Socio-demographic and modifiable risk factors of diabetes and hypertension among resource constrained patients from rural areas in Mdantsane Township in South Africa

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Abstract

Background: Recently, developing countries have shown a dramatic increase in non-communicable diseases (NCDs). The burden of NCDs in South Africa has increased over the past years resulting in an estimated 37% of all-cause mortality and 16% of disability-adjusted life years. Currently, diabetes mellitus (DM) and hypertension (HTN) are the two most prevalent NCDs associated with the rapid increase in mortality.

Objective: To demonstrate the socio-demographic and modifiable risk factors of diabetes mellitus (DM) and hypertension (HTN) among South African adults.

Methods: A cross-sectional analytical study was conducted in the Cecilia Makiwane Hospital serving the residents of Mdantsane. Relevant socio-demographic data, anthropometric measurements, triplicate blood pressure, fasting blood glucose and lipogram analysis were obtained from 265 outpatients.

Results: Multivariate analysis shows that; salt intake, smoking, elevated triglycerides and decreased high-density lipoprotein levels were significantly associated with DM with adjusted odds ratio of 0.18 (p=0.002), 0.26 (p=0.048), 2.19 (p=0.006) and 0.38 (p=0.001), respectively. Overweight and obesity were significantly associated with hypertension with odds ratio of 0.03 (p=0.01) and 0.06 (p=0.006), respectively.

Conclusion: The burden of DM and HTN on society can be drastically reduced with simple lifestyle changes, development of preventative strategies, large-scale screening and better disease management in South Africa.

Keywords: Diabetes, hypertension, rural areas, Mdantsane Township, South Africa.

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Introduction

Non-Communicable Diseases (NCDs) have currently been identified as the leading cause of death worldwide. In the past decade developing countries have shown a dramatic increase in NCDs. The burden of NCDs in South Africa has increased over the past years resulted in an estimated 37% of all cause mortality and 16% of disability-adjusted life years. Currently, Diabetes Mellitus (DM) and hypertension (HTN) are the two most prevalent NCDs associated with the rapid increase in mortality.

DM is defined as a chronic health condition associated with elevated blood sugar levels, whilst HTN is characterized by a systolic blood pressure ≥ 140 mmHg and a diastolic blood pressure ≥ 90 mmHg. DM often co-exists with HTN since they both share common disease mechanisms and, in some instances, the one condition exacerbates the other. Currently, 425 million people are diagnosed with diabetes, whilst it is estimated that over a billion people worldwide are af-
fected with HTN.* Both diseases have strongly been associated with an increased risk of kidney failure, obesity, stroke, blindness, nerve damage and cardiovascular disease (CVD).\(^2,15-18\)

DM and HTN have been shown to have a major impact on public health funding consuming a significant proportion of public health spending. However, these are described as lifestyle diseases, thus they can be prevented or managed by drugs and lifestyle modification.\(^19-21\) Modifiable risk factors associated with DM and HTN include: tobacco use, alcohol consumption, physical activity and unhealthy diets.\(^22\) An unhealthy diet is defined, according to Forouzanfar et al.\(^22\), as a diet which is high in sodium, low in vegetables, low in fruit, low in whole grains, low in nuts and seeds, and low in seafood omega-3. Low- and middle-income countries are the most affected by these risk factors.\(^23,24\) The African region has been identified to have the highest burden of DM and HTN.\(^30,14\) In Africa, DM is estimated at 15.5 million adults aged between 20-79 years\(^31\) and HTN is estimated at 46% in adults >25 years.\(^30\) The ever-increasing numbers of individuals diagnosed with these diseases are of great concern across the world, especially in middle- and low-income countries.\(^30\) The present study highlights the burden and associated risk factors of DM and HTN in Mdantsane, a resource constrained township of South Africa. In South Africa, the burden of NCDs is predicted to increase substantially in the next decades if the necessary preventative measures are not taken.\(^25\) Furthermore, strategies need to be implemented to effectively manage these diseases.\(^26\) Currently, there are limited studies exploring the prevalence and risk factors of DM and HTN in South Africa, especially within the economically disadvantaged population. The aim of this study was to investigate the socio-demographic and modifiable risk factors of diabetes and hypertension in one of the rural areas in South Africa, with resource constrained patients. Modifiable risk factors found significantly associated with diabetes and/or hypertension could be used to promote health education as a primary intervention.

Methods

Study area and design

A cross-sectional descriptive study was conducted in the Cecilia Makiwane Hospital (Mdantsane, South Africa) from July 2017 – October 2017. Mdantsane is located in the Buffalo Municipality and is a low-income residential township with a population of approximately 150000.\(^27\) The objectives of the study were explained to all participants and each participant signed a consent form indicating voluntary participation in the study. Information sheets were provided in both English and IsiXhosa languages. Prior to sampling, participants underwent physical examination and medical history was recorded.

Study population and sampling

Inclusion criteria for participants in this study were individuals aged ≥18 years and have been diagnosed with hypertension and/or diabetes for more than a year prior to the study. Exclusion criteria included pregnant women, patients diagnosed with type 1 diabetes and acute illnesses. Age, sex, monthly income, level of education, lifestyle profile (i.e. physical activity, smoking status, alcohol and diet), and family history of disease prevalence were obtained through interview from all of the participants. The use of anti-hypertensive and antidiabetic medications along with the durations of disease(s) was obtained from the patients’ medical records. Eligible participants (N=265) were recruited sequentially at the study setting over the study period.

Data collection

A trained research nurse conducted anthropometric measurements of: weight to the nearest 0.1 kg, height to the nearest of 0.1 cm using a stadiometer, waist circumference, hip circumference and upper-arm circumference was measured using a tape measure. Measurements were taken with all participants wearing minimal clothing and no shoes. Blood pressure (BP) was measured using a validated automated digital blood pressure monitor (Microlife® BP A100 Plus). BP was recorded in triplicate and the average was used for analysis. Blood glucose was measured using Accutrend® test strips. Body Mass Index (BMI) for each patient was calculated as weight (kg) divided by height (m)\(^2\) and was categorised based on WHO criteria: underweight (<18.5 kg/m\(^2\)), normal weight (18.5-24.9 kg/m\(^2\)), overweight (25.0-29.9 kg/m\(^2\)) and obese (30 or greater kg/m\(^2\)). Patients with systolic BP (SBP) of ≥140 mmHg and ≥90 diastolic BP (DBP) were identified as hypertensive and patients with systolic and diastolic BP below 140 mmHg and 90 mmHg respectively were identified as normotensive.
Laboratory assessment
Fasting venous blood was obtained for all patients. The lipid profile which includes: total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL) and high-density lipoprotein (HDL) for each participant was categorized according to the guidelines of the Heart and Stroke Foundation of South Africa. In addition to this, the glycosylated haemoglobin (HbA1c) was assayed from blood samples of diabetic participants. All blood samples were sent to the clinical laboratory centre, i.e. National Health Laboratory Services (NHLS) of Cecilia Makiwane hospital and the East London private hospital.

Statistical analysis
Statistical analysis was performed using Statistical Package for Social Science (SPSS) version 25 for Windows (SPSS Inc., Chicago, IL, USA). The clinical laboratory data and anthropometric measurements were expressed as mean (n) ± standard deviation (SD). Differences between groups were assessed using chi-square test for statistical significance. Risk factors associated with DM and HTN are presented as percentages with the odds ratios (ORs) and 95% confidence intervals (CIs). The p-value ≤0.05 were considered statistically significant.

Results
In the study cohort, a total of 265 outpatients (of which n=175 were female and n=90 were male) were interviewed during a 3-month study (Table 1). The mean ages of men and women were 59.96±11.19 and 61.32±11.60 years, respectively. Other demographic, anthropometric and clinical laboratory measurements of the study participants are indicated in (Table 1).

Table 1: Characteristics of the study subjects in Mdantsane, Eastern Cape (July 2018).

| Parameter                      | Female (n=175) | Male (n=90) | Total (n=265) |
|-------------------------------|---------------|-------------|---------------|
| Age (years)                   | 59.96±11.19   | 61.32±11.6  | 60.42±11.32   |
| Weight (Kg)                   | 87.45±21.46   | 81.62±16.06 | 85.46±19.94   |
| Height (cm)                   | 159.93±6.22   | 168.10±11.66| 162.72±9.30   |
| BMI (Kg/m²)                   | 34.18±8.27    | 29.77±12.93 | 32.68±10.29   |
| HbA1c (%)*                    | 10.40±2.80 (n=85) | 10.48±3.91 (n=32) | 10.42±3.12 (n=117) |
| FBG (mmol/l)*                 | 12.65±5.11 (n=85) | 13.11±3.92 (n=32) | 12.78±4.80 (n=117) |
| Systolic blood pressure (mmHg) | 155.67±20.53  | 157.04±21.65| 156.14±20.88  |
| Diastolic blood pressure (mmHg) | 92.56±13.18   | 93.87±13.45 | 93.00±13.26   |
| Heart rate (pbm)              | 84.14±13.60   | 80.01±14.43 | 82.74±13.99   |
| TC (mmol/L)                   | 5.02±1.27     | 4.53±1.14   | 4.86±1.25     |
| HDL (mmol/L)                  | 1.30±0.36     | 1.35±0.44   | 1.31±0.39     |
| LDL (mmol/L)                  | 2.63±1.14     | 2.35±0.98   | 2.54±1.09     |
| TG (mmol/L)                   | 1.71±1.01     | 1.88±1.06   | 1.77±1.03     |

Table 2 and 3 indicates the socio-demographic and modifiable risk factors of non-diabetic and diabetic groups as well as among non-hypertensive and hypertensive groups. It is important to note that approximately 40% of the study cohort was co-morbid. In both NCDs, the proportion of females is higher than males, however, sex was only shown to be significantly associated amongst diabetic patients (p-value = 0.043). Amongst diabetic patients, smoking status, salt intake, TG and HDL were all significantly associated with disease incidence with p-values of 0.015; 0.004, 0.012 and 0.003 respectively (Table 2). All other factors, i.e. age,
educational level, physical activity, alcohol consumption, TC and LDL were not significantly associated with DM (Table 2). BMI was the only modifiable risk factor that showed significant association amongst hypertensive patients with a p-value of <0.0001 (Table 3). Factors not significantly associated with HTN were: sex, age, educational level, smoking status, physical activity, salt intake, and alcohol consumption, TC, TG, LDL and HDL (Table 3).

Table 2: Socio-demographics and Modifiable risk factors among diabetes (n=265).

| Variables          | Subgroups          | Non-diabetic (n=148) | Diabetic (n=117) | X², P Value |
|--------------------|--------------------|----------------------|------------------|-------------|
| Gender             | Male               | 58 64.4              | 32 35.5          | 4.08, 0.040 |
|                    | Female             | 90 51.4              | 85 48.6          |             |
| Age                | Less than 50 years | 28 63.6              | 16 36.4          |             |
|                    | More than 50 years | 120 54.3             | 101 45.7         | 1.30, 0.260 |
| Educational level  | No formal education| 12 60.0              | 8 40.0           |             |
|                    | Primary education  | 34 54.0              | 29 46.0          |             |
|                    | Secondary education| 97 58.1              | 70 41.9          | 4.78, 0.190 |
|                    | Higher education   | 4 28.6               | 10 71.4          |             |
| Smoking status     | Never smoked       | 99 52.1              | 91 47.9          |             |
|                    | Quit smoking       | 29 56.9              | 22 43.1          |             |
|                    | Current smoker     | 20 83.3              | 4 16.7           |             |
| Physical activity  | More than 3 times/week | 8 50.0            | 8 50.0          |             |
|                    | 1-2 times/week     | 119 54.6             | 92 43.4          | 0.25, 0.880 |
|                    | No physical activities | 21 55.3        | 17 44.7          |             |
| Salt intake        | No salt intake     | 11 37.9              | 18 62.1          |             |
|                    | Normal salt intake | 103 53.9             | 88 46.1          | 11.15, 0.004 |
|                    | Increased salt intake | 34 75.6         | 11 24.4          |             |
| Alcohol consumption| Never drank        | 78 54.9              | 64 45.1          | 3.63, 0.160 |
|                    | Quit drinking      | 40 50.6              | 39 49.4          |             |
|                    | Occasional drinking| 30 68.2              | 14 31.8          |             |
| BMI (Kg/m²)        | <18.5              | 4 57.1               | 3 42.9           |             |
|                    | 18.5-24.9          | 21 55.3              | 17 44.7          |             |
|                    | 25.0-29.9          | 37 53.6              | 32 46.4          | 0.28, 0.960 |
|                    | ≥30                | 86 57.3              | 64 42.7          |             |
| TC (mmol/L)        | Increased          | 52 46.8              | 59 53.2          |             |
|                    | Normal             | 96 56.8              | 58 43.2          | 0.15, 0.700 |
| TG (mmol/L)        | Increased          | 52 46.3              | 59 53.7          |             |
|                    | Normal             | 95 62.3              | 58 37.7          | 6.28, 0.012 |
| HDL (mmol/L)       | Decreased          | 74 67.3              | 36 32.7          |             |
|                    | Normal             | 69 48.6              | 73 51.4          | 8.81, 0.003 |
| LDL (mmol/L)       | Increased          | 50 56.8              | 38 43.2          |             |
|                    | Normal             | 98 55.4              | 79 44.6          | 0.05, 0.820 |

TC= Total Cholesterol, TG= Triglyceride, HDL= High density lipoprotein, LDL= Low density lipoprotein, mmol= mill mole, L= litre. Location: Mdantsane, Eastern Cape (July 2018)
Table 3: Factors affecting the Modifiable risk factors of hypertension in study subjects (n=265).

| Variables               | Subgroups      | Group          | Non-hypertensive | Hypertensive | X², P value |
|-------------------------|----------------|----------------|------------------|--------------|-------------|
|                         |                | n= 13          | %                | n= 252       | %          |
| Gender                  | Male           | 6              | 6.6              | 84           | 93.3        | 0.91, 0.34  |
|                         | Female         | 7              | 4                | 168          | 96          |             |
| Age                     | Less than 50 years | 4              | 9.1              | 40           | 90.9        | 1.98, 0.16  |
|                         | More than 50 years | 9              | 4.1              | 212          | 95.9        |             |
| Educational level       | Uneducated     | 0              | 0                | 20           | 100         |             |
|                         | Primary        | 4              | 6.3              | 59           | 93.7        |             |
|                         | Secondary      | 8              | 4.8              | 159          | 95.2        | 1.46, 0.69  |
|                         | High education | 1              | 7.1              | 13           | 92.9        |             |
| Smoking status          | Never smokers  | 8              | 4.2              | 182          | 95.8        |             |
|                         | Quit smokers   | 4              | 7.8              | 47           | 92.2        | 1.17, 0.56  |
|                         | Current smokers| 1              | 4.2              | 23           | 95.8        |             |
| Physical activity       | More than 3 times / week | 0           | 11.1             | 16           | 88.9        |             |
|                         | 1-2 times/ week | 11             | 4.3              | 200          | 95.7        | 0.88, 0.64  |
|                         | No physical activities | 2           | 5.3              | 36           | 94.7        |             |
| Salt intake             | No salt intake | 0              | 0                | 29           | 100         |             |
|                         | Normal salt intake | 10            | 5.2              | 181          | 94.8        | 1.84, 0.40  |
|                         | Increased salt intake | 3           | 6.7              | 42           | 93.3        |             |
| Alcohol consumption     | Never drank    | 4              | 2.8              | 138          | 97.2        | 3.32, 0.19  |
|                         | Quit drinking  | 5              | 6.3              | 74           | 93.7        |             |
|                         | Occasional drinker | 4           | 9.1              | 40           | 90.9        |             |
| BMI (Kg/m²)             | <18.5          | 2              | 28.6             | 5            | 71.4        | 21.34, <0.0001 |
|                         | 18.5-24.9      | 6              | 15.8             | 32           | 84.2        |             |
|                         | 25.0-29.9      | 1              | 1.4              | 68           | 98.6        |             |
|                         | ≥30            | 4              | 2.7              | 146          | 97.3        |             |
| TC (mmol/L)             | Increased      | 5              | 4.9              | 98           | 95.1        | 0.001, 0.98 |
|                         | Normal         | 8              | 4.9              | 154          | 95.1        |             |
| TG (mmol/L)             | Increased      | 4              | 3.5              | 107          | 96.5        | 0.69, 0.41  |
|                         | Normal         | 9              | 5.8              | 145          | 94.2        |             |
| HDL (mmol/L)            | Decreased      | 2              | 1.8              | 108          | 98.2        | 2.37, 0.12  |
|                         | Normal         | 8              | 5.6              | 134          | 94.4        |             |
| LDL (mmol/L)            | Increased      | 4              | 4.5              | 84           | 95.5        | 0.04, 0.85  |
|                         | Normal         | 9              | 5.1              | 168          | 94.9        |             |

TC= Total Cholesterol, TG= Triglyceride, HDL= High density lipoprotein, LDL= Low density lipoprotein, mmol= millmole, L= litre. Location: Mdantsane, Eastern Cape (July 2018)

Table 4 and 5 describe the univariate and multivariate analyses for diabetes and hypertension. The univariate results show a risk association between diabetes and smoking status, salt intake, TG and HDL (Table 4). The results gave an indication that smoking status has an impact on diabetes using never smoked as the reference, those who quit smoking had significantly lesser odds (p-value = 0.824) of diabetes in comparison to those who are currently smokers (p-value = 0.048) (Table 4). Furthermore, an increased salt intake, increased TG and a decreased HDL-C also demonstrated significantly higher odds (p-value = 0.01) of diabetes. Gender was not significantly associated with diabetes (p-value = 0.210). In table 5, an increased BMI in comparison to the underweight (as per WHO standards) has higher odds of hypertension (p-value=0.012 and p-value=0.006). In addition to this, participants who have normal BMI have lower odds of hypertension (p-value = 0.420).

Multivariate logistic regression analysis showed that after adjusting for all significant factors, an increased salt intake and BMI were significantly associated with DM and HTN respectively (Table 4 and 5).
### Table 4: Univariate and Multivariate analysis for risk factors of Diabetes status

| Factors            | Diabetic N (%) | Non-Diabetic N (%) | Unadjusted Odds ratio | Adjusted odds ratio | P-value |
|--------------------|----------------|--------------------|-----------------------|---------------------|---------|
| **Sex**            |                |                    |                       |                     |         |
| Male               | 32 (35.6)      | 58 (64.4)          | 1                     | 1                   | 1       |
| Female             | 90 (51.4)      | 85 (48.6)          | 1.71 (1.01-2.89)*     | 1.55 (0.78-3.1)     | 0.212   |
| **Salt intake**    |                |                    |                       |                     |         |
| No salt intake     | 18 (62.1)      | 11 (37.9)          | 1                     | 1                   | 0.009   |
| Normal salt intake | 88 (46.1)      | 103 (53.9)         | 0.52 (0.23-1.17)      | 0.54 (0.19-1.08)    | 0.075   |
| increased salt intake | 11 (24.4) | 34 (75.6)          | 0.2 (0.07-0.54)*      | 0.18 (0.06-0.55)*   | 0.002*  |
| **Smoking status** |                |                    |                       |                     |         |
| Never smoke        | 91 (47.9)      | 99 (52.1)          | 1                     | 1                   | 1       |
| Quit smoking       | 22 (43.1)      | 29 (56.9)          | 0.83 (0.44-1.54)      | 1.09 (0.51-2.36)    | 0.824   |
| Current smokers    | 4 (16.7)       | 20 (83.3)          | 0.22 (0.07-0.66)*     | 0.26 (0.07-0.98)    | 0.048*  |
| **TG-Cholesterol** |                |                    |                       |                     |         |
| Normal level       | 58 (37.7)      | 96 (62.3)          | 1                     | 1                   | 1       |
| Increased level    | 59 (53.2)      | 52 (46.8)          | 1.88 (1.15-3.08)*     | 2.19 (1.3-3.8)      | 0.006*  |
| **HDL-Cholesterol** |               |                    |                       |                     |         |
| Normal level       | 73 (51.4)      | 69 (48.6)          | 1                     | 1                   | 1       |
| Decreased level    | 36 (32.7)      | 74 (67.3)          | 1.06 (0.27-0.77)*     | 0.38 (0.22-0.67)    | 0.001*  |

*P-value <0.05. Location: Mdantsane, Eastern Cape (July 2018)
Table 5: Univariate and Multivariate analysis for risk factors of hypertension

| Factors         | Hypertensive N (%) | Non-hypertensive N (%) | Unadjusted Odds ratio | Adjusted odds ratio | P-value |
|-----------------|--------------------|------------------------|-----------------------|---------------------|---------|
| BMI             |                    |                        |                       |                     |         |
| <18.5           | 5 (71.4)           | 2 (28.6)               | 1                     | 1                   |         |
| 18.5-24.9       | 32 (84.2)          | 6 (15.8)               | 0.47 (0.07-3.0)       | 0.35 (0.048-2.56)   | 0.304   |
| 25.0-29.9       | 68 (98.6)          | 1 (1.4)                | 0.04 (0.003-0.48)*    | 0.03 (0.002-0.44)*  | 0.010*  |
| ≥30             | 146 (97.3)         | 4 (2.7)                | 0.07 (0.01-0.47)*     | 0.06 (0.007-0.447)* | 0.006*  |

Smoking status

|               | Never smoke | Quit smoking | Current smokers |
|---------------|-------------|--------------|-----------------|
| Never smoke   | 182 (95.8)  | 47 (92.2)    | 23 (95.8)       |
| Quit smoking  | 8 (4.2)     | 4 (7.8)      | 1 (4.2)         |
| Current smokers |           |              | 0.99 (0.012-8.3) |

Alcohol consumption

|               | Never drank | Quit drinking | Occasional drinker |
|---------------|-------------|---------------|--------------------|
| Never drank   | 138 (97.2)  | 74 (93.7)     | 40 (90.9)          |
| Quit drinking | 4 (2.8)     | 5 (6.3)       | 4 (9.1)           |
| Occasional drinker |    | 2.33 (0.61-8.95) | 3.45 (0.83-14.4) |

*P-value <0.05

Location: Mdantsane, Eastern Cape (July 2018)

Discussion

South Africa has been reported to have the highest incidence of DM in the African continent. Amongst the modifiable risk factors, significant association was shown with tobacco intake, increased salt intake, TG and HDL. Tobacco smoking is well established as a risk factor for multiple diseases and has been associated with DM in multiple cohort studies. The present study showed that smoking was associated with the probability of developing DM. This finding is consistent with previous studies conducted in Korea. Current smokers and ex-smokers display a greater probability of developing DM than non-smokers, however in this study, the increased risk of ex-smokers were not statistically significant. Previous studies conducted by Jee et al. and Hur et al. also reported the increased risk of ex-smokers as insignificant.

The WHO (2016) recommends that patients with DM should reduce their dietary salt intake. The precise relationship between dietary salt intake and DM is not well defined, however, excessive salt intake is well associated with hypertension and CVDs. In the present study, an increased salt intake was significantly associated with the higher incidence of DM. Previous studies also demonstrated an association between high dietary salt intake and DM. Increased TG levels have been associated with an increased risk of DM and in this study cohort, similar results were observed. In addition, this study also found that the odds of having DM were increased with a decrease in HDL. Similar findings have been reported in African, European and United States communities. Lower levels of HDL concentrations have been associated with many diseases such as CVDs, nephropathy and coronary heart disease. Although, levels of TC and LDL in diabetic individuals are reportedly comparable with that found in non-diabetics, low levels of HDL and elevated TG have been reported in T2DM patients as the probable cause of CVD. It has also been observed that HDL alone might not be a good indicator of increase DM risk since most of the subjects had lower total cholesterol. Moreover, lower levels of HDL in the present study might be because of the lower cholesterol. A high BMI is a risk factor that is often associated with
DM, however, in this study; it was significantly associated with HTN, since DM and HTN co-exist in approximately 40% of the study cohort, this could be an explanation for this observation. Furthermore, many studies suggest that a high BMI contributes to hypertension. It is well established that smoking increases the risk of hypertension; however, the significance of this association may differ between populations. In this study, no significant association was observed between hypertension and smoking status. These findings are contrary to other studies.

The following limitations need to be considered; the cross-sectional design and recruitment of participants from one study centre might limit the generalisation of the findings. In addition, the scope of this study needs more samples drawn from broader population across the country to conclude on an association that exists between DM and HTN with the discussed variables.

Conclusion
DM was associated with smoking and salt intake; whilst hypertension was associated with increasing BMI. Development of best practices for affordable and effective programs in screening, prevention, detection and treatment of DM and HTN is essential. In order to reduce the burden of NCDs, comprehensive intervention strategies should be implemented across the country. Future studies with larger sample size should be done to identify or generate local modifiable risk factors for the development of DM and HTN.

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Ethical clearance
Ethical approval for this study was approved by the ethics committees of the University of the Western Cape (UWC) and the Eastern Cape Department of Health (Ethics Reference Number: BM/16/5/19).

Declaration of authorship
MB, LX, BP, OVA, RJ conceived and designed the study; LX acquired and prepared the data; LX and MMM analysed and interpreted the data; LX and ZAO drafted the manuscript; LX, ZAO and MMM revised the manuscript for important intellectual content; all authors gave approval of the version to be submitted and agree to be accountable for all aspects of the work.

Competing interests
All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.

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