Hypertension and diabetes mellitus: a collision of two heavyweight non-communicable diseases

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Introduction: Patients living with type 2 diabetes mellitus (PLWD) are at an increased risk of developing hypertension (HPT). The presence of HPT in PLWD (PLWDH) accelerates diabetes-related complications (DRC). Scarce data exist from South Africa on the impact of HPT in PLWD.

Methods: Data were captured from Edendale Hospital diabetes clinic datasheets from January 1, 2019 to December 31, 2019 and analysed to determine differences in demographic, clinical and biochemical variables between PLWD and PLWDH.

Results: Data from 822 PLWD were analysed, the majority having HPT (713, 86.74%). The prevalence of HPT, resistant HPT (RHPT) and the number of antihypertensives used increased with age and diabetes duration. PLWDH had statistically poorer lipid control (LC), higher creatinine, waist circumference (WC), increased prevalence of sensory peripheral neuropathy, non-proliferative and proliferative retinopathy, cerebrovascular accidents, proteinuria and renal impairment. The significant majority of PLWDH were not meeting diabetes targets (glycaemic, lipid, BMI, WC). The bulk of PLWDH were on combination antihypertensive therapy (p < 0.001) and performed significantly better than monotherapy for glycaemia, LC, BMI and WC. Proteinuria and blood pressure (BP) improved significantly as the number of antihypertensives increased. One-fifth (151, 18.37%) of PLWDH had RHPT; this was more common in females (p < 0.001). PLWD with RHPT had a significantly higher LDL cholesterol, BMI, and urine protein–creatinine ratio (p < 0.001). Over one-quarter (29.87%) of the PLWDH without HPT had a BP over 140/90 mmHg.

Conclusion: It was shown that HPT, RHPT and obesity are significant comorbidities in PLWD and increase the risk of DRC. The majority of PLWDH are not meeting targets, which places them at increased risk of DRC. BP, glycaemic and LC and proteinuria improved in those on combination antihypertensive therapy. A significant proportion of PLWD without HPT had elevated BP, and thus were potentially undiagnosed hypertensives needing intervention.

Keywords: BMI, COVID-19 infection, diabetes mellitus, glycaemic control, hypertension, lipid control, macrovascular complications, microvascular complications, obesity, proteinuria, resistant hypertension, waist circumference

Introduction

Non-communicable diseases (NCDs) are placing a tremendous burden on the South African population, both at patient and at fiscal levels.1–3 Diabetes mellitus (DM), hypertension (HPT) and obesity, three of the major NCDs, have been shown to possess interrelated pathophysiology. Patients living with DM without HPT (PLWD) are at a twofold increased risk of developing HPT, which is secondary to hyperinsulinemia.4–5 The presence of HPT in these PLWD increases and accelerates the risk of developing both micro- and macro-vascular complications.4–6 Obesity is related to the development of both HPT and DM on the basis of insulin resistance.7–8

HPT is a global pandemic affecting approximately 35% of the South African population. The majority of patients with HPT living in South Africa, other parts of Africa and in developing countries are either uncontrolled or undiagnosed.9–10 Studies have demonstrated that a significant proportion (up to 70%) of PLWD have HPT.11 Control of blood pressure (BP) in PLWD is paramount, as illustrated by the United Kingdom Prospective Diabetes Study (UKPDS), which showed that tight blood pressure control decreases the overall risk of death, complications of DM and progression of retinopathy.11

The South African diabetes and hypertension guidelines have proposed a blood pressure target of less than 140/90 mmHg in PLWD without albuminuria and less than 130/80 mmHg for those with albuminuria.12–13

The purpose of this descriptive, comparative study was to describe and compare the current state of diabetes control achieved in PLWD with and without HPT in type 2 DM patients visiting the Edendale Hospital diabetes clinic from January 1, 2019 to December 31, 2019. Clinical and biochemical data collected from patient data sheets were used to perform these comparisons between patients living with diabetes and hypertension (PLWDH) and PLWD. In this study, we delved deeper into the prevalence of resistant hypertension (defined as a blood pressure reading of greater than 140/90 despite being on three antihypertensive medications on a maximal dose, one of which is a diuretic) among these PLWDH.13 We also assessed and reported on the number of PLWDH that were achieving the Society of Endocrinology, Metabolism and Diabetes of South Africa (SDEMDSA) targets for blood pressure, glycaemic and lipid control, body mass index (BMI), waist circumference (WC) and urine proteinuria. We compared clinical and biochemical variables between the cohort of PLWDH who were and those who were not achieving target BP.

The results of this study help identify the prevalence of uncontrolled hypertension amongst these PLWD and can help the government better identify strategies and implement measures to improve BP control in PLWD.
Methods

Edendale Hospital is a regional hospital based in Pietermaritzburg, KwaZulu-Natal, South Africa. In 2012, a diabetes datasheet was introduced into this diabetes clinic, which ensured that for all patients who were seen for consultation at this clinic this was done in a comprehensive and structured manner. This datasheet has been approved by the University of KwaZulu-Natal Biomedical Research and Ethics Committee (BCA 194/15).

This was a retrospective, quantitative, observational, analytic cross-sectional study and was approved by the University of KwaZulu-Natal Biomedical Research and Ethics Committee (BREC 2589/2021). Data were captured from these diabetes datasheets for all patients living with type 2 diabetes mellitus who were seen for consultation at this diabetes clinic from January 1, 2019 to December 31, 2019. The following demographic, clinical and biochemical variables were captured and interrogated for this study: age (years), duration of DM, presence of HPT, names and dosages of antihypertensive therapy, HIV status, glycated haemoglobin (HbA1c), systolic and diastolic blood pressures (mmHg), total cholesterol, triglyceride, HDL and LDL cholesterol (mmol/l), creatinine (mmol/l), glomerular filtration rate (GFR), random blood glucose (mmol/l), waist circumference (cm), body mass index (kg/m2), complications of DM (retinopathy—proliferative and non-proliferative), peripheral sensory neuropathy, nephropathy defined by GFR < 60, cerebrovascular accident (CVA), glaucoma/cataracts, and urine protein creatinine ratio (PCR).

The 2017 SEMDSA targets for glycaemia, lipids, blood pressure, BMI, waist circumference and urine PCR in PLWD were used for this study.12

The Adam® MDW-300L scale (Adam Equipment Inc, Oxford, CT, USA), was used to measure height, weight and BMI while an Accu-Chek Active® glucometer (Roche Diabetes Care Inc, Indianapolis, IN, USA) was used to measure random blood glucose. The Mindray® VS-800 machine (Mindray Medical International, Shenzhen, China) was utilised to obtain patient blood pressure and pulse.

The Bio-Rad® D-10 machine (Bio-Rad Laboratories, Hercules, CA, USA), which was National Glycohemoglobin Standardization Program-accredited, was used by the National Health Laboratory Services (N HLS) to calculate the HbA1c values, to ensure the HbA1c standardisation. The NHLS classifies a urine protein–creatinine ratio (PCR) of < 0.015 as normal.

GFR (ml/min/1.73 m²) was calculated using the Modified Diet in Renal Disease (MDRD) formula: GFR=186 × (creatinine (mmol/l)/88.4) −1.154 × (age) −0.203 × (0.742 if female) × (1.210 if black).14

Data collection and statistical analysis

Descriptive statistics (mean and standard deviation or median and interquartile range as appropriate) was used to describe the sample groups. Continuous variable group means were compared using unpaired t-tests for normally distributed data; otherwise, non-parametric (Mann–Whitney U) methods were used. A p-value of < 0.05 was regarded as statistically significant.

Results

A total of 822 PLWD were seen for consultation during the study period, the majority (713, 86.74%) having hypertension. PLWDH were significantly older than those PLWD (p < 0.001). We demonstrated that the prevalence of HPT increased with age (Figure 1) and duration of DM (Table 1). Within this cohort of PLWDH, female patients predominated (p < 0.001). Approximately one-sixth of the PLWDH were HIV-infected (109, 15.29%). We showed that PLWDH had significantly poorer control of triglycerides (p = 0.008) and higher creatinine levels (p < 0.001). There was no significant difference noted in glycaemic control between PLWD and PLWDH. We showed that PLWDH had significantly higher waist circumferences (WC) when compared with the PLWD cohort (p < 0.001), with females higher than men (p < 0.001). A significant proportion of PLWDH had evidence of a GFR < 60 (43.34% vs. 8.26%, p < 0.001, respectively). PLWDH also had a greater prevalence of diabetes-related complications when compared with PLWD (sensory peripheral neuropathy, non-proliferative and proliferative retinopathy, CVA, GFR < 60, higher urine PCR, p < 0.001). (Table 1).

Antihypertensive medication used in PLWDH

Table 2 demonstrates that the majority of PLWDH were on combination therapy. These PLWDH on combination therapy performed significantly better than those on monotherapy in terms of glycaemic and lipid control, target BMI, blood pressure and waist circumference.

Figure 1: Association between age and hypertension in PLWD.
Table 1: Demographics of PLWD with and without hypertension

| Demographics                                      | No (n = 109, 13.26%) | Yes (n = 713, 86.74%) | p-value |
|---------------------------------------------------|-----------------------|-----------------------|---------|
| Median ± IQR: Age (years)                         | 41 (35–49)            | 59 (53–67)            | < 0.001 |
| Age categories (years), n (%):                    |                       |                       |         |
| • ≤ 30                                            | 12 (11.01)            | 2 (0.28)              | 0.01    |
| • 30–40                                           | 42 (38.53)            | 28 (3.39)             | 0.09    |
| • 41–50                                           | 32 (29.36)            | 111 (15.57)           | < 0.001 |
| • 51–60                                           | 14 (12.84)            | 258 (36.18)           | < 0.001 |
| • 61–70                                           | 6 (5.50)              | 202 (28.33)           | < 0.001 |
| • 71–80                                           | 3 (2.75)              | 87 (12.20)            | < 0.001 |
| • ≥ 90                                            | 0                     | 23 (3.23)             | < 0.001 |
| n (%):                                            |                       |                       |         |
| • Males                                           | 43 (39.45)            | 183 (25.67)           | < 0.001 |
| • Females                                         | 66 (60.55)            | 530 (74.33)           | < 0.001 |
| • HIV-infected                                     | 20 (18.34)            | 109 (15.29)           | < 0.001 |
| Duration of DM (years)                            | 4 (1–10)              | 10 (4–17)             | < 0.001 |
| Median ± interquartile range (IQR):               |                       |                       |         |
| • Systolic BP (mmHg)                              | 121 (118.5–133.5)     | 137 (122–157)         | < 0.001 |
| • Diastolic BP (mmHg)                             | 80 (69–85.5)          | 79 (70–88)            | 0.523   |
| • HbA1c (%)                                       | 9.4 (7.7–10.8)        | 9.4 (7.6–11.2)        | 0.962   |
| • Total cholesterol (mmol/l)                      | 4.3 (3.6–5.2)         | 4.5 (3.7–5.3)         | 0.259   |
| • Triglyceride (mmol/l)                           | 1.37 (0.93–2.01)      | 1.63 (1.1–2.4)        | 0.008   |
| • LDL cholesterol (mmol/l)                        | 2.45 (1.83–3.2)       | 2.38 (1.75–3.12)      | 0.869   |
| • HDL cholesterol (mmol/l)                        | 1.16 (1.0–1.37)       | 1.19 (0.99–1.43)      | 0.694   |
| • Creatinine (umol/l)                             | 69 (61–81)            | 89.5 (69–128.5)       | < 0.001 |
| • Random blood glucose (mmol/l)                   | 9.3 (5.8–14)          | 10.7 (7–15.1)         | 0.259   |
| • Waist circumference (cm):                       | 102 (90–112.5)        | 108 (99–118)          | 0.009   |
| • Males                                           | 97 (80–110)           | 99 (90–108.5)         | 0.343   |
| • Females                                         | 104.5 (95–114)        | 110 (102–120)         | 0.003   |
| • BMI (kg/m²):                                    | Total                 |                       |         |
| • Total                                           | 31 (26–36.5)          | 32.75 (28–38)         | 0.383   |
| • Males                                           | 27 (22–33)            | 28 (25–33)            | 0.455   |
| • Females                                         | 34 (30–39)            | 34 (30–39)            | 0.946   |
| • Urine PCR – Overall                             | 0.94 (0.01–0.03)      | 0.03 (0.016–0.094)    | 0.005   |
| • Female                                          | 0.012 (0.009–0.023)   | 0.028 (0.016–0.08)    | 0.010   |
| • Male                                            | 0.024 (0.012–0.03)    | 0.059 (0.016–0.144)   | 0.021   |
| N (%) of pts with GFR (ml/min/1.73m²):            |                       |                       |         |
| • < 15                                            | 0                     | 18 (2.53)             | < 0.001 |
| • 15–30                                           | 1 (0.92)              | 75 (10.51)            | < 0.001 |
| • 30–45                                           | 2 (1.83)              | 100 (14.03)           | < 0.001 |
| • 45–60                                           | 6 (5.50)              | 116 (16.27)           | < 0.001 |
| • > 60                                            | 87 (79.82)            | 326 (45.72)           | < 0.001 |
| • Combined, n (%) of pts with GFR < 60            | 9 (8.26)              | 309 (43.34)           | < 0.001 |
| Complications, n (%):                             |                       |                       |         |
| • Sensory peripheral neuropathy                   | 26 (23.85)            | 318 (44.60)           | < 0.001 |
| • Non-proliferative retinopathy                   | 3 (2.75)              | 76 (10.65)            | < 0.001 |
| • Proliferative retinopathy                       | 0                     | 22 (3.09)             | < 0.001 |
| • Cataract                                        | 4 (3.67)              | 77 (10.80)            | < 0.001 |
| • Glaucoma                                        | 1 (0.92)              | 20 (2.81)             | < 0.001 |
| • CVA                                             | 2 (1.83)              | 30 (4.21)             | < 0.001 |
| Therapy, n (%):                                   |                       |                       |         |
| • Oral antidiabetic drugs                         | 56 (51.37)            | 342 (47.97)           | < 0.001 |
| • Insulin monotherapy                             | 94 (86.24)            | 623 (87.37)           | < 0.001 |
| • Oral antidiabetic drugs + insulin combination   | 41 (37.61)            | 254 (35.62)           | < 0.001 |
| n (%) of pts performing self-monitoring of blood glucose (SMBG) | 77 (70.64) | 557 (78.12) | < 0.001 |
Table 2: Classes of antihypertensive therapy

| Factor                        | *HCT, N = 26 | Enalapril, N = 74 | HCT + wnalapril, N = 245 | Amlodipine, N = 40 | Amlodipine+ HCT combined, N = 270 | Hydralazine alone, N = 1 | Doxazocin XL alone, N = 2 | HCT + wnalapril+ amlodipine combined, N = 163 | HCT + enalapril+ Norvasc ± hydralazine ± doxazocin XL, N = 59 |
|-------------------------------|--------------|-------------------|--------------------------|-------------------|----------------------------------|--------------------------|--------------------------|-----------------------------------------------|-------------------------------------------------|
| Systolic BP                   | 149.5 (118–167) | 133.5 (120–156) | 131 (119–148)           | 138 (133–152)     | 135 (120–154)                    | 125 (125)                | 159.5 (155–164)            | 132 (120–148)                        | 132 (121–152)                                  |
| Diastolic BP                  | 83.5 (74–92)  | 81 (71–89)       | 79 (70–87)              | 77 (70–85)        | 80 (70–88)                       | 59 (59)                  | 77 (65–89)                | 79 (70–88)                           | 80 (70–86)                                    |
| Target BP Achieved in patients with urine PCR < 0.015 | 1 (3.85) | 3 (4.05) | 17 (6.94) | 3 (7.5) | 17 (6.3) | 0 | 0 | 12 (7.36) | 8 (13.56) |
| Target BP Achieved in patients with urine PCR > 0.015 | 1 (3.85) | 11 (14.86) | 27 (11.02) | 4 (10) | 29 (10.74) | 0 | 0 | 18 (11.04) | 6 (10.17) |
| Target achieved, n (%)        |              |                   |                        |                   |                                  |                          |                          |                                |                                                |
| HbA1c ≤ 7%                    | 4 (15.38)    | 11 (14.86)       | 37 (15.10)             | 4 (10.0)          | 46 (17.04)                       | 1 (100)                  | 0                         | 26 (15.95)                           | 12 (20.33)                                    |
| Total cholesterol < 4.5 mmol/l| 10 (38.46)   | 33 (44.59)       | 117 (47.76)            | 21 (52.5)         | 129                              | 1 (100)                  | 1 (50)                    | 82 (50.31)                           | 30 (50.85)                                    |
| LDL cholesterol < 1.8 mmol/l  | 3 (11.54)    | 12 (16.22)       | 38 (15.51)             | 10 (25)           | 48                               | 0                        | 0                         | 28 (17.18)                           | 8 (13.56)                                     |
| HDL > 1 mmol/l in males       | 4 (15.38)    | 9 (12.16)        | 32 (13.06)             | 5 (12.5)          | 40                               | 0                        | 0                         | 23 (14.11)                           | 10 (16.95)                                    |
| HDL > 1.2 mmol/l in females   | 8 (30.77)    | 21 (28.38)       | 71 (28.98)             | 11 (27.5)         | 89                               | 0                        | 1 (50)                    | 51 (31.29)                           | 20 (33.90)                                    |
| Triglyceride < 1.7 mmol/l     | 13 (50)      | 38 (51.35)       | 117 (47.76)            | 18 (45)           | 138                              | 1 (100)                  | 1 (50)                    | 80 (49.08)                           | 32 (54.24)                                    |
| BMI < 25 kg/m²                | 6 (23.08)    | 9 (12.16)        | 27 (11.02)             | 5 (12.5)          | 35                               | 0                        | 0                         | 18 (11.04)                           | 10 (16.95)                                    |
| Waist < 94 cm males           | 4 (15.38)    | 5 (6.76)         | 26 (10.61)             | 2 (5)             | 31                               | 0                        | 0                         | 17 (10.43)                           | 6 (10.17)                                     |
| < 80 cm in females            | 0            | 0                | 0                       | 1 (2.5)           | 2                                | 0                        | 0                         | 0                                  | 0                                              |

*HCT = hydrochlorothiazide.
The number of antihypertensives used by PLWDH increased as the age and duration of DM increased (Figures 2 and 3).

Table 3 demonstrates that a more significant proportion of males were on combination versus monotherapy ($p < 0.001$). Proteinuria, as detected by elevated urine PCR, decreased as the number of antihypertensives increased. A significant number of patients on combination therapy had a GFR < 60. Diabetic sensory peripheral neuropathy and non-proliferative retinopathy were more common in patients on monotherapy ($p < 0.001$ and $p = 0.03$, respectively). A significantly lesser number of PLWDH on four or more (≥ 4) antihypertensive agents performed self-monitoring of blood glucose. This cohort of PLWDH had better blood pressure, lipid and BMI control. Blood pressure and glycaemic control improved significantly with the successive addition of antihypertensives ($p < 0.001$ and $p = 0.045$, respectively). The significant majority of PLWDH failed to achieve a target waist circumference as advocated by SEMDSA diabetes guidelines.

PLWDH who were on combination antihypertensive agents had significantly better glycaemic control (Figure 4).

The significant majority of PLWDH were not meeting targets (glycaemic, lipid, BMI, waist circumference) set by the SEMDSA diabetes guidelines. Only one-fifth of PLWDH had a normal urine PCR < 0.015. Just over one-third of PLWDH (35.56%) with renal impairment, whereas half (49.69%) of PLWDH without renal impairment, had reached their target blood pressure (Table 4).

Table 5 shows that PLWDH had significantly poorer glycaemic and lipid control, BMI, waist circumference and increased proteinuria.

Female PLWDH were predominantly uncontrolled when compared with their male counterparts ($p < 0.001$). Both systolic and diastolic blood pressures were statistically higher in the uncontrolled cohort. This uncontrolled group of PLWDH had poorer lipid control, waist circumference (especially in females) and had higher levels of proteinuria and a significantly greater prevalence of non-proliferative retinopathy. Patients with uncontrolled hypertension had DM for a greater duration of time and were older when compared with the controlled hypertensives (Table 6).

Approximately one-fifth (151, 18.37%) of PLWDH had resistant hypertension (RHPT), which was more common in females ($p < 0.001$). Eighteen PLWDH with HIV infection (11.92%) had RHPT. Patients with RHPT had significantly higher blood pressure and glycated haemoglobin levels than those without RHPT (Table 6).
Table 3: Monotherapy vs. combination therapy

| Factor | All monotherapy, N = 143 | Dual therapy, N = 217 | Triple therapy, N = 163 | More than triple therapy, N = 47 | p-value |
|--------|--------------------------|-----------------------|-------------------------|---------------------------------|---------|
| Age categories (years): | | | | | |
| ≤ 30 | 8 (48–67) | 8 (49–65) | 8 (49–66) | 8 (49–67) | 0.999 |
| 30–40 | 15 (10.49) | 20 (9.22) | 18 (11.04) | 6 (12.77) | 0.05 |
| 40–50 | 23 (16.08) | 40 (18.43) | 26 (15.95) | 6 (12.77) | < 0.001 |
| 50–60 | 46 (32.17) | 76 (35.02) | 58 (35.58) | 19 (40.43) | < 0.001 |
| 60–70 | 38 (26.57) | 47 (21.66) | 33 (20.24) | 8 (17.02) | < 0.001 |
| 70–80 | 12 (8.39) | 25 (11.52) | 20 (12.27) | 6 (12.77) | 0.03 |
| ≥ 80 | 5 (3.50) | 8 (3.68) | 7 (4.29) | 2 (4.25) | 0.28 |

Median ± IQR: Age (years)

- Males: 38 (26.6) vs. 60 (27.65) vs. 46 (28.2) vs. 15 (31.91) < 0.001
- Females: 105 (73.4) vs. 157 (72.35) vs. 117 (71.8) vs. 32 (68.09) < 0.001
- HIV-infected: 20 (14) vs. 44 (20.28) vs. 29 (17.8) vs. 3 (6.38) < 0.001
- Duration of DM (years): 9 (3–15) vs. 10 (4–17) vs. 10 (4–16.5) vs. 7 (4–14) 0.344
- 1–5 years, n (%) | 54 (37.76) vs. 59 (27.19) vs. 44 (26.99) vs. 14 (29.79) < 0.001 |
- 6–10 years, n (%) | 26 (18.18) vs. 52 (23.96) vs. 40 (24.54) vs. 13 (27.66) < 0.001 |
- 11–20 years, n (%) | 43 (28.10) vs. 61 (28.11) vs. 47 (28.83) vs. 9 (19.15) < 0.001 |
- ≥ 20 years n (%) | 15 (11.54) vs. 34 (15.67) vs. 21 (12.88) vs. 6 (12.77) < 0.001 |

Median ± IQR:

- Systolic BP (mmHg) | 139 (121–157) vs. 132 (119.5–151) vs. 132 (120–148) vs. 129 (120–151) 0.304 |
- Diastolic BP (mmHg) | 80 (71–88) vs. 79.5 (69–88) vs. 79 (70–88) vs. 80 (70–86) 0.907 |
- HbA1c (%) | 9.6 (7.75–11.2) vs. 8.75 (7.35–10.8) vs. 8.9 (7.4–10.6) vs. 8.4 (7–9.5) 0.041 |
- Total cholesterol (mmol/l) | 4.5 (3.8–5.3) vs. 4.45 (3.6–5.3) vs. 4.36 (3.6–5.2) vs. 4.4 (3.6–5) 0.681 |
- Triglyceride (mmol/l) | 1.58 (1.06–2.64) vs. 1.61 (1.2–4.2) vs. 1.53 (0.9–2.39) vs. 1.43 (0.87–2.35) 0.419 |
- LDL cholesterol (mmol/l) | 2.29 (1.7–2.98) vs. 2.32 (1.78–3.16) vs. 2.29 (1.71–3.16) vs. 2.4 (1.91–2.26) 0.635 |
- HDL cholesterol (mmol/l) | 1.19 (0.98–1.41) vs. 1.2 (0.95–1.43) vs. 1.2 (0.98–1.43) vs. 1.16 (0.93–1.4) 0.941 |
- Creatinine (umol/l) | 83 (67–125) vs. 87 (67–122) vs. 81 (67–114) vs. 87 (69–115) 0.873 |
- Random blood glucose (mmol/l) | 11.25 (7.85–15.95) vs. 9.6 (6.7–14.3) vs. 9.5 (6.4–14.3) vs. 9.5 (6.5–14.2) 0.08 |
- Waist circumference (cm) – overall | 107 (97.5–117) vs. 107 (98–114) vs. 106 (96–114) vs. 104 (95–113) 0.872 |

Number of pts with:

- GFR (ml/min/1.73m²)
  - ≤ 15 | 2 (1.40) vs. 6 (2.76) vs. 3 (1.84) vs. 0 0.08 |
  - 15–30 | 12 (8.39) vs. 23 (10.6) vs. 13 (7.98) vs. 5 (10.64) 0.006 |
  - 30–45 | 19 (13.29) vs. 26 (11.98) vs. 18 (11.04) vs. 8 (17.02) 0.03 |
  - 45–60 | 17 (11.89) vs. 33 (15.21) vs. 26 (15.95) vs. 6 (12.77) < 0.001 |
  - > 60 | 72 (50.35) vs. 108 (49.77) vs. 87 (53.37) vs. 24 (51.06) < 0.001 |

- Combined < 60 | 50 (34.97) vs. 88 (40.55) vs. 60 (36.81) vs. 19 (40.43) < 0.001 |

- Complications, n (%):
  - Sensory peripheral neuropathy | 60 (41.96) vs. 91 (41.94) vs. 63 (38.65) vs. 13 (27.66) < 0.001 |
  - Non-proliferative retinopathy | 17 (11.89) vs. 18 (8.29) vs. 14 (8.59) vs. 4 (8.51) 0.03 |
  - Proliferative retinopathy | 2 (1.40) vs. 6 (2.76) vs. 5 (3.07) vs. 1 (2.13) 0.18 |
  - Cataract | 12 (8.39) vs. 30 (13.82) vs. 19 (11.66) vs. 4 (8.51) < 0.001 |

(Continued)
pressures, LDL cholesterol, BMI in females and urine PCR levels. Approximately half (49.01%) of patients living with RHPT had a GFR < 60. Patients with RHPT had a higher prevalence of retinopathy (non-proliferative and proliferative) and cerebrovascular accidents. Notably, a more substantial number of patients with RHPT were performing SMBG (82.12% vs. 76.01%, \( p < 0.001 \), respectively) (Table 7).

Like hypertension, RHPT became more prevalent with increasing age and duration of DM (Figures 5 and 6).

Over one-quarter (29.87%) of the PLWD (without hypertension) had a blood pressure reading of over 140/90.

| Factor                              | All monotherapy, \( N = 143 \) | Dual therapy, \( N = 217 \) | Triple therapy, \( N = 163 \) | More than triple therapy, \( N = 47 \) | \( p \)-value |
|-------------------------------------|---------------------------------|-----------------------------|------------------------------|-------------------------------------|--------------|
| • Glaucoma                          | 7 (4.90)                        | 3 (1.38)                    | 1 (0.61)                     | 1 (2.13)                            | 0.05         |
| • CVA                               | 7 (4.90)                        | 7 (3.23)                    | 6 (3.68)                     | 4 (8.51)                            | 0.80         |
| Patients performing SMBG (n, %)     | 109 (76.22)                     | 172 (79.26)                 | 126 (77.30)                  | 36 (76.6)                           | < 0.001      |

Targets reached:

- \( \text{HbA1c} \leq 7\% \): 20 (13.99) vs. 36 (16.59), \( p = 0.002 \)
- Total cholesterol < 4.5 mmol/l: 66 (46.15) vs. 99 (45.62), \( p = 0.001 \)
- Triglyceride < 1.7 mmol/l: 71 (49.65) vs. 104 (47.93), \( p = 0.001 \)
- LDL cholesterol < 1.8 mmol/l: 25 (17.48) vs. 34 (15.67), \( p = 0.001 \)
- HDL cholesterol > 1.0 mmol/l in males: 18 (12.59) vs. 28 (12.9), \( p = 0.003 \)
- HDL cholesterol > 1.2 mmol/l in females: 41 (28.67) vs. 68 (31.34), \( p = 0.001 \)
- BP < 140/90 mmHg: 68 (47.55) vs. 121 (55.76), \( p < 0.001 \)
- BP < 130/85 mmHg: 50 (34.97) vs. 84 (38.71), \( p < 0.001 \)
- BMI < 25 kg/m\(^2\): 20 (13.99) vs. 23 (10.6), \( p = 0.16 \)
- BMI < 25 kg/m\(^2\) in males: 10 (6.99) vs. 12 (5.53), \( p = 0.41 \)
- BMI < 25 kg/m\(^2\) in females: 10 (6.99) vs. 11 (5.07), \( p = 0.48 \)
- Normal waist circumference: 12 (8.39) vs. 20 (9.22), \( p = 0.01 \)
- Waist circumference < 94 cm in males: 11 (7.69) vs. 20 (9.22), \( p = 0.01 \)
- Waist circumference < 80 cm in females: 1 (0.70) vs. 0, \( p = 0.39 \)

### Table 4: Number (%) of PLWDH meeting targets

| Known HPT n (%) | Yes | No | \( p \)-value |
|-----------------|-----|----|--------------|
| GFR < 60+ BP < 130/85 \( N = 309 \) | 110 (35.56) | 199 (64.40) | < 0.001 |
| GFR > 60+ BP < 140/90 \( N = 326 \) | 162 (49.69) | 164 (50.31) | 0.91 |
| HbA1c ≤ 7\% | 105 (15.77) | 561 (84.23) | < 0.001 |
| Total cholesterol < 4.5 mmol/l | 316 (47.88) | 344 (52.12) | 0.28 |
| Triglyceride < 1.7 mmol/l | 340 (51.91) | 315 (48.09) | 0.33 |
| LDL cholesterol < 1.8 mmol/l | 118 (27.31) | 314 (72.69) | < 0.001 |
| HDL cholesterol: | | | |
| > 1.0 mmol/l in males | 93 (62.42) | 56 (37.58) | 0.002 |
| > 1.2 mmol/l in females | 217 (53.71) | 187 (46.29) | 0.14 |
| BMI < 25 kg/m\(^2\) | 74 (11.53) | 568 (88.47) | < 0.001 |
| Waist circumference (cm): | | | |
| Males < 94 | 56 (34.15) | 108 (65.85) | < 0.001 |
| Females < 80 | 5 (1.07) | 462 (98.93) | < 0.001 |
| Urine PCR < 0.015 | 43 (21.94) | 153 (78.06) | < 0.001 |

Within the PLWDH cohort, around 50% had poorly controlled blood pressure irrespective of the type of antidiabetic medication taken.

Approximately one-sixth of PLWDH had optimal glycaemic control irrespective of the type of antidiabetic medication taken. This proportion was lower in PLWD.
Patients with concomitant hypertension and diabetes had a higher prevalence of proteinuria.

PLWDH on all three modalities of diabetes therapy had better glycaemic control than the PLWD.

Those PLWD had better control of BP, lipid and waist circumference control across all three antidiabetic therapeutic modalities (Table 8).

Discussion

HPT remains a significant contributor to premature mortality globally. South Africa has the highest prevalence of HPT in sub-Saharan Africa, with the majority of these hypertensive patients being either uncontrolled or undiagnosed.\(^{10,15-16}\) PLWD are at increased risk of developing HPT and, when present, this will increase the risk of developing diabetes-related micro- and macro-vascular complications.\(^{4-6}\) Furthermore, uncontrolled blood pressure in PLWD has been shown to increase the chances of overall mortality, complications of DM and the development of retinopathy.\(^{11}\) The prevalence of HPT in DM ranges globally from 40% to 60%.\(^{17,18}\) Our study showed a much higher prevalence of HPT in PLWD (86.74%). This figure resembles those from other low- to middle-income countries (LMICs) like Thailand (78.4%), Morocco (70.4%) and Cameroon (66.4%) and aptly describes the burden that the combination of HPT and DM poses on these LMICs.\(^{19-21}\)

In this study, we showed that the prevalence of HPT in PLWD increased with both patient age and duration of DM, thus highlighting the importance of routine blood pressure screening in PLWD. Earlier detection and control of HPT will translate into improved diabetes-related morbidity and mortality. Results of our study showed, like others undertaken globally, that PLWDH had a significant higher control of lipids, had higher waist circumference, this especially in females, had higher creatinine levels and a greater number of patients with GFR < 60. These PLWDH also had a higher prevalence of both micro- and macro-vascular complications (peripheral sensory neuropathy, retinopathy [both non-proliferative and proliferative]), cerebrovascular accidents (CVA) and renal dysfunction (increased urine PCR and a more significant number of patients having GFR < 60).\(^{4-6}\) Our cohort of PLWDH had a higher prevalence of obesity when compared with PLWD. Obesity is related to the development of both DM and HPT.\(^{7-8}\) These findings illustrate that PLWDH are high-risk patients, and that in addition to glycaemic control they need intensive BP control to minimise overall morbidity and mortality. Both cohorts (PLWD and PLWDH) had suboptimal glycaemic control, highlighting the need for strategies to improve glycaemic control, one of which would be weight loss as both cohorts had a high prevalence of obesity.

The significant majority of PLWDH failed to meet lipid, glycaemic, BMI and waist circumference targets set out by the South

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**Table 5: Number (%) of PLWDH versus PLWD meeting targets**

| Factor | Known hypertension (n = 713) | No history of hypertension (n = 109) | p-value |
|--------|------------------------------|-----------------------------------|---------|
| GFR < 60+ BP < 130/85 N = 115 | 110 (95.65) | 5 (4.35) | < 0.001 |
| GFR > 60 + BP < 140/90 N = 231 | 162 (70.13) | 69 (29.87) | < 0.001 |
| Hba1c < 7% | 105 (87.5) | 15 (12.5) | < 0.001 |
| Total cholesterol < 4.5 mmol/l | 316 (84.72) | 57 (15.28) | < 0.001 |
| Triglycercide < 1.7 mmol/l | 340 (83.54) | 67 (16.46) | < 0.001 |
| LDL cholesterol < 1.8 mmol/l | 118 (88.06) | 16 (11.94) | < 0.001 |
| HDL cholesterol: | | | |
| • > 1.0 mmol/l in males | 93 (83.04) | 19 (16.96) | < 0.001 |
| • > 1.2 mmol/l in females | 217 (87.15) | 32 (12.85) | < 0.001 |
| BMI < 25 kg/m² | 74 (80.43) | 18 (19.57) | < 0.001 |
| Waist circumference (cm): | | | |
| • Males < 94 | 56 (75.68) | 18 (24.32) | < 0.001 |
| • Females < 80 | 5 (83.33) | 1 (16.67) | 0.10 |
| Urine PCR < 0.015 | 43 (68.25) | 20 (31.75) | 0.004 |
African diabetes guidelines. These results also serve to highlight the impact of obesity in the management of both PLWD and PWLDH. As part of an effective integrated management plan for patients with both DM and HPT, much emphasis needs to be placed on lifestyle modification (diet and exercise) and weight loss to improve control of both DM and HPT. The majority of PLWDH had evidence of proteinuria, implying renal impairment and increased cardiovascular risk.

Control of blood pressure was shown in the UKPDS study to be vitally essential to decrease both micro- and macrovascular complications in PLWD. This was illustrated in our research,
Table 7: Resistant hypertension

| Factor                        | Yes                  | No                  | p-value |
|-------------------------------|----------------------|---------------------|---------|
| Median ± IQR:                 |                      |                     |         |
| Age (years)                   | 60 (53–66)           | 57 (48–66)          | 0.029   |
| Age categories (years):       |                      |                     |         |
| ≤ 30                          | 2 (1.30)             | 12 (1.8)            | 0.007   |
| 30–40                         | 11 (7.3)             | 59 (8.8)            | < 0.001 |
| 40–50                         | 13 (8.6)             | 130 (19.4)          | < 0.001 |
| 50–60                         | 58 (38.4)            | 214 (31.9)          | < 0.001 |
| 60–70                         | 44 (29.1)            | 164 (24.4)          | < 0.001 |
| 70–80                         | 21 (13.9)            | 69 (10.3)           | < 0.001 |
| 80–90                         | 2 (1.3)              | 21 (3.1)            | < 0.001 |
| ≥ 90                          | 0                    | 2 (0.3)             | 0.16    |
| N (%)                         |                      |                     |         |
| Males                         | 35 (23.2)            | 191 (28.5)          | < 0.001 |
| Females                       | 116 (76.8)           | 480 (71.5)          | < 0.001 |
| HIV infected patients         | 18 (11.92)           | 111 (16.54)         | < 0.001 |
| Duration of DM (years)        | 12 (5–20)            | 9 (3–16)            | 0.005   |
| 1–5                           | 40 (26.49)           | 224 (33.38)         | < 0.001 |
| 6–10                          | 24 (15.89)           | 148 (22.06)         | < 0.001 |
| 11–20                         | 48 (31.79)           | 196 (29.21)         | < 0.001 |
| > 20                          | 33 (21.85)           | 73 (10.88)          | < 0.001 |
| Median ± IQR:                 |                      |                     |         |
| Systolic BP (mmHg)            | 155 (144–169)        | 129 (117–148)       | < 0.001 |
| Diastolic BP (mmHg)           | 89 (78–96)           | 77 (69–85)          | < 0.001 |
| HbA1c (%)                     | 9 (7.8–10.6)         | 9.4 (7.6–11.2)      | 0.112   |
| Total cholesterol (mmol/L)    | 4.6 (3.8–5.5)        | 4.5 (3.7–5.3)       | 0.430   |
| Triglyceride (mmol/l)         | 1.58 (1.11–2.34)     | 1.61 (1.06–2.34)    | 0.803   |
| LDL cholesterol (mmol/l)      | 2.52 (1.99–3.33)     | 2.32 (1.71–3.11)    | 0.028   |
| HDL cholesterol (mmol/l)      | 1.27 (1.05–1.48)     | 1.16 (0.98–1.42)    | 0.109   |
| Creatinine (umol/l)           | 85 (69–133)          | 85 (67–120)         | 0.242   |
| Random blood glucose (mmol/l) | 10.6 (6.8–14.7)      | 10.5 (6.9–15.1)     | 0.974   |
| Waist circumference (cm)      | 109 (99–119)         | 107 (97–116)        | 0.392   |
| Males                         | 97 (87–108)          | 99 (90–110)         | 0.889   |
| Females                       | 113 (102.5–122.5)    | 110 (101–118)       | 0.178   |
| BMI (kg/m²)                   |                      |                     |         |
| Males                         | 29 (26–32)           | 28 (24–33)          | 0.232   |
| Females                       | 36 (30–40)           | 34 (29–39)          | 0.042   |
| Urine PCR                     | 0.043 (0.025–0.136)  | 0.025 (0.013–0.071) | 0.019   |

Number of pts with GFR (ml/min/1.73 m²):

|                  |                      |                     |         |
|                  | < 15                 | 6 (3.97)            | 12 (1.79) | 0.16  |
|                  | 15–30                | 18 (11.92)          | 58 (8.64) | < 0.001 |
|                  | 30–45                | 15 (9.93)           | 87 (12.97)| < 0.001 |
|                  | 45–60                | 24 (15.89)          | 98 (14.61)| < 0.001 |
|                  | > 60                 | 74 (49.01)          | 339 (50.52)| < 0.001 |
|                  | Combined < 60        | 63 (41.72)          | 255 (38.0) | < 0.001 |

Complications:

|                  |                      |                     |         |
|                  | Sensory peripheral neuropathy | 59 (39.07) | 285 (42.47) | < 0.001 |
|                  | Non-proliferative retinopathy | 19 (12.58) | 60 (8.94) | < 0.001 |
|                  | Proliferative retinopathy | 5 (3.31)           | 17 (2.53) | 0.010   |
|                  | Cataract              | 16 (10.6)          | 65 (9.69) | < 0.001 |
|                  | Glaucoma              | 3 (1.99)           | 18 (2.68) | 0.001   |
|                  | CVA                   | 8 (5.30)           | 24 (3.58) | 0.005   |

Number of pts performing SMBG

|                  |                      |                     |         |
|                  | 124 (82.12)          | 510 (76.01)         | < 0.001 |
Figure 5: Prevalence of resistant hypertension with increasing age.

Figure 6: Relationship between duration of diabetes and prevalence of resistant hypertension.

Table 8: Types of antidiabetic therapy used in all PLWD

| N (%) of pts achieving: | Known hypertensive | | No hypertension | | |
|-------------------------|--------------------|-------------------|-------------------|-------------------|-------------------|
|                         | Oral antidiabetics (OADs) alone | Insulin alone | OADs + Insulin | p-value | OADs alone | Insulin alone | OADs + Insulin | p-value |
| BP < 140/90 mmHg         | 173 (50.58)        | 308 (49.44)       | 128 (50.39)       | < 0.001 | 43 (76.79)        | 72 (76.66)      | 32 (78.05)         | < 0.001 |
| BP > 140/90 mmHg         | 169 (49.42)        | 315 (50.56)       | 126 (49.61)       | < 0.001 | 13 (23.21)        | 22 (23.44)       | 9 (21.95)          | 0.05    |
| HbA1c < 7%               | 45 (14.33)         | 99 (16.75)        | 39 (16.25)        | < 0.001 | 7 (14)            | 12 (13.48)       | 4 (10.53)         | 0.12    |
| HbA1c ≥ 7%               | 269 (85.67)        | 492 (83.25)       | 201 (83.75)       | < 0.001 | 43 (86)           | 77 (86.52)       | 34 (89.47)        | < 0.001 |
| Total cholesterol < 4.5 mmol/l | 158 (49.07)        | 276 (47.92)       | 119 (49.58)       | < 0.001 | 27 (50.94)        | 49 (53.06)       | 19 (46.34)         | < 0.001 |
| Total cholesterol ≥ 4.5 mmol/l | 164 (50.93)        | 300 (52.08)       | 121 (50.42)       | < 0.001 | 26 (49.06)        | 40 (44.94)       | 22 (53.66)        | 0.05    |
| Triglyceride < 1.7 mmol/l | 157 (47.32)        | 298 (52.01)       | 117 (49.37)       | < 0.001 | 32 (60.38)        | 58 (65.17)       | 23 (56.17)        | < 0.001 |
| Triglyceride ≥ 1.7 mmol/l | 160 (52.68)        | 275 (47.99)       | 120 (50.63)       | < 0.001 | 21 (39.62)        | 31 (34.83)       | 18 (43.9)         | 0.14    |
| HDL cholesterol:         |                     |                   |                   |         |                   |                   |                   |         |
| Males                    |                     |                   |                   |         |                   |                   |                   |         |
| • < 1.0 mmol/l           | 26 (35.14)         | 46 (35.11)        | 17 (29.82)        | < 0.001 | 5 (29.41)         | 14 (51.85)       | 5 (45.45)         | 0.03    |
| • ≥1.0 mmol/l            | 48 (64.86)         | 85 (64.89)        | 40 (70.18)        | < 0.001 | 12 (70.59)        | 13 (48.15)       | 6 (54.55)         | 0.25    |
| Females                  |                     |                   |                   |         |                   |                   |                   |         |
| • < 1.2 mmol/l           | 91 (46.91)         | 159 (45.43)       | 63 (44.68)        | < 0.001 | 14 (53.85)        | 22 (42.31)       | 12 (54.55)        | 0.17    |
| • ≥1.2 mmol/l            | 103 (53.09)        | 191 (54.57)       | 78 (55.32)        | < 0.001 | 12 (46.15)        | 30 (57.69)       | 10 (45.45)        | < 0.001 |
| LDL < 1.8 mmol/l         | 62 (48)            | 104 (48)          | 48 (48)           | < 0.001 | 6 (15)            | 15 (5)           | 5 (33.3)          | 0.03    |
| • Males                  | 21 (33.87)         | 37 (35.85)        | 18 (37.5)         | 0.02    | 1 (16.67)         | 2 (13.33)        | 0 (0)             | 0.37    |
| • Females                | 41 (66.13)         | 67 (64.22)        | 30 (62.5)         | < 0.001 | 5 (83.33)         | 13 (66.67)       | 5 (100)           | 0.06    |
| LDL ≥ 1.8 mmol/l         | 144 (275)          | 107 (275)         | 0.001             | 25 (49) | 20 (49)           | 0.001             |         |
| • Males                  | 36 (25)            | 64 (33.75)        | 27 (25.23)        | < 0.001 | 12 (48)           | 21 (42.86)       | 9 (45)            | 0.06    |
| • Females                | 108 (75)           | 211 (73.73)       | 80 (74.77)        | < 0.001 | 13 (52)           | 28 (57.14)       | 11 (55)           | 0.01    |
| BMI < 25 kg/m²            | 39 (12.62)         | 61 (11.07)        | 28 (12.23)        | 0.001   | 11 (21.57)        | 14 (15.91)       | 7 (18.92)         | 0.31    |
| BMI > 25 kg/m²            | 270 (87.38)        | 490 (88.93)       | 201 (87.77)       | < 0.001 | 40 (78.43)        | 74 (84.09)       | 30 (81.08)        | < 0.001 |

Waist circumference (cm):

| Males                    | 28 (93.33)         | 50 (94.34)        | 23 (100)          | 0.002   | 10 (90.9)         | 12 (92.31)       | 4 (80)            | 0.14    |
| Females                  | 2 (6.67)           | 3 (5.66)          | 0                | 0.25    | 1 (9.1)           | 1 (7.69)         | 1 (20)            | >0.05   |
| Urine PCR < 0.015        | 23 (23.71)         | 36 (22.09)        | 16 (24.62)        | 0.02    | 9 (47.37)         | 17 (40.48)       | 6 (50)            | 0.05    |
| Urine PCT ≥ 0.015        | 74 (76.29)         | 127 (77.91)       | 49 (75.38)        | < 0.001 | 10 (52.63)        | 15 (59.52)       | 6 (50)            | 0.14    |
| GFR < 60 ml/min/1.73 m²  | 152 (48.72)        | 279 (50.54)       | 122 (53.04)       | < 0.001 | 7 (13.73)         | 6 (7.06)         | 4 (10)            | 0.66    |
| GFR ≥60 ml/min/1.73 m²   | 160 (51.28)        | 273 (49.46)       | 108 (46.96)       | < 0.001 | 44 (86.27)        | 79 (92.94)       | 36 (90)           | < 0.001 |
which showed that the cohort of PLWD with uncontrolled BP had significantly poorer lipid, BMI and waist circumference measurements, a higher prevalence of proteinuria, non-proliferative retinopathy, and increased duration of DM. These findings strengthen the case for the use of combination therapy in PLWDH to achieve tighter BP control. Female PLWDH had a higher prevalence of uncontrolled BP than males. This can be explained by the higher prevalence of obesity in females in South Africa.24

RHPT is more common in PLWD and those with obesity.7,25,26 When present in DM, RHPT carries a poorer prognosis.27 Approximately one-fifth of our PLWDH had resistant HPT, which was more common in females, while one-eighth of the HIV-infected PLWDH had resistant hypertension. Our prevalence of RHPT in PLWDH was similar to results published by the RIACE study.28 Patients with RHPT in our research had poorer LDL cholesterol, higher BMI—this especially in females, and a higher prevalence of proteinuria with lower GFR values. They also had lower HbA1c values compared with those PLWDH without RHPT. This can be explained by the fact that our study also showed these patients with resistant HPT were performing significantly more SMBG than their counterparts without resistant HPT. Studies have shown that SMBG improves glycaemic control.29,30 Another plausible explanation for this improved glycaemic control in patients with RHPT is that these patients are seen more frequently for their blood pressure control and hence receive more clinician guidance on overall diabetes control. In this study, the prevalence of RHPT, similar to HPT, increased with advancing patient age and duration of DM. This finding needs to be borne in mind when managing older patients who have DM for more extended time periods in our diabetes clinics.

A notable finding of our study was that over a quarter of PLWDH, without a history of HPT, had blood pressure readings of > 140/90 mmHg. This is an area of diabetes care that must be actively explained by the higher prevalence of obesity in females in South Africa.24

PLWDH on all modalities of anti-diabetes therapies had better glycaemic control than PLWD. In contrast, PLWD had better control of lipid, blood pressure and waist circumference than those PLWDH. This improved glycaemic control in PLWDH probably reflects the effect that increased frequency of diabetic clinic visits in those with DM and HPT than those with DM alone.

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