# THE METABOLIC SYNDROME:

# DOES IT EXIST IN AFRICANS IN TRANSITION IN THE NORTHWEST PROVINCE

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Thesis submitted for the degree of Philosphiae in the School of Physiology, Nutrition and Consumer Sciences of the Potchefstroomse Universiteit vir Christelike Hoër Onderwys.

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# ABSTRACT

## THE METABOLIC SYNDROME: DOES IT EXIST IN AFRICANS IN TRANSITION IN THE NORTHWEST PROVINCE?

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**Background:**

The term 'metabolic syndrome' is used to describe the clustering in a person of risk factors which is associated with the chronic diseases of lifestyle. Considerable evidence exists that insulin resistance is the underlying common factor in the development of the metabolic syndrome. At present, urbanisation occurs very rapidly in the South African population. According to the literature, urbanisation is accompanied by the adoption of Western lifestyles and dietary habits. Therefore, overnutrition, the prevalence of risk factors, morbidity and mortality from chronic diseases of lifestyle are expected to increase among urbanising communities.

**Objectives:**

1. The questions addressed were whether the metabolic syndrome exists in the African population of the Northwest province and if it does, what are the characteristics of this syndrome in this population?
2. The hypothesis tested in this study was that despite the concept of "healthy obesity" in black women (Walker *et al.*, 1991) the metabolic syndrome will also develop in black South Africans when they adopt Western lifestyles.

**Study design:**

This study was part of the larger THUSA-study. THUSA was a cross-sectional study of 1854 "apparently healthy"African men and women volunteers, recruited from 37 randomly selected sites in the Northwest province and stratified for age, gender and level of urbanisation. A sub-sample of all the fasted subjects, 193 men and 233 women, between the ages of 15 and 65 years was selected to investigate the characteristics of the metabolic syndrome.

**Research methods:**

A variety of research techniques were used by a multidisciplinary team to collect the data. The results were statistically analysed by using the SPSS 9.0 programme, performing non-parametric statistical tests. Spearman's correlations were used to identify relationships between risk factors of chronic diseases of lifestyle and insulin sensitivity. The GLM Multivariate procedure was used to investigate interactions between risk markers for the chronic diseases of lifestyle and the insulin sensitivity index. Cross-tab statistics were used to calculate odds ratios. Logistic regression analyses were used to investigate the influence of lifestyle factors in the development of the metabolic syndrome. These relationships were used to investigate conditional probabilities in the predictive value of variables for early detection in the development of the metabolic syndrome.

**Results:**

The influence of urbanisation on this population was reflected in a deterioration in lipid profiles, an increased body mass index (BMI) and percentage body fat (calculated from girths), increased iron status and an increase in insulin resistance.

Although age was inversely associated with insulin sensitivity in the women, no linear association between insulin resistance and age was found. An increase in serum urea levels in women was associated with insulin resistance which should be further investigated as it may hold a key between kidney function and hypertension in African women. A progressive increase in the risk factors for type 2 diabetes (NIDDM), coronary heart disease (CHD) and obesity was detected in these subjects from a condition of high insulin sensitivity towards high insulin resistance. However, these risk factors were still within the boundaries of normal ranges (Chapter 6).

Clusters of two and more (up to five in men and six in women) traditional risk factors for the metabolic syndrome were also found in these "apparently healthy" subjects. Clustering of two and more risk factors occurred in 25% of the men and in 32% of the women. These clusters of risk factors were found despite the absence of insulin resistance, although clusters of more than two risk factors occurred more frequently in

the insulin resistant subjects.

Serum total cholesterol seemed to be a predictor for the clustering of risk factors at levels higher than 4.4 mmol/L in men and 4.8 mmol/L in women. However, large confidence intervals were observed and results should be interpreted with care. Physical activity seemed to be protective against the clustering of risk factors in the women. Raised plasma fibrinogen levels seemed to be involved in the developing of insulin resistance in the women and in the clustering of risk factors in the men. High consumption of food energy seemed to be indicative of the development of insulin resistance in the women while in the men it seemed to be protective against the clustering of risk factors. This contradiction might be an indication of the importance of food composition rather than quantity in the development of the metabolic syndrome, or it could be related to the fact that "overnutrition" as indicated by a mean BMI of 26.9 $kg/m^2$ was present in the women, while "undernutrition" (mean BMI of 20.5 $kg/m^2$) was more prevalent in the men. An increase in energy intake would represent further overnutrition in women, while in men it would result in more adequate or optimal nutrition.

**Conclusions:**

- Insulin resistance and the clustering of risk factors occurred in the study population.
- Insulin resistance was not the underlying common factor in all the clusters of risk factors for the metabolic syndrome in these subjects. Therefore, the term "multiple metabolic syndrome,"suggested by Liese *et al.* (1998), will probably be more appropriate to use for this study population.
- Obesity and an inactive lifestyle seem to be risk factors for the development of insulin resistance and a"multiple metabolic syndrome" in these women of the study population.

**Recommendations:**

The results of this study emphasised obesity as a risk factor in the development of chronic diseases of lifestyle and the importance of physical activity and its protective role against the clustering of risk factors of chronic diseases in black women. Physical activity does not necessarily implicate gymnasium exercises or participation in sport, but also includes walking, dancing and physical labour. In the men the emphasis was on "healthy" or adequate nutrition. Proper education on the benefits of an active lifestyle and

healthy food choices should be included in health intervention programmes. The data generated in this study provides a platform for future research programmes to define criteria for suitable health intervention programmes for the Northwest province. The study raised a number of questions that should be addressed in future research:

1. Evaluation of appropriate cut-off values for total serum cholesterol and serum ferritin levels to predict risk profiles for the development of the "multiple metabolic syndrome" in the Africans of the Northwest province.
2. Serum urea as the possible link between insulin resistance and hypertension in black women, needs to be investigated.
3. The optimum dietary composition to be protective against the development of the "multiple metabolic syndrome" in this population should be investigated.
4. The involvement of fibrinogen in the development of the metabolic syndrome in this population should be investigated in more detail.

# ABSTRAK

## DIE METABOLIESE SINDROOM: KOM DIT VOOR TYDENS DIE VERSTEDELIKING VAN AFRIKANE IN DIE NOORDWES PROVINSIE?

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**Agtergrond:**

Die term 'metaboliese sindroom' word gebruik om in 'n persoon die voorkoms van 'n versameling van risikofaktore wat geassosieer kan word met chroniese lewenstylsiektetoestande te beskryf. Bewyse bestaan dat die onderliggende gesamentlike faktor in al hierdie siektetoestande, wat deel uitmaak van die metaboliese sindroom, insulienweerstand blyk te wees. Verstedeliking vind tans teen 'n vinnige tempo in die Suid-Afrikaanse bevolking plaas. Volgens die literatuur gaan verstedeliking gepaard met die aanvaarding van Westerse leefwyse en eetgewoontes. Oorvoeding, stygende voorkoms van risikofaktore vir chroniese siektes, mortaliteit en morbiditeit kan dus in gemeenskappe wat verstedelik verwag word.

**Doelstellings:**

1. Die vrae waarop antwoorde gesoek is, was of die metaboliese sindroom in die Afrikane van die Noordwes provinsie wat in 'n proses van verwestering is voorkom en indien wel, wat is die kenmerke van hierdie sindroom in dié spesifieke populasie?
2. Die hipotese wat in hierdie studie ondersoek is, was dat tenspyte van die konsep van "gesonde oorgewig" in swart vrouens (Walker *et al.*, 1991), die metaboliese sindroom wel in swart vrouens wat 'n westerse lewenswyse aanleer sal ontwikkel.

**Studie-ontwerp:**

Hierdie studie was deel van die groter THUSA-studie. THUSA was 'n dwarssnitstudie van 1854 "oënskynlik gesonde" swart manlike en vroulike vrywilligers wat gewerf is uit

37 ewekansig geselekteerde plekke in die Noorwes provinsie en gestratifiseer is volgens ouderdom, geslag en vlak van verwestering. 'n Kleiner steekproef van al die vastende proefpersone, 193 mans en 233 vrouens tussen die ouderdomme van 15 en 65 jaar is ingesluit in hierdie studie waarin die kenmerke van die metaboliese sindroom ondersoek is.

**Navorsingsmetodes:**

'n Verskeidenheid navorsingstegnieke is deur 'n multidissiplinêre span gebruik om data te versamel. Die resultate is met nie-parametriese statistiek met behulp van die SPSS 9.0 pakket verwerk. Spearman-korrelasiekoëffisiënte is gebruik om verwantskappe tussen risikofaktore vir chroniese lewenstylsiektes en insuliensensitiwiteit te identifiseer en die "GLM Multivariate" prosedure om interaksies tussen die risikomerkers van die chroniese lewenstylsiektes en die insuliensensitiwiteitsindeks te bepaal. Oorkruis tabuleringstatistieke, 'n stapsgewyse meervoudige, liniêre regressie-analise en logistiese regressie-analises is gebruik om voorwaardelike voorspellingswaardes aan risikomerkers toe te ken ten einde vroegtydig die ontwikkeling van die metaboliese sindroom te kan voorspel.

**Resultate:**

Die invloed van verwestering op hierdie populasie is weerspieël in 'n verswakkende lipiedprofiel, verhoogde liggaamsmassa-indeks en persentasie liggaamsvet ( bereken deur van omtrekke gebruik te maak), verhoogde ysterstatus en 'n verhoogde insulienweerstand.

Geen reglynige verband tussen insulienweerstand en ouderdom kon gevind word nie, ten spyte van die negatiewe korrelasie tussen insuliensensitiwiteit en ouderdom wat in die vrouens waargeneem is. 'n Verhoogde serum-ureumvlak in hierdie vrouens was positief verwant aan 'n insulienweerstand wat verder ondersoek te behoort word, daar dit moontlik lig kan werp op die moontlike verband tussen nierfunksie en hipertensie in swart vrouens. 'n Geleidelike verhoogde risiko vir tipe 2 diabetes, koronêre hartvatsiektes en obesitieit is in hierdie proefpersone bespeur vanaf 'n toestand waar insuliensensitiwiteit prominent is tot waar insulienweerstand ter sprake is. Hierdie risikofaktore was egter steeds binne die normale reikwydtes (Hoofstuk 6).

Die voorkoms van twee en meer tradisionele risikofaktore vir die metaboliese sindroom (tot vyf in mans en ses in vrouens) is in 25% van die mans en 32% van die vrouens in hierdie "oënskynlik gesonde" proefpersone gevind. Alhoewel hierdie "opstapeling" van risikofaktore in een persoon meer geredelik in die teenwoordigheid van insulienweerstand voorgekom het, het dit ook voorgekom in die afwesigheid daarvan.

Totale serumcholesterolvlakke van bo 4.4 mmol/L in mans en 4.8 mmol/L in vrouens het 'n voorspeller vir die ontwikkeling van die metaboliese sindroom geblyk te wees. Groot vertrouensintervalle is egter waargeneem en resultate moet versigtig geïnterpreteer word. In die vrouens het fisiese aktiwiteit 'n beskermende rol gespeel teen die ontwikkeling van die metaboliese sindroom. Hoë-plasmafibrinogeenvlakke het geblyk 'n rol te speel in die ontwikkeling van insulienweerstand in die vrouens en die metaboliese sindroom in die mans. In mans was 'n hoë-energie-inname beskermend teen die ontwikkeling van die metaboliese sindroom. Daarteenoor het 'n hoë-energie-inname insulienweerstand in die vrouens bevorder. Hierdie oënskynlike paradoks dui waarskynlik op die belangrikheid van die samestelling van voedsel in die ontwikkeling van die metaboliese sindroom eerder as die hoeveelheid wat ingeneem word. Dit kan egter ook herlei word tot die feit dat "oorvoeding," soos geïmpliseer deur 'n gemiddelde liggaamsmassa- indeks van 26.9 $kg/m^2$ in die vrouens en "ondervoeding," (gemiddelde liggaamsmassa-indeks van 20.5 $kg/m^2$) in die mans voorgekom het. 'n Hoër energie-inname sal waarskynlik tot verdere obesiteit in die vrouens lei, terwyl dit in die mans tot 'n verbetering in voedingstatus sal lei.

**Gevolgtrekkings:**

- Insulienweerstand sowel as die metaboliese sindroom het in hierdie populasie voorgekom.
- Insulienweerstand was nie die onderliggende gemeenskaplike faktor in alle gevalle waar "opeenstapeling" van risikofaktore vir die metaboliese sindroom in 'n persoon voorgekom het nie. Daar word dus voorgestel dat die gebruik van die term "metaboliese sindroom" in hierdie studiepopulasie vervang word met 'n meer beskrywende term naamlik die "meervoudige metaboliese sindroom" soos voorgestel deur Liese *et al.*(1998).

- Obesiteit en 'n onaktiewe lewenswyse blyk risikofaktore te wees in die ontwikkeling van beide insulienweerstand en die "meervoudige metaboliese sindroom" in hierdie vrouens.

**Aanbevelings:**

Die bevindinge in hierdie studie het bevestig dat obesiteit, ook in swart vrouens, as 'n risikofaktor vir chroniese lewenstylsiektes beskou kan word en ook dat 'n aktiewe lewenstyl belangrik is in die voorkoming van die "meervoudige metaboliese sindroom" in swart vrouens. 'n Fisies-aktiewe lewenstyl impliseer nie noodwendig oefeninge in 'n gimnasium of deelname aan 'n georganiseerde sport nie, maar sluit ook stap, dans en fisiese arbeid in. In die mans het die bevindinge die klem laat val op gesonde voeding en voedingstatus. Effektiewe onderrig in die voordele van 'n aktiewe lewenstyl en gesonde eetgewoontes moet derhalwe ingesluit word in gesondheidsbevorderende programme. Die inligting wat in hierdie studie bekom is kan met vrug gebruik word in daarstel van sulke programme vir die Noordwes provinsie. Die inligting kan ook gebruik word om die volgende aanbevelings aangaande verdere navorsing te maak:

- Die vasstelling van toepaslike normale reikwydtes vir totale serumcholesterol, en -ferritin vir die gebruik as voorspellers in die ontwikkeling van die meervoudige metaboliese sindroom in hierdie populasie, moet verder ondersoek word.
- Die betrokkenheid van serumureum in die ontwikkeling van hipertensie in insulienweerstandbiedende swart vrouens moet verder ondersoek word.
- Die optimale dieetsamestelling vir hierdie populasie wat beskermend kan wees teen die ontwikkeling van die meervoudige metaboliese sindroom behoort ondersoek te word.
- Die rol wat fibrinogeen in die ontwikkeling van die "meervoudige metaboliese sindroom" in hierdie populasie speel, behoort verder ondersoek te word.

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**DEFINITIONS:**

For the purpose of this study the following terms are defined as:

1 Metabolic syndrome: The clustering of risk markers for NIDDM, CHD and obesity with insulin resistance as common underlying factor (Reaven, 1988).

2. Insulin sensitivity: A high insulin index as calculated by 10 000 ÷ [fasting insulin ($\mu$U/ml) X fasting glucose (mmol/L)]. (Donahue *et al.*, 1988).

**Quartiles of the insulin sensitivity index**

| Gender | Insulin sensitivity Quartiles Donahue *et al.*, 1988 | Quartile range | Std. Deviation | N |
|---|---|---|---|---|
| Men | 1 Low sensitivity | <=113 | 30.3 | 33 |
| | 2 | >113 <=149.5 | 11.4 | 33 |
| | 3 | >149.5 <=191.5 | 12.0 | 34 |
| | 4 High sensitivity | >191.5 | 37.1 | 33 |
| | | | | |
| Women | 1 Low sensitivity | <=87.7 | 18.5 | 44 |
| | 2 | >87.7 <= 117.5 | 8.8 | 44 |
| | 3 | >117.5 <=158.95 | 12.2 | 44 |
| | 4 High sensitivity | >158.95 | 61.04 | 44 |
| | | | | |

The relationship between fasting glucose and insulin is the basis of calculation of insulin sensitivity.

When both glucose and insulin levels are low, a high insulin sensitivity index indicates that low glucose levels can be maintained with low insulin.

In this study, subjects who fell in the top quartile (4) of the insulin sensitivity index distributions, were classified as being insulin sensitive.

3. Insulin resistance: An alternative expression for a decreased insulin sensitivity (Colagiuri and Brand Miller, 1997).

When both glucose and insulin levels are high, the insulin sensitivity will be low, indicating that despite a high insulin secretion, low (natural) blood glucose levels cannot be maintained. This condition is referred to as insulin resistance.

In this study, subjects who fell in the bottom quartile (1) of the insulin sensitivity index distributions, were classified as being insulin resistant.

4. Africans: Black (Negroid) South Africans

## LIST OF ABBREVIATIONS:

| | |
|---|---|
| ARIC-study | Atherosclerosis Risk in Communities |
| BD | Body density |
| BMI | Body mass index |
| BP | Blood pressure |
| CHD | Coronary heart disease |
| CHS | Cardiovascular Health Study |
| CVD | Cardiovascular disease |
| cm | Centimetres |
| Creat | Creatinine |
| DBP | Diastolic blood pressure |
| DM | Diabetes mellitus |
| DNA | Deoxyribonucleic acid |
| Fe | Iron |
| FE satur | Iron saturation |
| FFA | Free fatty acids |
| Fib | Fibrinogen |
| g | Gram |
| g/d | Gram per decilitre |
| Gluc $T_0$ | Fasting glucose |
| Gluc $T_{120}$ | Two hour glucose |
| GLM | General linear model |
| GTT | Glucose tolerance test |
| Hc | Haematocrit |
| HDL-C | High-density lipoprotein |
| Hip-max | Maximum hip circumference |
| HIV | Human immunodeficiency virus |
| IGT | Intolerant glucose test |
| IHD | Ischemic heart disease |
| IRAS | Insulin Resistance and Atherosclerosis Study |
| IR | Insulin resistance |
| IS | Insulin sensitivity |
| IS Q1 | Insulin sensitivity quartile 1 |
| IS Q2 | Insulin sensitivity quartile 2 |
| IS Q3 | Insulin sensitivity quartile 3 |
| IS Q4 | Insulin sensitivity quartile 4 |
| IU/l | International units per litre |
| KJ | Kilojoules |
| Kg | Kilogram |
| $Kg/m^2$ | Kilogram per square metre |
| L | Litre |
| LD | Lactate dehydrogenase |
| LDL-C | Low-density lipoprotein cholesterol |
| LDL:HDL | Low-density lipoprotein, high-density lipoprotein ratio |
| med | Medium |
| mm | Millimetres |

| | |
|---|---|
| MMS | Multiple metabolic syndrome |
| mmHg | Millimetres of mercury |
| mmol/L | Millimol per litre |
| n | Number / sample size |
| NAS NRC | National Academy of Science, National research Council |
| NIDDM | Non-insulin-dependent diabetes mellitus |
| P | Probability (level of significance) |
| Pl | Plasma |
| PAI | Plasminogen activator inhibitor |
| R | Rand (currency) |
| S | Serum |
| SBP | Systolic blood pressure |
| st. | Standard or education grade |
| SD | Standard deviation |
| Sig | Significance |
| Stats | Statistics |
| Stratum 1 | Urbanisation level: rural |
| Stratum 2 | Urbanisation level: farm living subjects |
| Stratum 3 | Urbanisation level: squatter dwellers |
| Stratum 4 | Urbanisation level: urban and upper urban citizens |
| TB | Tuberculosis |
| T-Bili | Total bilirubin |
| TC | Total cholesterol |
| TG | Triglycerides |
| TIBC | Total iron binding capacity |
| THUSA | Transition and Health during Urbanisation of South Africans |
| USA | United States of America |
| VLDL | Very low density lipoprotein |
| Waist-hip min | Minimum waist circumference |
| WHO | World Health Organisation |
| WHR | Waist to hip ratio |
| y | Years |
| % | Percentage |
| $\mu$mol/L | Micro mol per litre |
| $\mu$U/L | Micro units per litre |
| $^0$C | Degree Celsius |