Cardiovascular Topics

Association of microalbuminuria with serum lipids and inflammatory markers in an adult population in the Dikgale Health and Demographic Surveillance System site, South Africa

Thabo Magwai, Perpetua Modjadji, Solomon Choma

Abstract

**Background:** There is evidence that microalbuminuria (urinary albumin excretion) is an early sign of vascular damage and an established risk factor for cardiovascular morbidity and mortality. This study investigated the magnitude of microalbuminuria and its association with serum lipids and inflammatory markers among a rural black population residing in the Dikgale Health and Demographic Surveillance System site, South Africa.

**Methods:** Data were collected from 602 presumably healthy participants (225 men and 377 women) aged ≥ 18 years. Biochemical data collection included serum lipids, glucose, insulin, high-sensitivity C-reactive protein (hs-CRP), urine albumin and creatinine. Anthropometry and blood pressure were also measured. Microalbuminuria was diagnosed with an albumin–creatinine ratio of ≥ 2.5 mg/mmol in men and ≥ 3.5 mg/mmol in women. Data were analysed using SPSS version 22.0.

**Results:** The mean age of participants was 48.63 ± 20.89 years. High percentages of microalbuminuria (35.7%), high levels of interleukin 6 (17.8%), hs-CRP (32.9%), triglycerides (TG) (26.1%), low-density lipoprotein cholesterol (52.2%) and total cholesterol (32.0%), and low levels of high-density lipoprotein cholesterol (29.1%) were observed in the population. Increased glucose levels (32.8%), insulin resistance (27.6%), hypertension (45.8%), overweight (26.8%) and obesity (25.4%) were also prevalent. Microalbuminuria was associated with high hs-CRP and TG levels in the men (adjusted odds ratios = 9.434, 95% confidence interval: 1.753 – 50.778, \( p = 0.01 \)).

**Conclusion:** High prevalence of microalbuminuria, hypertension, insulin resistance, overweight and obesity, as well as abnormal levels of serum lipids and inflammatory markers were observed in the population. Microalbuminuria was associated with high hs-CRP and TG levels among men.

Keywords: microalbuminuria, serum lipids, inflammatory markers, rural HDSS site, South Africa

Submitted 18/5/20, accepted 6/1/21
Cardiovasc J Afr 2022; online publication www.cvja.co.za
DOI: 10.5830/CVJA-2021-055

In 2018, the World Health Organisation (WHO) reported that South Africa faces a quadruple burden of disease resulting from communicable diseases (HIV/AIDS and tuberculosis), maternal and child mortality, non-communicable diseases (NCDs) such as hypertension and cardiovascular diseases (CVDs), diabetes mellitus, cancer, mental illnesses and chronic lung diseases such as asthma, as well as injury and trauma. Most of the CVD deaths (80%) occur in low- to middle-income countries.

In South Africa, NCDs are estimated to account for 43% of the total adult deaths, while CVDs account for almost a fifth (18%) of these deaths. One in three South African adults (33.7%) has hypertension, which can increase the risk of heart attack, heart failure, kidney disease or stroke, while 31.3% of adults are obese. Contributing factors to CVDs are urbanisation and the population burden of vascular risk factors, such as hypertension, hypercholesterolaemia, low-grade inflammation, as well as diabetes, smoking and obesity.

Microalbuminuria (MA) is an established risk factor for cardiovascular morbidity and mortality and for end-stage renal disease in individuals with associated cardiovascular risk conditions such as hypertension or and diabetes mellitus. The leakage of albumin into the urine is thought to be linked to enhanced capillary permeability for albumin in the systemic vasculature and this might lead to haemodynamic strain and instability, which then starts the atherosclerotic process, eventually leading to adverse cardiovascular events. Another explanation could be endothelial dysfunction, since abnormalities in the endothelial glyocalix can contribute to both MA and the pathogenesis of atherosclerosis, therefore...
providing a link between MA and CVDs. In a South African study, the prevalence of MA was reported to be 58% in the general population, 51% in a diabetic population and 43% in a hypertensive population.

One of the most significant markers of inflammation appearing during atherosclerosis is C-reactive protein (CRP). This is found in the liver in response to the development of an inflammatory condition or is due to infection. There is a significant relationship between an increased high-sensitivity CRP (hs-CRP) and local disturbances in the structure and function of blood vessels, particularly with abnormal lipid status. MA has been associated with high levels of hs-CRP and interleukin 6 (IL-6).

Several studies have also reported that chronic low-grade inflammation is associated with MA and the risk of atherosclerosis. Furthermore, MA was also found to be associated with serum total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C).

Contradicting results wherein MA was not associated with CRP, IL-6 and serum lipids have been reported. Some studies have attributed the contradiction of associations to differences in the study approach, the method of diagnosing MA, control for confounders, or differences in sample size. Although the mechanism leading to MA is unclear, the literature documents that endothelial dysfunction may be responsible. Associations of endothelial dysfunction with MA, dyslipidaemia and low-grade inflammation long have been reported among patients with conditions such as hyperlipidaemia. MA, together with low-grade inflammation and dyslipidaemia, are the risk factors for CVDs. Hence, the hypothesis that high levels of serum lipids and inflammatory markers are associated with MA.

MA has been reported to be more prevalent in blacks compared to whites in an American population. This is thought to be due to socio-economic discrepancies, access to healthcare, differences in glycaemic control, or a possible biological or genetic difference in the populations. This makes the investigation of MA in a black population essential.

Despite the current burden of NCDs, including CVDs, in South Africa, there is a paucity of data on the prevalence of MA in the black South African population. Globally, most studies on MA focused separately on either MA and inflammatory markers or MA and serum lipids. As a result, not many studies have reported on the association among these three cardiovascular risk factors. This study was undertaken to determine the prevalence of MA among a presumably healthy black population, and further to determine the association of MA with inflammatory markers and serum lipids. It is noteworthy that MA, together with an evaluation of inflammatory markers and serum lipids, may have a potential role in improving cardiovascular risk prediction.

Methods

A cross-sectional study using a quantitative method was conducted in a rural black population to determine the association of inflammatory markers and serum lipids with MA. This study is part of a larger study titled ‘Prevention, control and integrated management of chronic diseases in a rural black population, South Africa’. The larger study aimed to identify specific risk factors for chronic diseases in a rural settlement in the Limpopo province, South Africa. The study used a WHO STEPS questionnaire to gather information on socio-economic status and risk factors for NCDs with questions covering different cardiovascular risk factors.

The study setting has previously been reported by Alberts et al. The study was conducted in the Dikgale Health and Demographic Surveillance System (DHSSS) site, a rural site in the Limpopo Province of South Africa, situated approximately 40 km north-east of Polokwane, the capital of Limpopo Province. The area constitutes communities typically made up of households clustered in villages with a population of approximately 36 000, speaking the local language of Sepedi. In 2009, the site was enlarged from eight to 15 villages. The area has poor infrastructure with minimal use of available electricity and shared or communal taps for water supply. The site has a socio-economic status characterised by high rates of unemployment and singlehood, and low rates of tertiary education. These living conditions are consistent with the findings of the South African National Health and Nutrition Examination Survey (SANHANES-I).

In a larger study, 2 981 participants were selected randomly from the DHSSS database. Only participants aged 18 years old and above were selected to participate in the study. Of the 2 981, only 1 407 participants completed the WHO STEPS questionnaire, of whom 878 were women and 525 were men. Only 817 of the participants were available to donate fasting blood samples. Reasons for the low participation were leaving for work early in the morning, unavailability after repeated visits, refusal to participate, death or emigration. The WHO STEPS questionnaire was first translated into Sepedi (a local language), and the field workers were then trained in the administration and understanding of the questionnaire during a pilot study to pre-test its feasibility among participants who did not form part of the main study.

The current study included participants who gave written consent to take part in the study, completed the WHO STEPS questionnaire, and gave both blood and urine samples. The study excluded participants with albumin/creatinine ratio (ACR) > 2.5 mg/mmol in males and > 3.5 mg/mmol in females, and participants with confounders such as renal disease (serum creatinine of ≥ 170 µmol/l), diabetes (glucose of ≥ 7.0 mmol/l and/or history of diabetes), pregnant women and HIV-positive participants. Furthermore, participants who were on medication for diabetes and HIV, or using lipid-lowering drugs were excluded to avoid interference with serum lipids. The final sample of 602 participants was obtained.

As part of the larger study, a spot urine sample was collected into a sterile urine jar from each participant. Blood was collected in silica-coated vacutainer tubes, EDTA-containing tubes and sodium fluoride tubes. Blood samples were centrifuged and immediately after centrifugation, serum lipids, hs-CRP, glucose, insulin, HIV status and creatinine were determined. The remaining serum was stored in cryotubes at −80°C for further determination of IL-6. The frozen samples were aliquoted to minimise freeze–thaw cycles on individual tubes, thus preserving the sample quality and integrity.

Serum hs-CRP levels were measured using the IMMAGE 800 immunochemistry system. Insulin and IL-6 were determined using the ACCESS 2 chemistry system. Serum lipid (TG, cholesterol, HDL-C and LDL-C) and glucose levels were
determined using the ILAB 300 plus chemistry system. Spot morning urine samples were collected using a sterile urine jar. Urine creatinine and albumin concentrations were measured using the ILAB 300 plus chemistry system and the ACR was calculated. Subjects with an ACR of 2.5–25 mg/mmol in males and 3.5–35 mg/mmol in females were considered microalbuminuric and subjects with an ACR of < 2.5 mg/mmol in males and < 3.5 mg/mmol in females were considered normoalbuminuric (NA). Subjects with MA were regarded as the cases and subjects with NA were regarded as controls for this study.

Anthropometry (weight, height and waist circumferences) were all measured according to the WHO procedures. Weight was measured using a calibrated smart D-quip electronic scale and recorded to the nearest 0.1 kg while height was measured using a stadiometer and recorded to the nearest 0.1 m. For both weight and height, two measurements were taken by two different and independent research assistants. The absolute technical error of measurement for WC was 0.012 cm. Abdominal obesity was defined by a waist circumference ≥ 80 cm for women and ≥ 94 cm for men.41

Blood pressure was measured using OMRON M-5 (OMRON UK) according to the WHO procedure. Blood pressure measurements were taken with participants in a seated position with a flexed elbow at the level of the heart. An appropriately tight blood pressure cuff was placed around the upper arm with its lower edge just above the antecubital fossa. The cuff was inflated to measure systolic blood pressure and released for diastolic blood pressure. Three measurements were taken and the average of the last two readings was reported. Participants with a systolic blood pressure (SBP) of ≥ 140 mmHg, diastolic blood pressure (DBP) of ≥ 90 mmHg and/or history of hypertension were considered hypertensive.42

This study was conducted according to the guidelines laid down in the Declaration of Helsinki43 and all procedures involving human subjects were approved by the Medunsa Research and Ethics Committee (MREC) [MREC/HS/102/2014:PG]. The nature of the study was explained to the subjects and written informed consent was obtained from parents and verbal assent from learners.

Statistical analysis

Data were analysed using the statistical package for social sciences (SPSS) version 22.0. Normally distributed data (Gaussian distribution) are presented as mean ± standard deviation and the skewed data were normalised through a logarithm transformed for further analysis and are presented as median (interquartile range). The Student’s t-test was used to compare serum lipids and inflammatory markers between participants with and without MA. Analysis of variance (ANOVA) was used to control for age in the comparison of parameters between participants with and without MA.

Multiple logistic regression analysis was used to determine the association of MA with serum lipids and inflammatory markers. A simple logistic regression was used to determine the bi-variate relationship between MA and predictors. Predictors with a p-value ≤ 0.250 were entered into the first adjusted model and those with the weakest prediction (with p > 0.250) were removed and the model was run again to get the last adjusted model. The model was used to control for known confounders measured in this study, such as age, gender, blood pressure, high glucose and creatinine levels, to mention a few. Adjusted odds ratios (AOR) with a 95% confidence interval (CI) were generated and used to determine the independent strength of the associations. Results are presented as AOR (95% CI). Significance was set at the probability level of p < 0.05.

Results

Table 1 presents demographic and biochemical data for males and females. In this population, women were found to be

<table>
<thead>
<tr>
<th>Variables</th>
<th>All (n = 602)</th>
<th>Female (n = 377)</th>
<th>Male (n = 225)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>48.63 ± 20.89</td>
<td>50.14 ± 19.82</td>
<td>46.22 ± 22.44</td>
<td>0.03</td>
</tr>
<tr>
<td>ACR (mg/mmol)</td>
<td>2.04 (1.05–4.71)</td>
<td>4.11 ± 5.39</td>
<td>3.18 ± 3.53</td>
<td>0.02</td>
</tr>
<tr>
<td>Glucose (mmol/l)</td>
<td>5.15 ± 0.84</td>
<td>5.16 ± 0.85</td>
<td>5.13 ± 0.83</td>
<td>0.71</td>
</tr>
<tr>
<td>Insulin (µIU/l)</td>
<td>6.25 (3.33–12.86)</td>
<td>6.42 (3.30–12.63)</td>
<td>6.50 (3.20–10.63)</td>
<td>0.33</td>
</tr>
<tr>
<td>HOMA</td>
<td>1.81 ± 1.33</td>
<td>1.85 ± 1.31</td>
<td>1.74 ± 1.36</td>
<td>0.31</td>
</tr>
<tr>
<td>IL-6 (pg/ml)</td>
<td>3.09 (0.96–4.94)</td>
<td>2.74 (1.96–3.81)</td>
<td>3.01 (1.81–4.84)</td>
<td>0.12</td>
</tr>
<tr>
<td>hs-CRP (mg/l)</td>
<td>1.50 (0.56–4.28)</td>
<td>1.83 (0.65–3.63)</td>
<td>1.26 (0.47–2.76)</td>
<td>0.01</td>
</tr>
<tr>
<td>TC (mmol/l)</td>
<td>4.45 ± 1.23</td>
<td>4.54 ± 1.29</td>
<td>4.33 ± 1.06</td>
<td>0.05</td>
</tr>
<tr>
<td>HDL-C (mmol/l)</td>
<td>1.34 ± 0.51</td>
<td>1.34 ± 0.59</td>
<td>1.33 ± 0.32</td>
<td>0.78</td>
</tr>
<tr>
<td>LDL-C (mmol/l)</td>
<td>2.54 ± 1.09</td>
<td>2.66 ± 1.04</td>
<td>2.41 ± 0.93</td>
<td>0.00</td>
</tr>
<tr>
<td>TG (mmol/l)</td>
<td>1.11 (0.73–1.68)</td>
<td>1.11 (0.72–1.70)</td>
<td>1.10 (0.74–1.58)</td>
<td>0.91</td>
</tr>
<tr>
<td>C/HDL ratio</td>
<td>3.52 ± 1.13</td>
<td>3.59 ± 1.16</td>
<td>3.39 ± 1.06</td>
<td>0.04</td>
</tr>
<tr>
<td>eGFR (ml/min/1.73 m²)</td>
<td>97.34 ± 24.07</td>
<td>93.65 ± 23.51</td>
<td>103.49 ± 23.80</td>
<td>0.00</td>
</tr>
<tr>
<td>Creatinine (µmol/l)</td>
<td>82.31 ± 19.81</td>
<td>79.28 ± 18.31</td>
<td>87.55 ± 21.17</td>
<td>0.00</td>
</tr>
<tr>
<td>MA, n (%)</td>
<td>215 (35.7)</td>
<td>128 (34.0)</td>
<td>87 (38.7)</td>
<td>0.24</td>
</tr>
<tr>
<td>Age (&lt; 40 years), n (%)</td>
<td>221 (36.7)</td>
<td>119 (31.6)</td>
<td>102 (45.3)</td>
<td>0.00</td>
</tr>
<tr>
<td>Age (40–59 years), n (%)</td>
<td>173 (28.7)</td>
<td>127 (33.7)</td>
<td>42 (20.4)</td>
<td>0.00</td>
</tr>
<tr>
<td>Age (&gt; 60 years), n (%)</td>
<td>208 (34.6)</td>
<td>131 (34.7)</td>
<td>77 (34.2)</td>
<td>0.39</td>
</tr>
<tr>
<td>High glucose (≥ 5.6 mmol/l), n (%)</td>
<td>197 (32.8)</td>
<td>128 (34.0)</td>
<td>69 (30.7)</td>
<td>0.39</td>
</tr>
<tr>
<td>High HOMA (&gt; 2.5), n (%)</td>
<td>166 (27.6)</td>
<td>106 (28.2)</td>
<td>60 (26.7)</td>
<td>0.69</td>
</tr>
<tr>
<td>High IL-6 (≥ 5 pg/ml), n (%)</td>
<td>32 (17.8)</td>
<td>14 (13.9)</td>
<td>18 (22.8)</td>
<td>0.12</td>
</tr>
<tr>
<td>High hs-CRP (≥ 3 mg/l), n (%)</td>
<td>198 (32.9)</td>
<td>146 (38.7)</td>
<td>52 (23.2)</td>
<td>0.00</td>
</tr>
<tr>
<td>High TC (≥ 5.0 mmol/l), n (%)</td>
<td>187 (32.0)</td>
<td>130 (35.5)</td>
<td>57 (26.1)</td>
<td>0.02</td>
</tr>
<tr>
<td>Low HDL-C (1.1 and 1.3 mmol/l), n (%)</td>
<td>167 (29.1)</td>
<td>85 (23.6)</td>
<td>82 (38.5)</td>
<td>0.00</td>
</tr>
<tr>
<td>High LDL-C (≥ 3.0 mmol/l), n (%)</td>
<td>295 (52.2)</td>
<td>195 (55.2)</td>
<td>100 (47.2)</td>
<td>0.06</td>
</tr>
<tr>
<td>High TG (≥ 1.7 mmol/l), n (%)</td>
<td>151 (26.1)</td>
<td>103 (28.1)</td>
<td>48 (22.5)</td>
<td>0.14</td>
</tr>
</tbody>
</table>

ACR, albumin:creatinine ratio; HOMA, homeostatic model assessment; IL-6, hs-CRP, high-sensitivity C-reactive protein; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglycerides; eGFR, estimated glomerular filtration rate; MA, microalbuminuria.
Women were also found to have a significantly higher hs-CRP compared to their male counterparts \( p = 0.03 \) and 0.02, respectively. More women were overweight and obese and had abdominal obesity (high WC) compared to men \( p = 0.000 \) and 0.01). Insulin levels were significantly higher in women with MA compared to women without MA \( [8.09 (4.62–15.60) \text{ vs } 6.11 (3.23–9.68 \mu IU/l)] \) after adjusting for age \( p = 0.00 \). In women with MA, HOMA was higher compared to those with NA \( [1.67 \pm 1.19 \text{ vs } 2.22 \pm 1.46 \% \text{ (cv) }] \) \( p = 0.01 \). Women with MA had a higher median TG compared to women without MA \( [96.17 \pm 22.64 \text{ vs } 88.76 \pm 24.47 \text{ µmol/l/min/1.73 m}^3] \) \( p = 0.00 \). Women with MA had a higher creatinine compared to women without MA \( [8.09 (4.62–15.60) \text{ vs } 6.11 (3.23–9.68 \mu IU/l)] \) after adjusting for age \( p = 0.00 \).

Table 2 presents anthropometric and blood pressure data in men and women. More women were found to have a higher body mass index and a higher WC compared to men \( p = 0.000 \) and 0.000, respectively. More women were overweight and obese and had abdominal obesity (high WC) compared to men \( p = 0.000 \) and 0.000, respectively. The levels of SBP were higher in men than in women \( p = 0.01 \).

Table 3 presents age and biochemical data by MA status in men and women. The table is split into males and females since the ACR was found to be significantly different between males and females in this study. This was done to control for the effect of gender on the association. Women with MA were significantly older than those without MA \( [53.66 \pm 19.90 \text{ vs } 48.25 \pm 19.55, p = 0.01] \). In women with MA, the prevalence of a high TC/HDL-C ratio was significantly higher in women than in men \( p = 0.00 \) and 0.00, respectively. More men were found to have a lower HDL-C compared to women \( p = 0.00 \). The prevalence of a high TC/HDL-C ratio was significantly higher in women than in men \( p = 0.00 \) and 0.00, respectively.
HOMA index levels were found in this study to be significantly higher in men with MA compared to women without MA (1.56 ± 1.18 vs 2.02 ± 1.57 units) (p = 0.00). Men with MA were found to have higher levels of insulin compared to men without MA [5.36 (3.18–9.30) vs 5.65 (3.20–5.18 μIU/l) (p = 0.04)]. The prevalence of overweight than those without MA (p = 0.02) and men with MA had a lower prevalence of obesity than those without MA (p = 0.00).

Table 4 presents anthropometric and blood pressure measurements by MA status in men and women. Women with MA had a significantly higher SBP compared to women without MA (125.28 ± 21.51 vs 134.94 ± 30.60 mmHg) (p = 0.00). Women had a higher prevalence of hypertension, SBP and DBP vs men with MA (p = 0.00, 0.00 and 0.01, respectively). Men with MA had a high prevalence of obesity (p = 0.02) and men with MA had a lower prevalence of overweight than those without MA (p = 0.02).

Table 5 presents predictors of MA in the total population with confounders controlled for in analysis. Participants with hypertension were more likely to have MA compared to their counterparts without hypertension [AOR 3.365 (95% CI: 1.111–10.188) (p = 0.03)]. Participants with a high insulin level (last quartile) were more likely to have MA than those in the last quartile of insulin [AOR 9.434 (95% CI: 1.753–50.778) (p = 0.01)].

Table 6 presents predictors of MA in men having controlled for confounders. Men with a high hs-CRP were less likely to have MA [AOR 0.204 (95% CI: 0.069–0.602) (p = 0.00)]. Men with a high HOMA were more likely to have MA than those with normal HOMA [AOR 2.982 (95% CI: 1.413–6.294) (p = 0.00)]. Men with high hs-CRP and TG levels were more likely to have MA compared to those with normal hs-CRP and TG levels [AOR 9.434 (95% CI: 1.753–50.778) (p = 0.01)].

Table 7 presents the predictors of MA in women. Women with a high glucose level were less likely to have MA [AOR 0.597 (95% CI: 0.356–0.976) (p = 0.04)]. Women with a high insulin level (last quartiles) were more likely to have MA than those in the first quartile [AOR 2.905 (95% CI: 1.436–5.877) (p = 0.00)].
Discussion

This study aimed to assess the prevalence of MA and further determine the association of MA with inflammatory markers and serum lipid levels in a rural black population in the Dikgale HDSS, South Africa. The study showed that women had significantly higher hs-CRP levels ($p = 0.01$) and a higher prevalence of high hs-CRP ($p < 0.001$) compared to men. Furthermore, women had a higher prevalence of high TG levels compared to men ($p = 0.02$), while men had a significantly higher prevalence of low HDL-C levels compared to women ($p < 0.001$). These findings are in agreement with a study conducted in north-east China that reported a high prevalence of high TG levels in women and a high prevalence of low HDL-C levels in men.44

Our study further showed that women had a high prevalence of overweight, obesity and abdominal obesity (high WC) compared to men ($p < 0.05$). This is consistent with a study conducted among participants from an urban Tanzanian population that reported a higher prevalence of obesity and abdominal obesity in women than in men.45

In this study, men with MA were found to have a significantly higher prevalence of a high HOMA compared to those without MA ($p = 0.01$), while women with MA were also found to have a higher prevalence of a high HOMA compared to those without MA ($p = 0.00$). Men with MA were found to have a lower prevalence of overweight and a higher prevalence of obesity compared to men without MA ($p < 0.05$). Women were found to have a higher prevalence of hypertension, high SBP and DBP compared to women without MA ($p < 0.05$). These results are in agreement with studies that reported that cardiovascular risk factors such as insulin resistance, obesity and hypertension were associated with MA.44-46

The prevalence of MA in this population was found to be 35.7%, which is similar to the prevalence of MA (39.7%) reported among diabetic patients attending the diabetes clinic at the Johannesburg Academic Hospital.49 In Nigeria, a study conducted at the cardiology out-patient clinic at the Ahmadu Bello University Teaching Hospital reported MA prevalence of 41.0% among patients with hypertension.50 On the other hand, the prevalence of MA in the current study was found to be lower than the 58.3% prevalence reported from a sub-analysis of a survey of 26 countries worldwide. In Botswana, the prevalence of MA has been estimated at 44.6%.51

The results of our study show that men with both high hs-CRP and high TG values were more likely to have MA compared to men with normal hs-CRP and TG levels. To the best of our knowledge this is the first study to report such an association between MA and serum TG and hs-CRP. The reason for this association is not known as only hs-CRP and TG were collectively associated with MA.

The interaction could explain the association of MA with chronic kidney disease (CKD) and CVD.52-54 CRP has been reported to be increased in patients with CKD compared to controls.54 Serum TG levels have been acknowledged by the American Medical Association as important risk factors for CVD and death.55-56 Furthermore, low-grade inflammation was found to be associated with the risk of developing CVD,55 and CRP has been established as an important predictor of cardiovascular events in CKD patients.57

Studies have reported that patients with both MA and high hs-CRP levels had low HDL-C levels.58-59 Although not similar to the present study, these studies further reported an association between MA, serum lipids and inflammatory markers. This could mean that in the current population, men with high CRP and TG levels are likely to have MA.

MA may be responsible for dyslipidaemia via the up-regulation of 3-hydroxy-3-methylglutaryl CoA reductase and an acquired deficiency of lecithin-cholesterol acyltransferase. CRP was found to promote the production of pro-inflammatory cytokines, thus leading to mesangial cell proliferation, matrix overproduction and increased vascular permeability, causing MA.23 This association could also be explained by the association of endothelial dysfunction with MA, dyslipidaemia and low-grade inflammation.52-56 Endothelial dysfunction precedes the development of MA by and has been found to be associated with inflammation and dyslipidaemia.52-57 Endothelial dysfunction has been reported as a risk factor for CVDs.58 MA is a marker of endothelial dysfunction.59 MA, dyslipidaemia and low-grade inflammation are cardiovascular risk factors.60-64 Therefore endothelial dysfunction might be associated with, or even a possible explanation of, the relationship between MA, dyslipidaemia and low-grade inflammation.

This study further showed that women with and without MA had similar levels of IL-6 and hs-CRP, while men with MA had lower hs-CRP levels compared to their counterparts without MA, but similar levels of IL-6. Studies have reported similar levels of inflammatory markers such as CRP and IL-6 and this is in agreement with the results of our study in the total population, where the levels were similar in those with and without MA. However, men with MA showed lower hs-CRP levels than those without MA. The reason for the low hs-CRP in men with MA is not known but could be due to the method of diagnosis of MA used in the present study, where we used only one urine sample, as opposed to three urine samples over a three-month period. The hypothesis that MA is associated independently with low-grade inflammation was not supported in this study.

In the present study, the levels of serum lipids such as TC, TG, HDL-C and LDL-C were found to be similar in participants with and without MA. The results of the study are in agreement with results of other studies, which found levels of TC, TG and LDL-C were similar in patients with and without MA.7,54 However, the difference was in the levels of HDL-C, which were increased in the hypertensive patients with MA in the above two studies, but in the present study, the levels were similar between those with and without MA. The comparable lipid levels also do not support the hypothesis that MA was independently associated with serum lipids in this population.

No significant association was found between MA and TG in participants in the total study population, among men and among women. The results are in agreement with other studies, which also found no association between MA and TG.7,50 In this population, MA was not independently associated with serum lipids and this can be attributed to physical activity, which was reported to be high in this population,7,52 and the diet that this population is thought to consume. An unhealthy lifestyle together with physical inactivity may increase the risk of MA.7,50 In a study conducted at the Dikgale HDSS site, the average physical activity was 11 615 steps per day (with a standard deviation of 5 139), showing that this population has a high level of physical activity.76
The study has shed light on the relationship among MA, serum lipids and inflammatory markers with confounders controlled in a rural black population. The results of the study will contribute to the discovery of markers that could possibly be used to determine which patients to screen for MA, since the screening procedure is long.

Limitations

The findings from this study should be considered in view of some limitations. Similar to other studies using a cross-sectional study design, we could not establish causality or temporality of events, and obtained at least three positive results a month apart, before a definite diagnosis, which requires a longitudinal study design. Nevertheless, we believe that the present study sheds light on the levels of MA in urine and it quantified MA among a presumably healthy black population. Furthermore, it determined the association of MA with inflammatory markers and serum lipids in a rural HDHSS site in South Africa. The results of this study cannot be generalised to other areas in South Africa, since this site is a very small rural area in one specific province and the situation may vary considerably in urban areas or with different racial populations. The reliability and validity measures for anthropometric measurements were not calculated in this study, so results are to be interpreted with caution.

Conclusion

Substantial proportions of MA, hypertension, insulin resistance, overweight and obesity, as well as high levels of serum lipids and inflammatory markers were observed in the population. Independently, serum lipids and inflammatory markers showed no association with MA in this population. However, MA was associated with high hs-CRP and TG levels among men.

We recommend in this population, participants should be screened for serum lipids, especially TG, and CRP and insulin sensitivity, and those with high TG and CRP levels, and insulin resistance should then be screened for MA, as the odds of them having MA are increased. There is a need for studies that will determine the association of MA, serum lipids and inflammatory markers while diagnosing MA with at least three urine samples over three months.

We thank the population of Dikgale HDSS site in South Africa for participating in the study. We acknowledge Professor Marianne Alberts, a mentor of the authors and the founder of the Dikgale HDSS site.

This study was funded by a Vlaamse Interuniversitaire Raad (VLIR) grant from Belgium.

References


55. Labreuche J, Deplanque D, Touboul P-J, Bruckert E, Amarenco P. Association between change in plasma triglyceride levels and risk of


