular disease, risk factors, fibrinogen, obesity

Introduction

Traditional risk factors of cardiovascular disease (CVD) include aging, hypertension, dyslipidemia, smoking, diabetes mellitus and obesity.[1] Fibrinogen and C-reactive protein (CRP) concentrations have also been proposed as markers of risk which should be screened for in an effort to better identify patients at high risk for cardiovascular events.[2] Additional markers or better markers of cardiovascular risk are still needed because evaluation of traditional risk factors, can insufficiently predict the incidence of CVD.[3] For instance, half of all myocardial infarctions occur in individuals with moderate to low risk based on assessment of lipid profile.[4,5]

With regard to the pathogenesis of CVD, the development of atherosclerosis is considered to be due, in part, to an inflammatory response.[6] Furthermore, inflammatory components are believed to contribute greatly to instability and rupture of atheromatous plaque that leads to atherothrombotic events.[7,8] Therefore, it may be hypothesized that inflammatory markers, such as high-sensitivity CRP (hsCRP) produced by hepatocytes in the liver,[9] may improve cardiovascular risk prediction adjunctive to the assessment of traditional risk factors. In support of this hypothesis, several large-scale epidemiological studies have reported a direct association between CRP concentrations and the risks of developing CVD.[10,11,12] Baseline levels of CRP have shown to predict the risk of future myocardial infarction, stroke and peripheral atherosclerosis among apparently healthy middle-aged men [13] and women [14] even after adjustment for other known cardiovascular risk factors. The relationship of CRP to CVD raises the question of how other risk factors relate to this marker. Few studies, however, have explored the interrelations between levels of CRP and other determinants of cardiovascular risk. In African women in particular, a study such as this has not yet been performed.

Subjects and methods

Subjects: The study is a cross-sectional design and formed part of the POWIRS project (Profiles of Obese Women suffering from the Insulin Resistance Syndrome), which was approved by the Ethics Committee of the North-West University (project number: 03M03). The study was conducted during March and April 2003. It was conducted in the North West province of South Africa and consisted of 102 African women

volunteers working at a governmental institution. Subjects were recruited by a dietician and the inclusion criteria were apparently healthy African women aged between 19 and 60 years. The dietician attempted to recruit only HIV negative subjects (according to their status as determined three months before the study), but the negative status of all subjects cannot be guaranteed. Pregnant and lactating women and those with oral temperatures above 37°C were excluded. Subjects were recruited according to their body mass index (BMI). Three groups of subjects were selected based on the BMI guidelines of the Report of a World Health Organization Consultation on Obesity:[15] i) normal range with BMI 18.5-24.9 kg/m²; ii) overweight with BMI 25-29.9 kg/m²; and iii) obese with BMI ≥ 30 kg/m². All subjects were fully informed about the objectives and procedures of the study prior to their inclusion and assistance was available to provide information in their home language. All subjects signed an informed consent form. Subjects identified with hypertension, diabetes or other abnormalities were referred to local clinics, hospitals or their physicians. All subjects received a short report regarding their health according to their individual measurements as assessed during the study.

During a period of three weeks, subjects were assessed at a Metabolic Unit Facility at the North-West University. Upon their arrival each participant received her own room, subject number and participant data sheet. Demographic and lifestyle questionnaires were completed. Questionnaires were issued during individual interviews conducted by the researchers and specially trained fieldworkers in the language of the subject's choice. The questionnaires included questions on marital status, language, education level, occupation, health history (also of close family members), years of smoking and drinking habits. All participants received an identical supper which excluded alcohol and caffeine at 19:00, went to sleep before 23:00 and fasted overnight.

Biochemical analysis: From 6:00 in the morning an urine sample was collected, followed by mass, stature and blood pressure measurements. Blood pressure readings were taken using a single headed stethoscope and a table-model mercury sphygmomanometer (Model ALPK2). Systolic blood pressure was based on the appearance of Korotkoff Phase I and diastolic blood pressure on Korotkoff Phase V. A fasting blood sample was taken and plasma glucose was measured with the hexokinase method (Inter assay CV-1.5%). The blood sampling was done by a registered nurse and

blood was taken from the *vena cephalica* using a sterile butterfly infusion set and syringes. For preparation of serum, blood was allowed to clot in glass tubes, centrifuged at 3500 rpm for 10 minutes (Universal 16™, Hettich) and transferred to 1.5 ml Eppendorff tubes. Plasma was collected in EDTA tubes and centrifuged at 3700 rpm for 10 to 15 minutes at 4°C (Universal 32R, Hettich). Citrated tubes were used to collect blood for the fibrinogen analyses. All serum and plasma samples were immediately stored at -84°C. CRP was measured using a high-sensitivity near infrared particle immunoassay by rate turbidimetry with a high sensitivity CRPH reagent (Beckman Coulter Inc., Nyon, Switzerland) in conjunction with an IMMAGE® Immunochemistry System (Cat. No. 474630) and Calibrator 5 Plus. Serum lipids were measured on a Vitros DT60 II Chemistry System with Vitros DT slides. Plasma fibrinogen was measured by a modified method of Clauss,[16] using the ACL-200 automated coagulation analyser and reagents from Instrumentation Laboratories (IL) Milan, Italy.

Anthropometric measurements: Body mass was measured by a Precision (A & D Company, Japan) electronic scale to the nearest 0.1 kg and stature with an Invicta stadiometer (IP 1465, UK) to the nearest 0.1 cm. All anthropometric measurements were taken by a qualified level II anthropometrist according to standardized methods as described by ISAK [17]. Girths were measured by a Lufkin (Cooper Tools, Apex, NC) unstretchable metal measuring tape to the nearest 0.1 cm and a Harpenden (British Indicators, UK) skinfold calliper with a constant pressure of 10 g/mm^2 was used for the measurements of the skinfolds to the nearest 0.2 mm.

Data analysis

All processed data were statistically analyzed by means of the software computer package StatSoft, Inc. (2003).[18] Data from one of the subjects were excluded from the data analysis because of the presence of infection, accompanied by an unusually high CRP concentration. Some of the traditional cardiovascular risk factors were defined as risks according to the following classifications: hypertension was defined as a systolic blood pressure of 140 mmHg or greater and/or a diastolic blood pressure of 90 mmHg or greater,[19] obesity was defined as a BMI ≥ 30 kg/m^2 [19] or a percentage body fat $\geq 25\%$ [20] calculated with the appropriate prediction equations based on seven skinfolds [21] or

waist circumference, height and weight.[22] Dyslipidemia was defined as triglycerides (TG) $\geq$ 1.5 mmol/L and or a low-density lipoprotein cholesterol (LDL-C)/high-density lipoprotein cholesterol (HDL-C) ratio > 3 and/or a total cholesterol (TC)/HDL-C ratio > 5,[23] fasting glucose $\geq$ 7 mmol/L[24] and fibrinogen $\geq$ 2.71 g/L.[25] Smoking was also classified as a risk factor.[26]

The distribution of CRP concentrations was positively skewed and hence CRP concentrations were log transformed for all analyses. Pearson correlation coefficients were used to analyze log-normalized CRP (lnCRP) concentrations as the dependent variable in relation to age, systolic blood pressure, diastolic blood pressure, BMI, percentage body fat, TC, LDL-C, TG, HDL-C, glucose, fibrinogen and years of smoking. A forward stepwise multiple linear regression analysis was used to determine the independent correlates of lnCRP concentrations. Subjects were divided into risk groups 1 to 6 according to the amount of risk factors present in their profile. The mean lnCRP was calculated for the covariates at their means and the 95 % confidence intervals were calculated for the lnCRP values. The intervals were then transformed back to CRP values.

Results

The mean (± standard deviation) and median value serum CRP of the subjects was 0.78 ± 1.29 mg/dL and 0.88 mg/dL respectively (Table 1). Figures 1 and 2 display the distribution of CRP and lnCRP among 101 apparently healthy African women. Table 2 shows the frequencies for each of the risk factors. Using the Pearson correlations analyis BMI, percentage body fat, fibrinogen and diastolic blood pressure levels were the only variables found to be associated with lnCRP at a practically significant level of $r \geq 0.5$ [27] and at a statistically significant level all of the variables correlated with lnCRP with $p < 0.05$ except for TC and LDL-C (Table 3). The results of the forward stepwise multiple linear regression analysis is shown in Table 4. BMI and fibrinogen were independently associated with lnCRP with $p \leq 0.05$ and together with HDL-C, systolic blood pressure; LDL-C and fasting glucose respectively explained 46% of the variance in lnCRP. The means of lnCRP and CRP were calculated for each of the risk groups and can be seen in Tables 5 and 6 respectively, together with the standard error (Std. E.) and 95% confidence intervals. The subjects in which all 6 of the risk factors presented

were found to have a 2 fold increase in plasma concentrations of CRP compared with the subjects with 4 risk factors and a 3 to 5 fold increase in plasma concentrations of CRP compared with the subjects with 3 or less risk factors.

Table 1: Descriptive statistics of CRP and lnCRP of a 101 apparently healthy African women

	N	Mean	Median	Minimum	Maximum	SD
lnCRP	101	0.78	0.88	-1.61	4.10	1.29
CRP	101	4.59	2.40	0.20	60.20	7.20

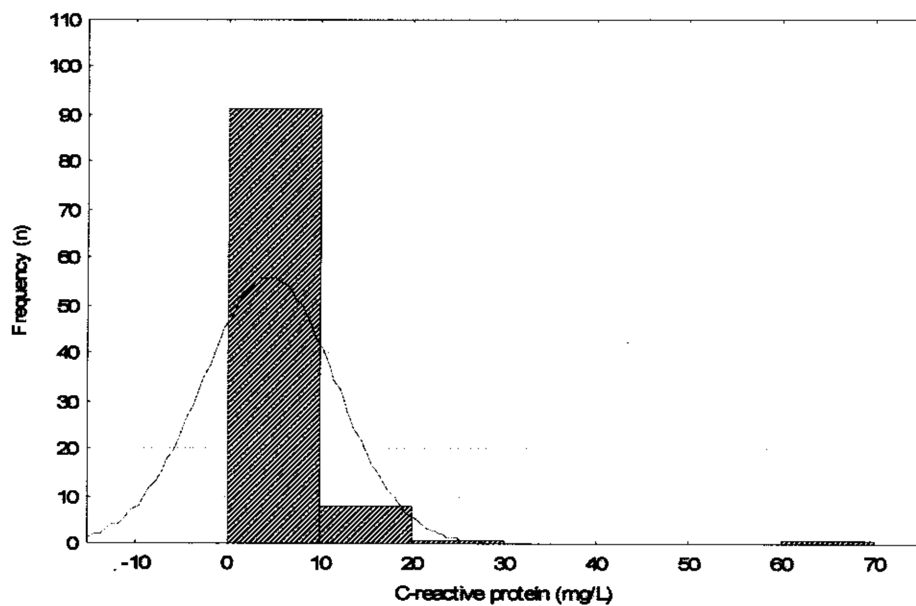

Figure 1: Distribution of CRP concentrations among a 101 apparently healthy African women

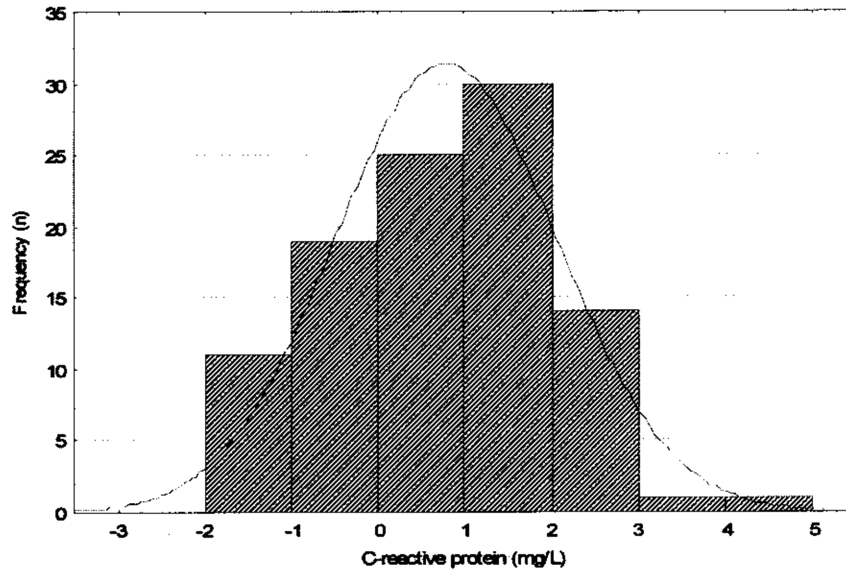

Figure 2: Distribution of log-normalized CRP concentrations among a 101 apparently healthy African women

Table 2: Frequency table for risk factors of a 101 apparently healthy African women

Risk factor	N	%
Hypertension: SBP ≥ 140 and/or DBP ≥ 90 mmHg	24	23.5
Obesity: BMI ≥ 30 kg/m² and/or % BF ≥ 25%	67	65.7
Smoking	7	6.9
Fasting blood glucose: ≥ 7 mmol/L	8	7.8
Dyslipidemia: TG ≥ 1.5 mmol/L and/or LDL-C/HDL-C > 3 and/or TC/HDL-C > 5	27	26.5
Fibrinogen: ≥ 2.71 g/L	95	93.1

* SBP (systolic blood pressure); DBP (diastolic blood pressure); BMI (body mass index); BF (body fat); TG (triglycerides); LDL-C (low-density lipoprotein cholesterol); HDL-C (high-density lipoprotein cholesterol); TC (total cholesterol)

Table 3: Pearson correlation coefficients between selected variables and hsCRP among a 101 apparently healthy African women

Variables	r	p
Age	0.22	p < 0.05
Body mass index	0.57**	p < 0.05
Fat percentage	0.55**	p < 0.05
Systolic blood pressure	0.31*	p < 0.05
Diastolic blood pressure	0.36*	p < 0.05
Total cholesterol	0.00	
Low-density lipoprotein cholesterol	0.06	
High-density lipoprotein cholesterol	-0.21	p < 0.05
Triglycerides	0.25	p < 0.05
Fasting glucose	0.31*	p < 0.05
Fibrinogen	0.47*	p < 0.05

** Practically significant ($r \geq 0.5$)
* Practically significant ($r \geq 0.3$)

Table 4: Forward stepwise multiple linear regression summary for lnCRP as the dependent variable among a 101 apparently healthy African women

Regression step	Independent variable	Beta	Std.Err. of Beta	t(92)	p-level
1	Body mass index	0.365	0.092	3.960	0.0002*
2	Fibrinogen	0.338	0.082	4.145	0.0001*
3	High-density lipoprotein cholesterol	-0.147	0.078	-1.879	0.0635
4	Systolic blood pressure	0.126	0.086	1.470	0.1450
5	Low-density lipoprotein cholesterol	-0.111	0.081	-1.372	0.1733
6	Fasting glucose	0.091	0.086	1.056	0.2938

* Statistically significant ($p \leq 0.05$)
** R = 0.67996844, R^2 = 0.46235708; adjusted R^2 = 0.42729341
≠ F (6, 92) = 13.186; p <0.00000; Std. Error of estimate: 0.97626

Table 5: lnCRP means for each of the risk groups in a 101 apparently healthy African women

Number of risk factors	N	Mean	Standard error	95% Confidence interval
1	6	0.294	0.506	-0.711 ; 1.299
2	26	0.125	0.248	-0.367 ; 0.616
3	34	0.961	0.210	0.545 ; 1.378
4	29	1.101	0.228	0.648 ; 1.555
5	3	1.223	0.737	-0.240 ; 2.686
6	3	1.879	0.718	0.454 ; 3.304

Table 6: CRP means for each of the risk groups in a 101 apparently healthy African women

Number of risk factors	N	Mean	Standard error	95% Confidence interval
1	6	1.342	1.659	0.491 ; 3.667
2	26	1.133	1.281	0.693 ; 1.852
3	34	2.616	1.233	1.725 ; 3.965
4	29	3.008	1.256	1.912 ; 4.733
5	3	3.340	2.090	0.786 ; 14.673
6	3	6.547	2.050	1.574 ; 27.231

Discussion

A strong positive correlation of CRP with obesity and fibrinogen levels was observed during the study, indicating a practical significance in the correlation between these variables. It is reported [28] that CRP concentrations are elevated in overweight adults, which raises broader questions about low-grade inflammation and coronary heart disease (CHD), suggesting that plasma CRP might at least partly mediate the effects of obesity on the development of CHD. Obesity is associated with a predisposition to hypertension, hyperlipidemia and diabetes mellitus. However, judging from the values of correlation coefficients, even though they were statistically significant, hsCRP was more closely correlated with BMI and percentage body fat than with blood pressure,

plasma glucose or serum lipids. Adipose tissue is known to secrete interleukin-6 (IL-6), the primary stimulant of CRP synthesis.[29] This suggests the existence of a direct mechanism by which obesity increases CRP independently of the effects of insulin resistance.[1] Although hepatic production of CRP is increased with acute infection and trauma, circulating level of hsCRP is stable within a person over long periods and reflects a chronic inflammatory process of the cardiovascular system.[30]

It has also been suggested that the association of various persistent infections with CHD may be mediated through increased fibrinogen. Recently, in a subset of the Physicians' Health Study, fibrinogen was found to be an independent risk factor for myocardial infarction [31] and in the Caerphilly and Speedwell studies,[32] fibrinogen was found to be a long-term predictor of coronary death and fatal and nonfatal myocardial infarction. An increased concentration of C-reactive protein in patients with angina is reported [33] and it is suggested that such an increase may represent an inflammation related to coronary atherosclerosis in which fibrinogen may act as an acute-phase protein. An elevation of both C-reactive protein and fibrinogen levels was a strong predictor of myocardial infarction and sudden death in patients with angina pectoris.[34] The CHD risk associated with these increases in acute-phase reactants seems to be linked to CRP.

Statistically significant relationships of CRP concentrations with age, smoking, HDL-cholesterol, systolic blood pressure, diastolic blood pressure, TG and diabetes mellitus were found. These findings indicate that the clustering of these risk factors may well increase CRP concentrations, resulting in chronic systemic inflammation which in turn, may cause the progression of atherosclerosis. Although statistically significant relationships were also found between CRP concentrations with TC and LDL-cholesterol by Tamakoshi and co-workers,[35] no such relationships were observed in this study. These findings could possibly, in part, be attributed to the more favourable lipid profile of black men and women.[36]

In a review of risk prediction [37] it was found that for men and women without coronary vascular disease, a CRP in the highest quartile gives an individual patient significant additional risk of developing cardiac diseases and that traditional cardiovascular risk factors, though they act independently of CRP, often give more than additive risks when combined with CRP. Having an increased total cholesterol and TC/HDL ratio carries a

worse prognosis for those with high CRP in men and women and those with the highest values of both have a relative risk of cardiac events of almost nine.[38] Assuming that hsCRP reflects future risk of CVD, intervention which reduces CRP may be effective in preventing the occurrence of cardiovascular events. The results of some studies [39, 40] suggest that correction of overweight may be effective in reducing plasma hsCRP. It has also been reported that moderate exercise reduces inflammation markers.[41, 42] Taken together, these physical activity and dietary approaches to correct obesity may be promising in inhibiting cardiovascular inflammation and future risk of developing CVD. Further studies in which therapeutic intervention adresses the problem of inactivity and poor dietary habits are needed to determine the role played by overweight and obesity in the mechanism of chronic systemic inflammation and CHD.

Conclusion

In order to prevent the incidence of cardiovascular events effectively, it is important to weigh the influence of each risk factor on the cardiovascular system. In this context, it must be taken into consideration that various cardiovascular factors are not independent of one another, but have direct relations. Effective prevention of CVD should be started with unravelling the network of multiple risk factors. In this respect, the relation of inflammatory markers to other risk factors is still not well understood. CRP concentrations could be related to the pathogenesis of atherosclerosis via the effects of inflammation on traditional risk factors, or the raised CRP concentrations may result from inflammation in the arterial wall associated with the atherosclerosis itself. Future studies are needed in order to provide clarity and a better understanding regarding these issues.

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5 SUMMARY, CONCLUSIONS AND RECOMMENDATIONS

5.1 SUMMARY
5.2 CONCLUSIONS
5.3 RECOMMENDATIONS

5.1 SUMMARY

The aim of this study was firstly to determine if there is a relationship between C-reactive protein (CRP) concentrations and body composition in 19 to 60 year old black women by means of body mass index (BMI), percentage body fat, waist circumference and waist-hip-ratio (WHR). The second aim was to determine the relationship of CRP concentrations to traditional cardiovascular risk factors in the study sample of 19 to 60 year old black women. Chapter 1 provided a brief introduction and outline of the problem statement that underlies the research questions, aims and hypotheses that form the basis of this study.

This dissertation is submitted in article format, as approved by the Senate of the North-West University (Potchefstroom Campus) and, therefore, includes one review article (Chapter 2) and two research articles (in Chapter 3 and 4 respectively) which will be presented to appropriate and accredited journals. Chapter 2 is a literature review, in the form of a review article on obesity as an inflammatory condition by Slabbert, S., de Ridder, J.H., Kruger, H.S. and Underhay, C. and will be presented for publication to Health SA Gesondheid Interdisciplinary Research Journal. The chapter firstly introduced the reader to the literature format of this article by means of an introduction. The introduction is followed by a section comprising of obesity as a public health problem together with its associated co-morbidities in different ethnic groups, focusing on black women in particular. This is followed by the threats posed by abdominal obesity and the possible link it may have to markers of inflammation like CRP and

interleukin-6, which in turn seems to be connected to coronary heart disease (CHD) and its associated risk factors. The chapter was concluded by focusing on weight-loss and physical activity as possible preventive and therapeutic measures which may be used to reduce and remedy the occurrence of elevated CRP concentrations and possibly lowering CHD risk.

The first research article entitled "The association between C-reactive protein concentrations and body composition in 19 to 60 year old black women" by Slabbert, S., de Ridder, J.H., Kruger, H.S., Underhay, C. and van Lieshout, M. will be presented for publication to Obesity Research. This article is included in Chapter 3. The main purpose of this study was to determine whether significant associations exist between C-reactive protein concentrations and body composition in 19 to 60 year old black women by means of various body composition variables.

The second article entitled "The relationship of C-reactive protein to traditional cardiovascular risk factors in 19 to 60 year old black women", by Slabbert, S., de Ridder, J.H., Kruger, H.S., Underhay, C. and Schutte, A. will be presented for publication to the South African Journal of Clinical Nutrition. This article is included in Chapter 4. The aim of this study was to determine the relationship of C-reactive protein to traditional cardiovascular risk factors in 19 to 60 year old black women..

All of the above mentioned articles have been written according to the guidelines of the specific journals and consist of an introduction, problem statement and the resulting research questions and purposes of the study. The research methods (subjects, measurement procedures and data analysis) were described, after which the results were presented and discussed. Each article concluded with research conclusions and implications.

5.2 CONCLUSIONS

The conclusions that are drawn from this research are presented in accordance with the set hypotheses (Chapter 1).

5.2.1 Hypothesis 1: *CRP concentrations show a relationship with body composition (BMI, percentage body fat, waist circumference and WHR) in 19 to 60 year old black women.*

Hypothesis 1 is accepted based on the research findings that BMI, percentage body fat, waist circumference and WHR were all significantly correlated with CRP throughout the anthropometric spectrum. BMI was found to be the strongest predictor of elevated CRP concentrations among the study population.

5.2.2 Hypothesis 2: *Certain traditional cardiovascular risk factors can be used as indicators of CRP concentrations in 19 to 60 year old black women.*

Hypothesis 2 is accepted based on the research findings that statistically significant correlations were found between CRP and all, except two of the selected variables, measured. BMI, percentage body fat and fibrinogen levels were associated with log-normalized CRP (lnCRP) at a practically significant level and BMI and fibrinogen were also found to be independently associated with lnCRP during a forward stepwise multiple linear regression analysis. This study also showed that within the population sample, women who presented with six of the traditional risk factors had a three to five-fold increase in CRP concentrations as compared to women with three or less risk factors.

5.3 RECOMMENDATIONS

The results from this study emphasise the importance of further research regarding obesity as a state of chronic systemic inflammation in black women, as there is clearly a shortage of literature that focuses on this research theme and within this ethnic group. With the race differences in mortality for CHD being greater among black than white women, it would be of interest to determine whether these differences can be ascribed to a genetic predisposition, or whether the high prevalence of obesity among these women is the key factor linking raised CRP concentrations to CHD. Another plausible explanation could be the finding that the presence of multiple risk factors among women in this study population is associated with an increased risk for elevated CRP

concentrations. Further research is needed, however, to support these findings and determine a possible mechanism through which the association between obesity, CRP and CHD can be explained.

The findings of this study give support to the possibility of weight-loss, by means of healthy dietary habits and physical activity, being a key promoter in reducing CRP concentrations. The need for more research to investigate the influence of a weight-loss intervention programme can, therefore, not be over emphasised, since it has already been proven to be a key factor in the prevention and treatment of obesity and CHD.

Certain shortcomings regarding this study can, however, be indicated:

- A cross-sectional design was used with the subjects being recruited according to their BMI classification. A longitudinal design where the subjects are randomly chosen to be included in the study would perhaps have been a more suitable approach. A longitudinal follow-up of the subjects and changes in CRP concentration with change in body composition would provide stronger evidence for a causal association between CRP and body composition variables.

- The study consisted of a small number of subjects in each of the BMI categories. Outliers, could, therefore, have had a much greater influence on the total group results than would have been the case with a larger population sample.

- The study's population sample consisted of a 101 women who were all recruited from the same institution and province, therefore, the results cannot be generalized to the larger population of black women, as certain discrepancies may occur.

APPENDICES

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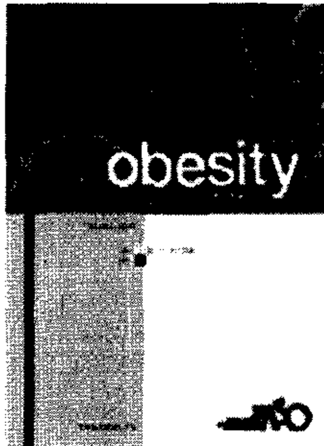
OBESITY RESEARCH



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Instructions to Authors

Instructions for Authors

Obesity Research publishes only material that has not been previously printed and is not under consideration for publication elsewhere, with the exception of an abstract that is less than 400 words in length. The North American Association for the Study of Obesity (NAASO) holds the copyright on all material appearing in Obesity Research.

Original Manuscripts report clinical and laboratory investigations, findings, and developments from both human and animal studies in all areas relevant to the science of obesity. Manuscripts should be between 1,500 and 5,000 words (i.e., 6-20 typewritten double-spaced pages), including tables, figure legends, and references necessary to support the data and their interpretation. The following features are essential: hypothesis testing, suitable controls, appropriate statistical methods, clear reporting of results, and conclusions supported by the results. Papers will be judged on their soundness, uniqueness and importance.

Short Communications are short critical articles on topics of general interest in obesity care. Short Communications should not attempt an exhaustive literature review, but should analyze a few carefully selected findings. The paper should be limited to 1200-1500 words in length including references and any graphics.

Perspective and Review topics should be presented to the editor-in-chief prior to submission to establish that the proposed subject falls within the guidelines of the journal and that a review in that field is not currently under preparation by another

author. Perspectives and Reviews should be a maximum of 7000 words including references.

Brief Genetic Analyses report genetic studies and gene profiling analyses relevant to obesity and related disorders that can be presented in a concise format. Suitable for presentation in this format are studies identifying new genes and their localization, observations on the molecular nature of allelic variants and their correlation with relevant clinical or physiological phenotypes, linkage or association studies, and gene or protein expression profiling using micro arrays or related approaches. Relevant DNA sequences must be deposited in one of the public-domain genetic databases and referenced in the published report. Manuscripts may be submitted before, but will be accepted for publication only after, formal sequence submission. Additional data, such as detailed marker analysis or tables of gene or protein expression data should be prepared in the form of an appendix that will be made available on the journal's Web site, along with the full text of the printed report. Large primary datasets, as may derive from micro array experiments, should be submitted in spreadsheet format whenever possible.

Brief Genetic Analyses should be written in the following format: 1) an abstract of no more than 200 words, containing essential introductory information and a summary of the results; 2) the main text of about 1200 words (excluding methods, legends, and references) and up to five tables or figures; 3) a brief methods section; and 4) no more than 20 references.

Brief Epidemiologic Reports are studies on the prevalence of overweight or obesity and related risk factors for a specific country or region that can be presented in a concise format. Suitable for presentation are studies that convey the descriptive epidemiology of obesity and associated demographic and lifestyle factors from national or regional surveys. In addition to any other definitions they elect to apply, authors are required to report prevalence using the WHO obesity classification for adults (WHO, 1995) and IOTF reference for children (Cole, 2000). To aid in future comparisons, prevalence by sex and by age group should be reported as follows. Children: 2-5 y, 6-11 y, 12-17 y, 18-20 y; Adults: 20-29, 30-39, 40-49, etc. where the data are adequate. Where sample sizes are small, collapsed categories based on the aforementioned are requested.

Brief Epidemiologic Reports should be written in the following format: 1) an abstract of no more than 200 words, containing essential descriptive information (population, place, time period) and a summary of the results; 2) a brief methods section that specifies the sampling design, basic survey methodology, and response rate; 3) the main text of about 1200 words (excluding methods, tables/figures, and references) and a total of 2 tables or figures; 4) no more than 20 references. To aid in future comparisons, prevalence by sex and by age group should be reported as follows. Children: 2-5 y, 6-11 y, 12-17 y, 18-20 y; Adults: 20-29, 30-39, 40-49, etc. where the data are adequate. Where sample sizes are small, collapsed categories based on the aforementioned are requested.

Letters to the editor are limited to opinions on topics published in the journal and should not exceed 500 words.

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Med 336:309-315, 1997) that authorship implies substantial contributions to conception and design or analysis and interpretation of data and drafting of the article or critical revision for important intellectual content.
All authors must disclose any duality or conflict of interest. All human investigation must be conducted according to the principles expressed in the "Declaration of Helsinki". All studies involving animals must state that guidelines for the use and care of laboratory animals of the author's institution or the National Research Council or any national law were followed.

Manuscript Format and Style Entire manuscript, including tables, figures, and figure legends, should be double spaced (including reference, tables, and figure legends) on one side of 8 ½ x 11" (21.6 x 27.9 cm) on non-erasable, white bond paper. Provide margins of at least one inch at top, bottom and both sides of each page. Arrange manuscript in the following order: title page, abstract, key words, introduction, research methods and procedures, results, discussion, acknowledgments, references, tables, and figure legends. Number pages consecutively, beginning with the title page. Do not send diskettes with initial submission.

Title Page should be brief (maximum of 95 characters including spaces) and include a short running title (less than 40 characters); first name, middle initial, last name, without degrees; institutional affiliations (in English) of each author during the study being reported; name, current address; telephone and fax number, and E-mail address of corresponding author.

Abstract should not exceed 250 words. It must be self-contained and clear without reference to the text and be written for a general journal readership. The abstract must be in a structured format with the following subheadings: Objective, purpose or hypothesis of study; Research Methods and Procedures, basic design, setting, number of participants and selection criteria, treatment or intervention and methods of assessment; Results, significant data found; Discussion; validity and clinical applicability.

Key Words Up to five index terms which are words not used in the title, but which are descriptive of the content and areas of interest in the manuscript. (The word obesity is not permitted as a key word.)

Introduction should state the rationale and background for the experiment.

Text Terminology and Style Text should be written in clear concise English and follow the recommendations for scientific writing found in Scientific Style and Format, the Council of Biology Editors (CBE) style manual (6th ed., 1994 Bethesda, MD, Council of Biology Editors). The authors are responsible for all statements made in their article or editorials, including any editing changes made by staff.

Acknowledgments should contain brief statements of assistance or support.

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style. The author's last name is followed by initials with no periods, then list the complete title of the article (chapter), then the journal (book), followed by the year, semicolon, volume, colon, and inclusive pages. References should be listed according to the following examples:

- Hunt SC, Daines MM, Adams TD, Hath EM, Williams RR. Pregnancy weight retention in morbid obesity. Obes Res. 1995;3:121-30.

- The National Task Force on Prevention and Treatment of Obesity. Towards preventions of obesity: research directions. Obes Res. 1994;2:571-84.

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Names and initials of all authors should be given unless there are more than six, in which case the first three names should be given followed by et al. First and last page numbers should be given.

Journal references should appear thus:
1. Price NC. Importance of asking about glaucoma. BMJ 1983; 286: 349-350.

Book references should be set out as follows:
1. Jeffcoate N. Principles of Gynaecology. 4th ed. London: Butterworth, 1975: 96-101.
2. Weinstein L, Swartz MN. Pathogenic properties of invading micro organisms. In: Sodeman WA jun, Sodeman WA, eds. Pathologic Physiology: Mechanisms of Disease. Philadelphia: WB Saunders, 1974: 457-472.

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THE POWIRS PROJECT

Dear Participant,

Welcome to the Metabolic Unit of the Potchefstroom University!

Thank you for participating in the POWIRS project. With your help it will be possible to create culturally sensitive programs to prevent health problems like obesity, diabetes, hypertension and stroke in the black community of South Africa.

WHAT IS THE POWIRS PROJECT?

POWIRS stands for the ***P***rofiles of ***O***bese ***W***omen with the ***I***nsulin ***R***esistance ***S***yndrome.

The aim of this project is to determine risk factors for the development of the insulin resistance syndrome, a condition which develops in obese people. The insulin resistance syndrome is a condition characterized by high blood pressure, high blood sugar levels and high blood fat levels. Diabetes, heart disease and stroke develop frequently in people suffering from the insulin resistance syndrome.

WHY IS THE POWIRS PROJECT IMPORTANT?

Obesity is a common problem in black women, especially in South Africa, where about 50% of these women are obese. Since obesity leads to the insulin resistance syndrome and eventually to diseases like diabetes, heart disease and stroke, we are concerned about the effect of obesity on the health of black women in South Africa.

In the POWIRS project we want to determine the factors leading to obesity and the insulin resistance syndrome in black South African women. The results of the project will enable The Department of Health and Developmental Social Welfare to develop culturally sensitive programs to prevent the development of obesity and the insulin resistance syndrome in black women.

WHAT WILL BE MEASURED IN THE POWIRS PROJECT?

Each person who participates in the project will complete a number of questionnaires to obtain information on:

Demographic background, eg income, education, area of living
Lifestyle habits, eg, physical activity, smoking, alcohol consumption
Medical background
Eating and drinking habits
Knowledge, attitude and behaviour about health, beauty and weight
Weight history
Mental health (psychological questionnaires)

A physical examination will be done to check for signs of malnutrition and to measure:

Weight, height, waist and hip circumferences and skin fold thickness
Temperature (orally)
Blood pressure

Blood samples will be taken to measure indicators of health, nutrition and disease, eg blood sugar, cholesterol, blood fats.

The results of all these measurements will give an indication of the health and nutrition status of the individual as well as his risks for diseases like stroke and sugar diabetes.

HOW COULD YOU BENEFIT FROM THE PROJECT?

A large number of indicators of nutrition and health will be measured, informing you about your health status and risk factors for stroke, sugar diabetes and overweight. We will give feedback on the results to you. If a problem is discovered, nutritional and / or social counselling will be given or you will be referred to a medical doctor if necessary, for treatment and prevention of development of a disease.
Each participant will receive an amount of R100.00.

HOW WILL YOU BE INVOLVED?

On arrival at the Metabolic Unit, you will receive a number and card and we will show you your room. The procedures of the project will be explained to you and you will

sign a consent form that you are willing to participate voluntarily in the project. Please take note that you may quit from the project any time you need to. All information collected from you as well as the results of the measurements will be kept strictly confidential. Please feel free to ask any questions at any time of the project.

The program for the evening will be as follows:
Your skin fold measurements will be taken and you will complete psychological and demographic questionnaires. At 19:00 supper will be served. ***Please do not eat anything else after supper. Only pure water may be taken.*** The reason for this is that you must be fasted for the blood tests to be done in the morning. The program continues the following morning. Please sleep before 23:00, because you will be wakened early.

Program for tomorrow morning:
Lady number 1 will be wakened at 6:00. She will give a urine sample. Then she will be weighed and her height, waist and hip circumferences and blood pressure measured. After this she may go back to her bed, and then the next lady will be wakened for the same procedures. Back in bed, the blood samples will be taken by a registered sister. Blood samples are taken with a very thin needle, so you will hardly feel it. This needle will be kept in your arm for two hours and will be removed after the last blood sample is being taken. This will not be painful; you won't feel the needle while it is in your arm.

Four blood samples will be taken, *one* sample every 30 minutes. It will be finished after *two hours*. After the first blood sample has been taken, you will receive a sugar drink. The other *three* blood samples to be taken will test how your body reacts to sugar. The sugar drink will also replace fluid lost by the body because of the blood taken. The amount of blood taken will be about 100 ml, which is far less than the amount usually given at blood donating, where they take 500 ml. Your body will immediately start to make new blood to replenish the blood taken out. We shall help your body to do so by giving you breakfast after the last blood sample has been taken.
During the 2 hours of the sugar test, you will complete questionnaires, asking you about your demographic background, lifestyle, eating habits, attitudes and knowledge about health, beauty and weight as well as questions on your weight history. The research team members will assist you in completing these questionnaires. After breakfast, you

will complete another psychological questionnaire. Thereafter lunch will be served for the hungry ones, after which you will be taken back home.
Thank you very much for your participation!

We hope you will enjoy the time with us!

THE RESEARCH TEAM

PROGRAM FOR THE POWIRS PROJECT

Program for the evening:

1. Explanation of procedures and signing of consent forms
2. Measurement of skinfolds
3. Completion of psychological and demographic questionnaires
4. Supper at 19:00
5. ***NOTHING MAY BE EATEN OR DRUNK AFTER SUPPER. ONLY PURE WATER IS ALLOWED***
6. Sleep before 23:00

Program for the next morning:

1. Lady number 1 wakened at 6:00
2. Urine sample, weighing, measurement of height, waist and hip circumferences and blood pressure.
   Lady 2 wakened for the same procedures. Then lady 3 and so on.
3. Back to bed
4. Blood sample taken
5. Sugar drink taken
6. Three more blood samples taken, every 30 minutes.
7. In between completion of questionnaires on physical activity, eating habits, attitude, knowledge on health, beauty and weight and weight history will be done.
8. Breakfast
9. Completion of psychological questionnaires
10. Lunch
11. Departure

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POWIRS PROJECT

RECRUITMENT AND INFORMED CONSENT FORM

Title of the project: The profiles of obese women suffering from the insulin resistance syndrome

Ethics Committee no: 03M03

Name: ______________________________ **Subject number:** _______

Adress: ____

Tel no: ____

Age: ______________________________

Are you pregnant ?___________________

Are you breastfeeding ? ______________

Do you suffer from diabetes ? hypertension ? other disease ?

____

INFORMED CONSENT

I, the undersigned ___________________
(full names in print), have read the details of the project or have listened to the oral explanation thereof, and declare that I understand it. I have had the opportunity to discuss relevant aspects with the researcher and declare that I voluntarily participate in the project. I hereby give consent to participate in the project.

____
Signature of participant

Witnesses:

1. ________________________ 2.________________________

Signed at ___________________ on ____________________

Demographic and lifestyle questionnaire

All information given in this questionnaire is confidential

1. Subject number			
2. Date			
3. Age:			
4. Age	20 – 24	(1)	
	25 – 29	(2)	
	30 – 34	(3)	
	35 – 39	(4)	
	40 – 44	(5)	
	45 +	(6)	

5. First language (please mark the correct block with a X)	Tswana	(1)
	Afrikaans	(2)
	English	(3)
	Sotho	(4)
	Xhosa	(5)
	Zulu	(6)
	Other	(7)
	Specify other (8)	

6. Second language	Tswana	(1)
	Afrikaans	(2)
	English	(3)
	Sotho	(4)
	Xhosa	(5)
	Zulu	(6)

	Other	(7)
	Specify other (8)	
7. What is your marital status?	Never married	(1)
	Married	(2)
	Divorced / separated	(3)
	Widowed	(4)
	Cohabiting	(5)
8. What is your highest qualification ?	Matric	(1)
	Diploma	(2)
	Degree	(3)
	Postdegree	(4)
9. What is your occupation ?		

10. Do you work: shifts, eg night shifts								(1)
office hours (± 8 hours per day)								(2)
mornings / part time (± 5 hours per day)								(3)
11. Are you pregnant ?		No (1)						Yes (2)
12. Are you breastfeeding ?		No (1)						Yes (2)
13. When did you have your last menstrual period (please give the date of the first day of your last period):		D	D	M	M	Y	Y	

Do you suffer from any of the following ?		
14. Hypertension	No (1)	Yes (2)
15. Diabetes	No (1)	Yes (2)
16. Stroke	No (1)	Yes (2)
17. Heart disease	No (1)	Yes (2)
18. Gout	No (1)	Yes (2)
19. Arthritis	No (1)	Yes (2)

20. Malaria	No (1)	Yes (2)
21. TB	No (1)	Yes (2)
22. Sexually transmitted disease	No (1)	Yes (2)
23. Head injury (previously)	No (1)	Yes (2)

Does anyone in your family suffer from:

24. Hypertension	No (1)	Yes (2)	Uncertain (3)
25. Diabetes	No (1)	Yes (2)	Uncertain (3)
26. Stroke	No (1)	Yes (2)	Uncertain (3)
27. Heart disease	No (1)	Yes (2)	Uncertain (3)
28. Gout	No (1)	Yes (2)	Uncertain (3)
29. Arthritis	No (1)	Yes (2)	Uncertain (3)
30. Malaria	No (1)	Yes (2)	Uncertain (3)
31. TB	No (1)	Yes (2)	Uncertain (3)
32. Sexually transmitted disease	No (1)	Yes (2)	Uncertain (3)

33. Do you take any medication ?	No (1)	Yes (2)

34. If yes, please list medication:

____
____
____
____

35. Do you take birth control tablets ?	No (1)	Yes (2)
36. Do you get a birth control injection ?	No (1)	Yes (2)
37. Have you ever been on anti-depressants ?	No (1)	Yes (2)
38. Have you ever been hospitalized for any psychiatric illness (eg depression, anxiety, panic attacks) ?	No (1)	Yes (2)

39. How many pregnancies did you have ? ____________		
40. Are your parents still alive ?		
Mother	No (1)	Yes (2)
Father	No (1)	Yes (2)
41. If your mother has died, what were the cause of death ? ____________________		
42. If your father has died, what were the cause of death ? ____________________		
43. Do you have other sources of income other than your job?	No (1)	Yes (2)
44. If yes, please name the source of income: ____________________		
45. Give an indication of your income per month (mark the correct block with a X):		
R 1 000 – R 2 0000		(1)
R 2 000 – R 3 000		(2)
R 3 000 – R 4 000		(3)
R 4 000 – R 5 000		(4)
> R 5 000		(5)
46. Does your work offer any benefits ?	No (1)	Yes (2)
47. If yes, please mark the benefits:		
Pension		(1)
Medical aid		(2)
Housing		(3)
Car		(4)
Allowance for car / housing / medical aid		(5)

Food (please list the foods)		(6)
48. Do you own property ?	No (1)	Yes (2)
49. If yes, what type of property, eg house, flat ? ______________________		
50. How many people live in your house (give the number of people):		Numb er
Children under 11 years		(1)
Children under 18 years		(2)
Adults (children older than 18 years,grand parents, brothers, sisters, wives, husbands, etc)		(3)
51. Do they contribute to your household costs?	No (1)	Yes (2)
52. In what way: food / money	Food (1)	Mon ey (2)
53. If money, how much money? ______________________		
54. Please name the members of your household:		

Member	*Age*	*Education*	*Present job*
(1)	(2)	(3)	(4)
(5)	(6)	(7)	(8)
(9)	(10)	(11)	(12)
(13)	(14)	(15)	(16)
(17)	(18)	(19)	(20)
(21)	(22)	(23)	(24)
(25)	(26)	(27)	(28)
(29)	(30)	(31)	(32)
(33)	(34)	(35)	(36)

55. In what type of area do you live (please tick the appropriate block with a X):

Township	(1)
Squatter camp	(2)
Traditional White area	(3)
Traditional Indian area	(4)
Other	(5)
Specify other (6)	
56. How long have you been living here (years)? ________________	
57. Where have you been living before:	
Township	(1)
Squatter camp	(2)
Traditional white area	(3)
Traditional Indian area	(4)
Other	(5)
Specify (6)	other
58. What type of house do you live in:	
Brick house	(1)
Informal housing (eg. shack / mokuku)	(2)
Other	(3)
Specify other (4)	

59. Do your stay away from your family when you work and go home only on weekends or holidays ?	No (1)	Yes (2)
60. If yes, where do you stay during when you work ? ____________________		
61. Do you smoke ?	No (1)	Yes (2)

If yes, mark what you smoke and indicate the amount per day / week	Type of smok ing	Amount per day / week
62. Cigarettes	(1)	(2)
63. Cigars	(1)	(2)
64. Tobacco (zoll)	(1)	(2)
65. Snuff	(1)	(2)
66. Pipe	(1)	(2)
67. Other, please specify: ____________________	(1)	(2)
68. For how long are you smoking (years) ? ______________		

69. If you don't smoke at the moment, have you been smoking regularly before ?	No (1)	Yes (2)
70. If yes, for how long have you been smoking before ? _______________		
71. Do you use alcohol ?	No (1)	Yes (2)

72. If yes, mark the type of alcohol you use:	
Traditional beer (homemade)	(1)
Tlokwe	(2)
Beer (commercial)	(3)
Spirits	(4)
Wine	(5)
Liqueur	(6)

Try to tell the amount of alcohol you use per day / per week:		Per day	Per week
73. Traditional beer (home made)	glass	(1)	(2)
74. Tlokwe	box	(1)	(2)
75. Beer (commercial)	quart / tin / dumpy	(1)	(2)
76. Spirits	tot / bottle	(1)	(2)
77. Wine	glass / bottle	(1)	(2)

78. Liqueur		glass / bottle		(1)	(2)
79. In my *childhood* (< 18 y) there were times when we didn't have enough food in the house:					
	Never (1)	Seldom (2)	Sometimes (3)	Often (4)	Always (5)
80. In my *adulthood* (> 18 y) there were times when we didn't have enough food in the house:					
	Never (1)	Seldom (2)	Sometimes (3)	Often (4)	Always (5)

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vir Christelike Hoër Onderwys

POWIRS PROJECT: FEEDBACK FORM

Subject number: ______________

BLOOD PRESSURE: __________ mm Hg

Normal ☐
Low ☐
High ☐

BLOOD IRON STATUS:

Haemoglobin : _____ g/dl

Normal ☐
Low ☐
High ☐

Haematokrit: _____ %

Normal ☐
Low ☐
High ☐

Please consult your doctor:
Yes ☐
No ☐

We will inform you of all the other results in a few month's time.

THE RESEARCH TEAM

ANTROPOMETRIE DATAKAART

Naam: ____________________ Van: ____________________

DOB: ______________ Ouderdom: _______ Geslag: _____

Proefpersoonnr.: ________ RHT: ____ Toetsdatum: ________

			Meting 1	Meting 2	Meting 3
1	Massa				
2	Lengte				
Omtrekke					
3	Maagomtrek:	a.) umbilicus			
4		b.) minimum			
5		c.) mid-xiphoïed-umbilicus			
6	Heupomtrek				
Velvoue:					
7	Triseps				
8	Subskapulêr				
9	Suprailiac				
10	Dy				
11	Abdomimaanl				
12	Pektoraal				
13	Mid-axillêr				