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Editorial Articles

- Effects of resistance training in adults with type-2 diabetes mellitus: a narrative review of randomised controlled trials
- Prevalence of microalbuminuria and associated factors among diabetic patients attending a general hospital in Central Uganda
- Evaluating red cell distribution width and kidney dysfunction in HIV-positive and HIV-negative adults with diabetes: insights from KwaZulu-Natal, South Africa
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- Monogenic diabetes in South Africa: clinical clues and lessons from seven cases
- Amyloid goitre in a patient with thyrotoxicosis: a diagnostic challenge

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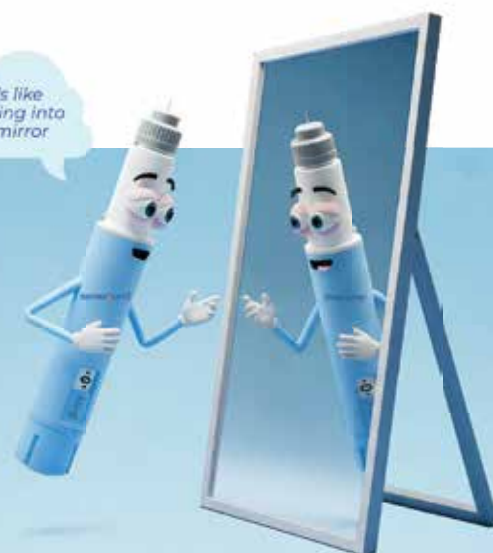
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References: 1. SEMAGARD Professional Information, July 2026. 2a. Sun Pharmaceutical Industries Ltd. Data on file: Semagard bioequivalence study [SEM01024]. 2b. Gopalakrishnan UA, Joshi AS, Giri R, et al. Semaglutide injection in Indian patients with type 2 diabetes mellitus: a randomised, phase III active-controlled study. *Diabetes Obes Metab*. 2026;0:1–10. doi:10.1111/dom.70891. 3. Sun Pharmaceutical Industries Ltd. Data on file: Semaglutide professional information. February 2023. 4. SAHPRA. Medicines and Related Substances Act, 1965 (Act 101 of 1965). Government Gazette 40869. Pretoria: Government Printer; 2017. 5. Sun Pharmaceutical Industries Ltd. Data on file: GLP-1 pricing. June 2026. 6. About us. Sun Pharma. Accessed June 10, 2026. <https://sunpharma.com/about-us/>.

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The Journal of Endocrinology, Metabolism and Diabetes of South Africa (JEMDSA) is the official journal of **SEMDSA** (Society for Endocrinology, Metabolism and Diabetes of SA), **DESSA** (Diabetes Education Society of SA), **NOFSA** (National Osteoporosis Foundation of SA), **SASOM** (SA Society of Obesity and Metabolism), **LASSA** (Lipid and Atherosclerosis Society of SA) and **PAEDS-SA** (The Paediatric and Adolescents Endocrine and Diabetes Society of SA).

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The journal further aims to provide a platform for clinical reviews and debate on practical and controversial issues in endocrinology, metabolism and diabetes. The journal aims to be instrumental in publishing and revising therapeutic protocols and national guidelines. Reviews will also be invited to address pertinent clinical and therapeutic issues for its practicing readership.

The print run of the journal is 2 000 and comprises the members of the various societies, namely general physicians, endocrinologists, diabetologists, diabetes nurse educators, lipidologists, bariatricians, paediatricians, gynaecologists (specialising in osteoporosis and infertility) and general practitioners with a special interest in endocrinology, metabolism and diabetes.

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EDITORIAL

This issue of the Journal of Endocrinology, Metabolism and Diabetes of South Africa highlights the breadth of endocrine and metabolic disease encountered in clinical practice across Africa. The papers span common conditions with significant public health implications, uncommon but important clinical presentations, and practical reviews that support evidence-based patient care. Together, they emphasise the importance of early diagnosis, recognising atypical presentations, and continually refining our clinical practice through research relevant to our setting.

Diabetic kidney disease (DKD) remains one of the most devastating complications of diabetes and is a leading cause of chronic kidney disease, end-stage kidney disease, cardiovascular disease, and premature mortality worldwide. The earliest clinically detectable manifestation is moderately increased albuminuria (microalbuminuria), which frequently precedes a decline in glomerular filtration rate by several years. Identifying microalbuminuria provides clinicians with a critical opportunity to intensify and optimise therapy to prevent disease progression. For this reason, both international and local diabetes guidelines recommend annual screening for albuminuria in people with diabetes. Kemigisha and colleagues provide valuable data on the prevalence of microalbuminuria and its associated factors among people with diabetes attending clinics in Central Uganda. Their findings add to the growing body of African evidence demonstrating that early kidney involvement is common and reinforce the importance of routine screening in clinical practice.

Hyperthyroidism is a common endocrine disorder with a wide spectrum of clinical manifestations, reflecting the pervasive effects of excess thyroid hormone on virtually every organ system. While most clinicians are familiar with its classic features, rarer presentations can easily be overlooked, with potentially serious consequences. Raichund and colleagues present a compelling case of thyrotoxic periodic paralysis, an uncommon but potentially life-threatening complication of hyperthyroidism. Prompt recognition is essential, as early diagnosis and appropriate treatment can rapidly reverse the paralysis and prevent potentially fatal cardiac arrhythmias.

Diabetes affects hundreds of millions of people worldwide, with the overwhelming majority having type 2 diabetes, followed by type 1 diabetes and gestational diabetes. Although monogenic forms of diabetes account for only a small proportion of cases, recognising them is of considerable clinical importance, as the diagnosis has important implications for treatment, prognosis, and genetic counselling of affected families. Raubenheimer and colleagues present a series of cases of monogenic diabetes, highlighting the clinical clues that should prompt clinicians to consider this diagnosis and providing practical guidance on its investigation and management. Their paper serves as an important reminder that identifying the correct diabetes subtype is fundamental to delivering truly personalised care.

The pharmacological management of type 2 diabetes has evolved substantially over the past two decades, driven by high-quality evidence from large randomised controlled trials. In contrast, while lifestyle interventions remain the cornerstone of diabetes care, the evidence supporting specific exercise modalities is often less definitive. Resistance training has emerged as a promising strategy, yet questions remain regarding its optimal role and benefits. Mtshali and colleague present a narrative review of randomised controlled trials evaluating the effects of resistance training in adults with type 2 diabetes, providing a timely synthesis of the available evidence and practical insights into whether this intervention can improve glycaemic control, physical function, and overall health outcomes.

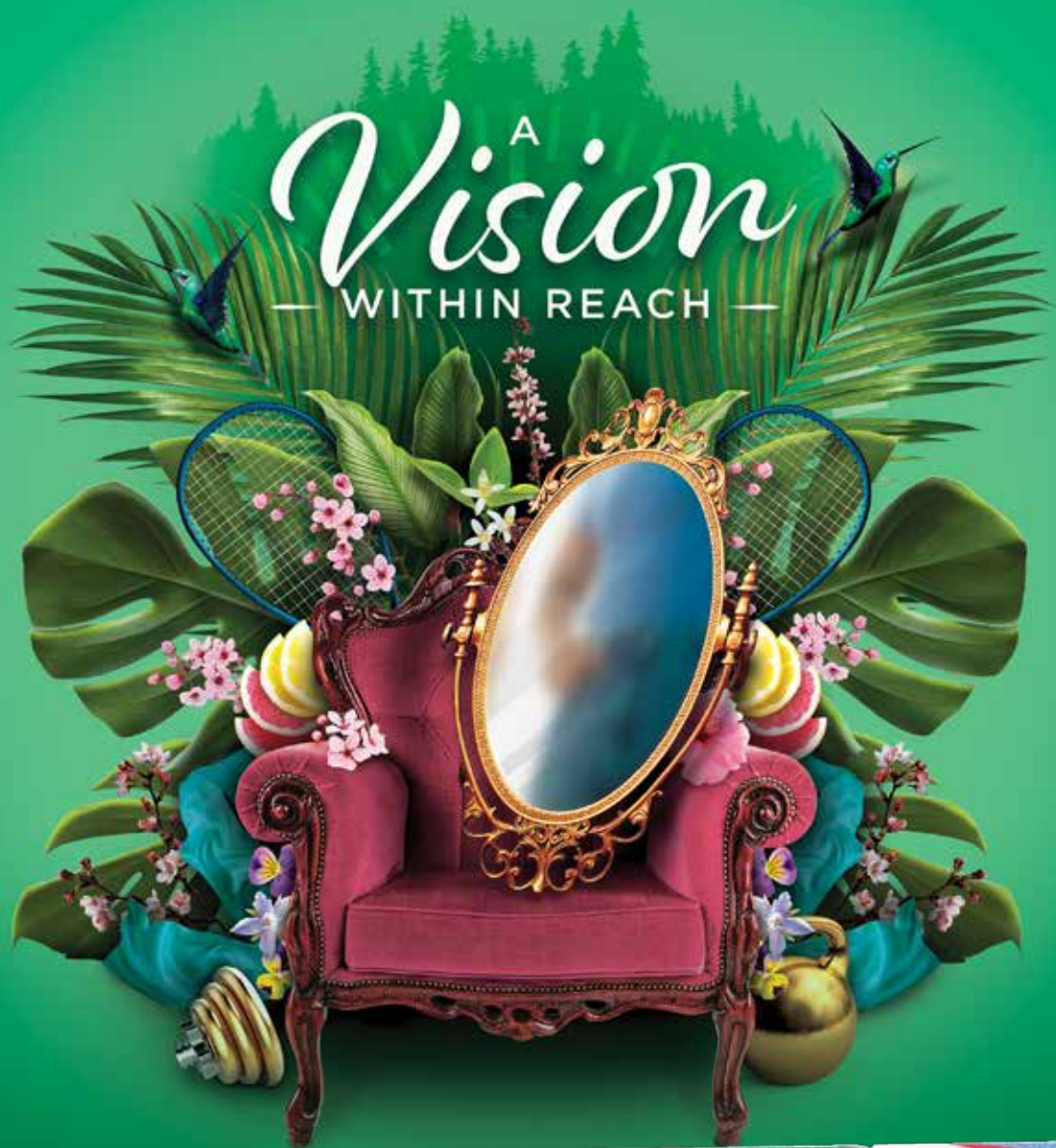
Most cases of thyrotoxicosis are caused by Graves' disease or toxic nodular thyroid disease. However, clinicians should remain alert to the rare infiltrative disorders of the thyroid that may present in unexpected ways. Talia and colleagues describe an unusual case of thyroid amyloidosis presenting with thyrotoxicosis, highlighting the importance of considering uncommon aetiologies when the clinical presentation is atypical. The case reminds us that maintaining a broad differential diagnosis remains a cornerstone of good endocrine practice.

Kidney disease remains one of the most important causes of morbidity and mortality among people living with HIV, particularly in sub-Saharan Africa, which bears the world's greatest HIV burden and is home to the largest antiretroviral therapy programme globally. Despite major advances in HIV care, the early identification of individuals at risk of progressive kidney disease remains a clinical priority. Red cell distribution width (RDW), a routinely reported and inexpensive haematological parameter, has emerged as a potential prognostic marker in a range of chronic diseases, including chronic kidney disease. Pillay explores the relationship between RDW and HIV-associated kidney disease, investigating whether this simple, readily available biomarker may assist in identifying patients at increased risk of kidney disease. Such accessible and cost-effective tools have particular relevance in resource-constrained settings, where they may facilitate earlier recognition of kidney disease and ultimately improve patient outcomes.

The diversity of papers in this issue reflects the breadth of endocrinology and metabolism, from common chronic diseases requiring earlier detection and optimisation of care to rare clinical entities that challenge diagnostic thinking. Collectively, these contributions reinforce the value of clinically relevant research generated within Africa to address the unique challenges faced by our healthcare systems. We hope that readers will find the articles both informative and applicable to their daily practice, ultimately contributing to improved care for people living with endocrine and metabolic disorders.

Joel A Dave

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Effects of resistance training in adults with type-2 diabetes mellitus: a narrative review of randomised controlled trials

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Background: Resistance training has been proposed as an effective non-pharmacological intervention for managing type-2 diabetes mellitus (T2DM). This review examines the effects of resistance training on metabolic parameters, muscle strength, and physical function in adults with T2DM.

Methods: A structured literature search was conducted in ScienceDirect, PubMed, and Google Scholar in accordance with PRISMA guidelines. Randomised controlled trials investigating resistance training interventions in adults with T2DM were included. Although a systematic search strategy was applied, findings were synthesised narratively due to heterogeneity in outcomes and limited data suitable for quantitative pooling.

Results: Five randomised controlled trials met the eligibility criteria. Resistance training interventions ranged from 15–85% of one-repetition maximum (1RM), performed three times per week for 40–60 minutes. Across studies, resistance training consistently improved muscle strength and physical function. However, findings related to metabolic parameters were inconsistent. Improvements in HbA1c and fasting glucose appeared dependent on baseline glycaemic status, intervention duration, and the presence of co-interventions such as dietary modification.

Conclusion: Resistance training reliably enhances muscle strength and functional performance in adults with T2DM, while its effects on glycaemic control remain variable. Given the narrative nature of the synthesis and heterogeneity of included studies, conclusions regarding metabolic outcomes should be interpreted with caution. Future research employing quantitative synthesis is required to clarify clinical significance.

Keywords: effects, HbA1c, fasting blood glucose, adults,, randomised trials, strength, physical function

Introduction

The pancreas plays a central role in regulating blood glucose through the secretion of insulin and glucagon.¹ These hormones function synergistically to maintain glucose homeostasis, particularly following food intake. Type-2 diabetes mellitus (T2DM) develops when insulin secretion, insulin action, or both become impaired, resulting in chronic hyperglycaemia.¹ T2DM is one of the most prevalent non-communicable diseases worldwide and continues to place a substantial burden on global health system.^{2–5}

T2DM is also age-related, and adults aged 40 years and older are at a higher risk of being diagnosed with the condition.^{6,7} In older adults, T2DM is linked to a gradual reduction in overall insulin sensitivity and worsening blood glucose regulation, a decline that is further intensified by the natural ageing process.⁸ Research suggests that a lack of exercise and an increase in abdominal obesity are primary factors contributing to insulin resistance.^{4,9} Furthermore, adults with T2DM often experience reduced muscle mass and strength, diminished physical function, and a higher risk of falls and bone fractures. To prevent and manage T2DM, significant lifestyle changes such as adopting a healthy diet and engaging in regular exercise are advised. Consistent physical activity (PA) is associated with disease prevention and enhanced overall health.^{9,10}

Resistance training has gained popularity as an effective treatment for several chronic diseases, including T2DM. It is considered a safe and efficient therapeutic approach for elderly and overweight individuals in managing the condition.^{2,11,12}

Research has shown that resistance training enhances muscle mass, bone mineral density, muscle strength, blood glucose regulation, and overall functional capacity.^{12,13} Hovanec et al.¹⁴ and Qadir et al.¹⁵ further highlighted that individuals living with T2DM gain from resistance training through increased muscle hypertrophy, improved muscle quality, greater strength for power development, and enhanced mobility, all of which support improved glycaemic control. According to Parsa et al.,¹¹ high-load resistance exercises performed once a week over eight weeks can significantly enhance strength development in the extremities of T2DM patients. Furthermore, heavy resistance exercise, such as weightlifting, can markedly improve muscle strength and function in this population.¹² Retaining both upper and lower muscle strength is essential for older adults to carry out daily tasks involving static or dynamic effort and to reduce the risk of falls.^{10,12}

Intervention programmes, particularly resistance training aimed at improving metabolic parameters, muscle strength, and physical function in adults with T2DM, are an urgent priority. Both supervised and unsupervised resistance training programmes have proven useful in achieving positive health outcomes, as reflected in improvements in metabolic parameters, muscle strength, and physical function. The effectiveness of resistance training interventions varies widely across studies, likely due to differences in participant characteristics, training intensity and duration, baseline metabolic control, and the inclusion of co-interventions such as dietary modification. There remains a need to critically evaluate and synthesise existing evidence. This review therefore aims to narratively synthesise available

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1. Richardson J et al. Clinical Relevance of Reapplication of Blood Samples During Blood Glucose Testing. Poster presented at the virtual 20th Annual Diabetes Technology Meeting (DTM), 12 November 2020. 2. Market Research Ascensia Diabetes Care, Hall & Partners online market research, conducted April/May 2015. 3. Klaff I et al. Accuracy and user performance of a new blood glucose monitoring system. Journal of Diabetes Science and Technology. 2021;15(6): 1382-1389. 4. CONTOUR® PLUS ELITE BGMS User Guide, Rev. 12/21

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randomised controlled trials examining the effects of resistance training on metabolic parameters, muscle strength, and physical function in adults with T2DM.

Methods

Data sources and search strategy

Electronic searches were conducted from inception until 14 June, 2024, on the following databases: Google Scholar, PubMed, and Science Direct. The keywords used in the database search were effects AND HbA1c AND fasting blood glucose AND adults AND randomised trials AND strength AND physical function. Reference lists of included articles and systematic reviews in the field were also searched manually for relevant studies.

Eligibility criteria

The inclusion and exclusion criteria were determined by PICO (participants, interventions, comparisons, and outcomes).⁹ To be included in this review, articles had to be of either randomised controlled trials (RCTs); written in English; including participants with clearly defined T2DM; evaluated on an exercise programme of resistance strength training using either weight training or own bodyweight; noting frequency, duration, and intensity with a follow-up period of 6-weeks or more; as well as articles reporting on the outcome measurements of metabolic parameters, i.e. fasting blood glucose and HbA1c, muscle strength, and physical function. Articles were excluded if the programmes comprised aerobic training, or were cross-sectional, case-control, case series studies, or abstracts only and review articles (Table 1).

Outcome measurements

The primary outcomes included metabolic parameters (HbA1c and fasting glucose), muscle strength, and physical function. Where applicable, muscle strength was assessed using one-repetition maximum (1RM), defined as the maximal load that can be lifted once with correct technique. Fasting glucose values were standardised to SI units (mmol/l).

Table 1: Eligibility criteria agreed upon by the authors for inclusion in the review

Characteristics Eligibility criteria	
Population	- Adults aged 18 and above - Both genders - Diagnosed with T2DM
Intervention	- Resistance training (supervised or unsupervised) - A minimum duration of 10 minutes of continuous activity bouts either in isolation or in combination with other lifestyle modifications - Including supervised gym-based low- to high-intensity interval training or home-based - Administered in any context (workplace, community, or school)
Comparison	Physical activity interventions before and after the trial period
Outcome Measurement	The primary or secondary outcome measurements should have included any of the following: metabolic parameters (HbA1c, fasting blood glucose), muscle strength, and physical function
Study design	Only randomised trial studies

Selection process

The search was carried out by one reviewer, after which duplicate records were removed using Mendeley Reference Manager. To assess eligibility, titles and abstracts were first screened by an independent researcher, followed by a full-text review of the selected articles. Data extraction was performed for each study, focusing on the following elements: details of the resistance training intervention, pre- and post-intervention outcome means, standard deviations of measured variables, FITT principle components, and year of publication.

Quality appraisal and data extraction

The current review used the JBI Critical Appraisal Checklist for Randomised Controlled Trials (RCTs) and Randomised Controlled Crossover (RCC) studies. Methodological quality was evaluated using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Randomized Controlled Trials. Due to heterogeneity and limited sample sizes, quantitative synthesis was not feasible, and findings were analysed narratively.

Results

Description of the included studies

Search results

Identification and selection of studies: Electronic searches yielded 13 840 articles. When duplicates and studies that did not meet the inclusion criteria were removed, five studies remained for qualitative analysis. The most common reasons for exclusion were animal studies, not resistance exercise intervention, systematic reviews, and only included abstracts (Figure 1).

Study characteristics

Trial settings and participants: Table 2 presents the characteristics of studies included in the review. Exercise programme settings included clinics and community areas. The total number of participants in the included trials ranged from 22 to 237. The mean age ranged from 60 to 92 years.

Intervention: Studies included in this review prescribed individualised resistance exercises. Of the five studies, one study, by Geirsdottir et al.,⁶ prescribed resistance training combined with dietary supplements, which consisted of a whey protein drink (20 g whey protein isolate + 20 g carbohydrates); a milk protein drink (20 g milk protein isolate + 20 g carbohydrates) or a carbohydrate drink (40 g carbohydrates). In another study, Dunstan et al.¹⁶ prescribed individualised resistance training combined with weight-loss eating. In addition, Dunstan et al.¹⁶ prescribed moderate-intensity exercise and Geirsdottir et al.⁶ prescribed high-intensity exercise. Cauza et al.¹⁷ reported on prescribed resistance and endurance training. Progressive resistance training uses light weights with exercises designed to target major muscle groups such as the legs, shoulders, and back. The duration of exercise sessions in both trials^{5,6} was 40–60 minutes. Both studies prescribed three non-consecutive exercise sessions per week for a duration of 12 and 24 weeks.^{5,6}

Study quality

The reviewed studies generally performed well on the JBI Critical Appraisal Checklist for RCTs. Groups were managed in the same way aside from the intervention, follow-ups were conducted, analyses reflected the original randomisation, and outcomes were measured consistently.

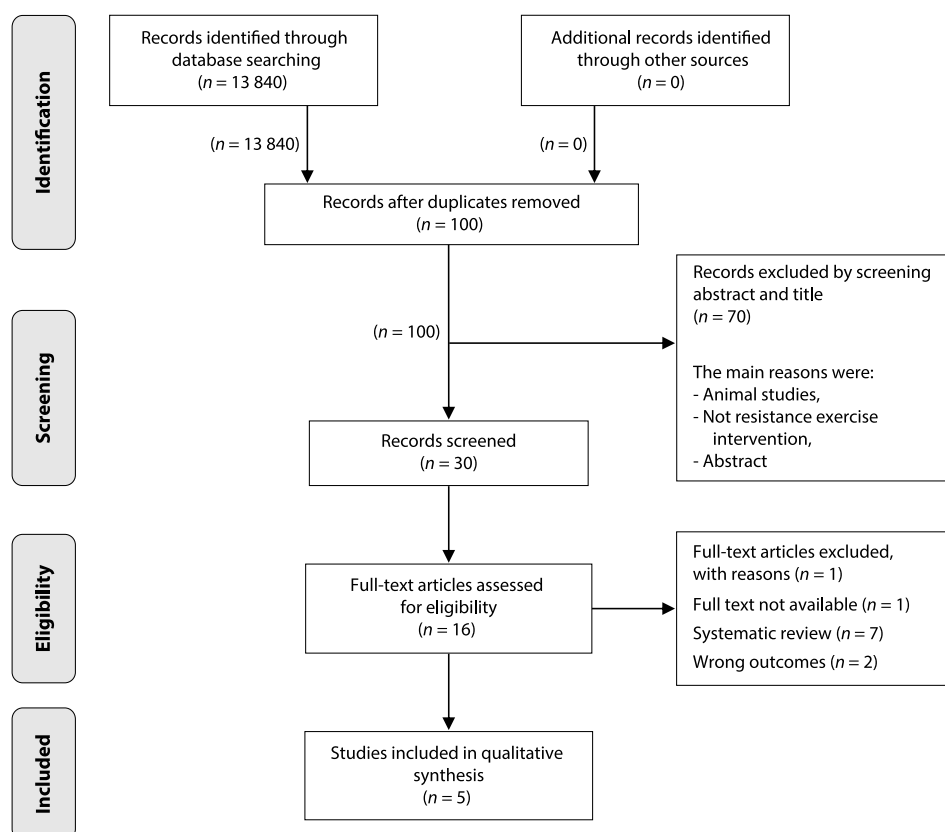


Figure 1: PRISMA 2009 flow diagram.

Study outcomes

Fasting blood glucose: Findings related to fasting glucose and HbA1c were inconsistent across studies. Four studies reported on the metabolic parameter fasting blood glucose and the studies reported positive findings. Dunstan et al.¹⁶ reported that during the 12 weeks no changes were detected in either group after 3 months, but a 1.4 mmol/l decrease ($p < 0.06$) was observed in the RT and WL group after 6 months. Geirsdottir et al.⁶ reported that fasting blood glucose increased from 7.83 ± 1.04 mmol/l to 8.20 ± 0.87 mmol/l, following 12 weeks of exercise training. Cauza et al.¹⁷ reported a significant decrease in fasting blood glucose (204 ± 16 mmol/l to 147 ± 8 mmol/l, $p < 0.001$) in the intervention group after 4 months of training. Hsieh et al.¹⁸ reported that the fasting blood glucose of the intervention group (7.2 ± 0.60 mmol/l to 7.1 ± 0.8 mmol/l) showed a minor improvement after 3 months of RT.

HbA1c: Four studies reported a significant reduction in HbA1c levels in the blood following 12 and 24 weeks of exercise training. The study by Dunstan et al.¹⁶ reported that the RT and WL programme was associated with a significant reduction in HbA1c at 3 months ($0.6 \pm 0.7\%$, $p < 0.01$) and 6 months ($1.2 \pm 0.9\%$, $p < 0.01$). Geirsdottir et al.⁶ reported that HbA1c increased from $6.83 \pm 0.95\%$ at baseline to $6.95 \pm 0.48\%$. Cauza et al.¹⁷ reported that a significant decline in HbA1c was observed only in the intervention group ($8.3\% \pm 1.7\%$ to $7.1\% \pm 0.2\%$, $p < 0.001$). The study by Kwon et al.¹² reported an unchanged HbA1c after the 12-week programme in both groups. According to Hsieh et al.,¹⁸ HbA1c increased from $6.83\% \pm 0.95\%$ at baseline to $6.95 \pm 0.48\%$ after 3 months of RT in the intervention group.

Muscle strength: The study by Dunstan et al.¹⁶ reported significant increases in both upper and lower body muscle strength throughout the intervention. The overall net percentage

change from baseline in upper body strength in the RT and WL group was 22.9% (95% CI 7.6–38.2, $p < 0.01$) at 3-months and 41.7% (95% CI 14.4–69.0, $p < 0.01$) at 6 months. For lower body strength, the net percentage change from baseline in the RT and WL group was 5.8% (95% CI 8.9–20.6, $p = 0.6$) at 3 months and 28.0% (95% CI 9.1–46.9, $p < 0.01$) at 6 months. In the study by Geirsdottir et al.,⁶ quadricep strength increased from 7.84 ± 2.07 kg at baseline to 9.22 ± 2.23 kg after the intervention, while grip strength significantly changed from 27.04 ± 7.37 kg at baseline to 32.16 ± 10.88 kg after the 12-week intervention. The study by Cauza et al.¹⁷ reported significant improvement in 1RM of all muscle groups following RT (22–48% of initial levels). Kwon et al.¹² also reported a significant increase in 1RM for the upper and lower body and arms and legs of the resistance training group (by 2.0 ± 4.3 kg and 10.1 ± 15.7 kg, respectively). The study by Hsieh et al.¹⁸ showed that the 1RM chest-press strength in the intervention group increased by 3.9 kg (95% CI 1.0–6.8, $p = 0.012$) after RT. The 1RM leg-press strength increased by 49.0 kg (95% CI 30.2–67.8, $p < 0.001$) in the intervention group after RT.

Physical function: Two trials examined the physical function of adults with T2DM. The study by Geirsdottir et al.⁶ reported significant results for the timed up-and-go test, which changed from 9.13 ± 2.68 seconds to 8.75 ± 3.21 seconds after 12 weeks of intervention. Hsieh et al.¹⁸ reported that the time to finish five sit-to-stands decreased in the intervention group by -2.2 seconds (95% CI -3.5 to -1.0 , $p = 0.002$).

Discussion

The current review shows that exercise training for 12 and 20 weeks improved metabolic parameters, muscle strength, and physical function, as reported by Dunstan et al.¹⁶ and Geirsdottir et al.⁶ Both short- and long-term exercises improve metabolic

Table 2: characteristics of studies included in the review ($n = 5$)

Source	Sample size (M/F)	Age (years)	Intervention			Findings
			Group	Intensity	Frequency and duration	
Dunstan et al. (2002)	28 (16/13)	66.9	RT + HE	50–60% 1RM 75%–85% 1RM	Three times a week for six months	Resistance training (RT) + healthy eating (HE) significantly lowered glycosylated haemoglobin (HbA1c), which changed from $(0.6\% \pm 0.7\%)$ at three months to $(1.2\% \pm 0.9\%)$ at six months The upper body strength in the RT and weight loss (WL) group changed from 22.9% to 41.7% For lower body strength, the net percentage change was from 5.8% to 28.0% after intervention For fasting blood glucose, the intervention group showed a 1.4 mmol/l decrease
Geirsdottir et al. (2012)	237 (98/139)	75.18	RT + supplements (S)	60% of 1RM 75–85% 1RM	Three times a week for three months	Glycosylated haemoglobin changed from $6.83\% \pm 0.95\%$ at baseline to $6.9\% \pm 0.48\%$ after intervention Fasting blood glucose did not show an improvement (7.83 ± 1.04 mmol/l, to 8.20 ± 0.87 mmol/l), after intervention Quadricep strength significantly changed from 7.84 ± 2.07 kg at baseline to 9.22 ± 2.23 kg after the intervention, whereas grip strength significantly changed from 27.04 ± 7.37 kg at baseline to 32.16 ± 10.88 kg after the intervention The timed up-and-go test significantly changed from 9.13 ± 2.68 s to 8.75 ± 3.21 s after intervention
Cauza et al. (2005)	22 (11/11)	56.2 ± 1.1	RT + endurance training (ET)	15–20% 1RM	three times a week for four months	A significant decline in HbA1c was observed only in the intervention group ($8.3\% \pm 1.7\%$ to $7.1\% \pm 0.2\%$, $p < 0.001$) Fasting blood glucose (204 ± 16 mmol/l to 147 ± 8 mmol/l, $p < 0.001$) also showed a significant decrease The improvement in maximum strength one-repetition maximum (1RM) of all muscle groups subjected to resistance training was highly significant (22–48% of initial levels)
Kwon et al. (2011)	28 (0/28)	56.4 ± 7.1	RT	40–50% 1RM	Three times a week for three months	Glycosylated haemoglobin was unchanged after the 12-week programme in both groups In the resistance training group, the 1RM for the upper and lower body and arms and legs of the resistance training group was increased significantly (by 2.0 ± 4.3 kg and 10.1 ± 15.7 kg, respectively)
Hsieh et al. (2018)	30 (11/19)	$71. \pm 2$ 4.3	RT	40–50% 1RM 75% 1RM	Three times a week for three months	Glycosylated haemoglobin changed from $6.83\% \pm 0.95\%$ at baseline to $6.9\% \pm 0.48\%$ after RT in the intervention group Fasting blood glucose of the intervention group (7.2 ± 0.60 mmol/l to 7.1 ± 0.8 mmol/l) also showed a minor improvement after RT The 1RM chest-press strength in the intervention group increased by 3.9 kg (95% confidence interval [CI] 1.0–6.8, $p = 0.012$) after RT The 1RM leg-press strength increased by 49.0 kg (95% CI 30.2–67.8, $p < 0.001$) in the exercise group after RT The time to finish five sit-to-stands decreased in the intervention group by -2.2 seconds (95% CI -3.5 to -1.0 , $p = 0.002$)

RT: resistance training; HE: healthy eating; HbA1c: glycosylated haemoglobin; S: supplements; ET: endurance training; 1RM: one repetition maximum.

parameters, strength, and physical function among adults with T2DM. Thus, both short- and long-term exercises may be applicable in the treatment of T2DM. Long-term exercise training may encourage individuals to adopt a physically active lifestyle.¹⁹ Despite research showing that resistance training enhances muscle strength in older adults with T2DM,²⁰ it was found that T2DM participants gained less strength than non-T2DM participants. The impairment in the basal hypothalamic–pituitary–adrenal axis functions as a limiting factor in strength development in older T2DM adults.

Studies lasting from several weeks to several months have demonstrated a decrease in HbA1c in individuals with T2DM following resistance exercise, though not all of them agree.^{12,21,22} According to Strasser et al.,²⁶ baseline HbA1c levels of more than 8.0% were associated with the biggest gains in glycaemic control. This may account for the lack of change in HbA1c among T2DM participants following the intervention, as it is greater than the average HbA1c in our T2DM group (6.8% at baseline). Microvascular complications are reduced by 35% for each percentage point that the HbA1c is lowered, according

to data from the UK Perspective Diabetes Study.²⁴ The study by Hsieh et al.¹⁸ reported a significant change in HbA1c ($6.83\% \pm 0.95\%$ at baseline to $6.9\% \pm 0.48\%$ after RT) in the intervention group following the 3 months of resistance training, and this concurred with the study by Sartore et al.⁷

The study by Dunstan et al.¹⁶ reported that after 4 months of resistance exercise, a 29% drop in fasting blood glucose was observed in T2DM participants (compared with baseline). Despite receiving medication therapy, the patients' baseline glucose levels were higher than 11 mmol/l, which may account for the significant improvements observed following training.⁵ Studies that have combined resistance and endurance training have also shown improvements in fasting blood glucose blood after training in individuals with T2DM who had baseline fasting blood glucose levels between 9.2 and 12.0 mmol/l, and this is consistent with the results of Cauza et al.^{17,25–28}

However, a study by Holten et al.¹³ found that, after a 6-week strength training programme, increases in participants' maximal leg muscle strength were comparable in older men with T2DM and healthy older men, which is consistent with the findings of Hsieh et al.¹⁸ in this review.¹³ The most consistent clinical finding across the included studies was an improvement in muscle strength, observed irrespective of programme duration or intensity. Improvements in glycaemic markers were variable and appeared strongly dependent on baseline HbA1c levels, intervention duration, and the presence of co-interventions such as dietary modification or combined endurance training.

Physiologically, resistance training may improve insulin sensitivity through increased skeletal muscle mass and enhanced glucose transporter (GLUT-4) expression; however, these mechanisms may be insufficient in isolation to produce measurable improvements in HbA1c in individuals with relatively controlled diabetes at baseline.⁹ Studies demonstrating improvements in glycaemic control generally involved participants with higher baseline HbA1c (> 8%) or incorporated longer intervention durations and additional lifestyle modifications.

The narrative nature of this synthesis, necessitated by heterogeneity and limited data aggregation, restricts the ability to draw definitive conclusions regarding glycaemic outcomes. Nonetheless, findings support the role of resistance training in improving functional health outcomes in adults with T2DM.

Conclusion

This review indicates that resistance training consistently improves muscle strength and physical function in adults with type-2 diabetes mellitus. However, evidence for improvements in metabolic parameters such as HbA1c and fasting glucose is inconsistent and appears dependent on baseline metabolic status and intervention characteristics. Given the narrative nature of the synthesis and the small number of heterogeneous studies, conclusions regarding glycaemic control should be interpreted with caution.

Limitations of the study

This review was limited to published studies and excluded unpublished data. The heterogeneity of interventions and outcome measures limited the ability to conduct meta-analysis. Additionally, several studies incorporated resistance training

alongside other interventions, making it difficult to isolate the effects of resistance training alone.

Acknowledgements – The author would like to thank my supervisor who made this journey easy to walk through, and the University of KwaZulu-Natal for its support.

Disclosure statement – No potential conflict of interest was reported by the authors.

Funding – This research received funding from the UKZN College of Health Sciences, the UKZN Talent Equity and Excellence Acceleration Scholarship, and the National Research Foundation of South Africa.

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Received:27-10-2025 Accepted: 04-03-2026

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Prevalence of microalbuminuria and associated factors among diabetic patients attending a general hospital in Central Uganda

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Introduction: Microalbuminuria is an early indicator of kidney damage and a strong predictor of diabetic nephropathy in diabetic patients. Its prevalence and associated factors vary across populations, necessitating region-specific studies. This study evaluated the prevalence of microalbuminuria and its associated factors among diabetic patients attending a general hospital in Central Uganda.

Methods: From September 2024 to December 2024, a structured questionnaire was used to carry out a descriptive and analytical cross-sectional study among patients with diabetes at Nakaseke General Hospital in Central Uganda. Blood and urine samples from each participant were also analysed for determination of HbA1c, serum gamma glutamyl transferase (GGT), and microalbumin respectively. Microalbuminuria was defined as urine microalbumin levels of 20–200 mg/L. Logistic regression analysis was used to assess associated factors.

Results: Of 298 participants, 220 (73.8%, 95% CI: 68.52–78.52) had microalbuminuria. The majority were females: 193 (64.8%). GGT levels were significantly higher in participants with microalbuminuria: 45.5IU/L (IQR: 33.5–57) than in those with normoalbuminuria: 39.5IU/L (IQR: 29–50), $p = 0.011$. HbA1c levels, indicative of glycaemic control, were noticeably greater in the microalbuminuria group: 8.2% (IQR: 7.2–9.65) as compared with those with normoalbuminuria: 7.6% (IQR: 6.9–9.1), $p = 0.012$. After adjustment for confounders, factors significantly associated with microalbuminuria were HIV-positive status (aOR = 3.20, $p = 0.030$), hypertension (aOR = 4.43, $p = 0.011$), and unemployment status (aOR = 2.32, $p = 0.023$).

Conclusion: Microalbuminuria is prevalent among patients with diabetes. Microalbuminuria is associated with elevated GGT, and HbA1c levels, HIV positivity, hypertension, and unemployment. Screening, more stringent glycaemic and blood pressure control, and targeted interventions are warranted in high-risk groups to prevent the onset of diabetic nephropathy.

Introduction

Microalbuminuria is defined as the urinary excretion of albumin ranging from 30 to 300 mg per day or an albumin-to-creatinine ratio (ACR) of 30–300 mg/g in at least two different spot urine samples.^{1,2} It serves as an early marker of diabetic nephropathy (DN), a major contributor to diabetes patients' end-stage renal disease (ESRD).^{3–5} In individuals with diabetes mellitus (DM), microalbuminuria is not only an indicator of kidney dysfunction but also a strong predictor of cardiovascular morbidity and mortality.⁶ Early detection of microalbuminuria permits prompt interventions such as blood glucose control, blood pressure management, and lifestyle modifications, which can slow the progression to overt nephropathy and reduce associated complications.⁷

The prevalence of microalbuminuria among individuals with diabetes is heterogeneous in the world, with rates ranging between 20% and 40% in industrialised countries.⁸ Systematic review has documented a pooled prevalence of 37.1% in sub-Saharan Africa, which testifies to the evolving burden of diabetes and its complications in the region.⁹ In East Africa, the prevalence is estimated to be between 9.8% and 54.3%

according to a few cross-sectional studies conducted in the region.⁹ In Uganda, there are still limited studies that have assessed the factors contributing to burden of microalbuminuria among patients with diabetes.

Several factors contribute to the development of microalbuminuria in patients with diabetes, including poor glycaemic control, hypertension, dyslipidaemia, obesity, and genetic predisposition.¹⁰ Recent evidence suggests that elevated serum gamma-glutamyl transferase (GGT) levels, a marker of oxidative stress and liver injury, correlate strongly with microalbuminuria in patients with diabetes.¹¹ Inadequate glycaemic control, reflected by elevated glycated haemoglobin (HbA1c) levels, remains a major impetus for diabetic nephropathy as chronic hyperglycaemia leads to glomerular damage through oxidative stress, inflammation, and endothelial dysfunction.¹² Despite these known risk factors, evidence on their role in microalbuminuria among Ugandan diabetic patients remains limited.

Past studies have generally incorporated renal complications in patients with diabetes without a specific focus on

microalbuminuria. Moreover, the relationship between serum concentrations of GGT, glycaemia, and microalbuminuria has not been clearly outlined in diabetic patients in the Ugandan context. The aim of this study was to determine the prevalence and determinants of microalbuminuria including serum GGT and the glycaemic control level in diabetic outpatients in a Central Ugandan general hospital. The findings provide critical data to inform early screening and specific interventions to relieve diabetic nephropathy burden among these individuals.

Methods

Study design, population, site, duration, and sampling technique

A descriptive and analytical cross-sectional study was conducted among diabetic patients at Nakaseke General Hospital between September 2024 and December 2024. Nakaseke Hospital is a public healthcare facility located in Nakaseke town, Nakaseke District, within the Luwero Triangle region. Geographically, the hospital is situated approximately 65 km north-west of Mulago National Referral Hospital and 35 km north-west of Bombo Military Hospital. The hospital provides a range of healthcare services, including diabetes clinics, an antiretroviral therapy (ART) clinic, orthopaedic services, and general medical care. The study involved male and female patients attending the diabetes clinic who provided written informed consent. The clinic primarily serves individuals already diagnosed with diabetes mellitus, including both type 1 and type 2 diabetes mellitus, who are under regular follow-up and receiving diabetic medication. Patients with missing medical history, those with a known diagnosis of kidney disease who were already receiving treatment for the condition, and those with communication impairments were excluded from the study. The participants were recruited consecutively in a manner such that all eligible individuals fulfilling the inclusion criteria were included until an adequate sample size was achieved.

Sample size determination

The Kish–Leslie formula¹³ was used to determine the minimum required sample size using the following assumptions; prevalence of microalbuminuria of 22.9% among patients with diabetes,³ 5% precision and a 95% confidence interval and a Z-statistic of 1.96.

$n = Z^2 P(1-P)/d^2$ where n is required sample size, Z is Z-statistic for a level of confidence, P is hypothesised prevalence, and d is precision.

$$n = 1.96^2 \times 0.229(1-0.229)/0.05^2 = 271.3.$$

By considering a 10% non-response rate, the minimum sample size for this study was 298 participants. Therefore, the minimum sample size of 298 study participants was considered for this study.

Study variables

Dependent variable

Microalbuminuria was the primary dependent variable.

Independent variables

The independent variables are categorised as sociodemographic factors, behavioural factors, clinical factors, and HIV and/or ART-related factors. The sociodemographic factors

include age, sex, residence, education level, religion, employed status, and marital status. The behavioural factors include smoking status, alcohol consumption, sleep duration, sleep quality, obstructive sleep apnoea, fruit and vegetable intake, and physical activity. Clinical factors will include comorbidities (hypertension, HIV, cardiovascular disease, dyslipidaemia), family history of comorbidities (hypertension, HIV, cardiovascular disease, dyslipidaemia), type of diabetes mellitus (DM), duration with DM, type of DM treatment, adherence to DM medication, family history of DM, anthropometric parameters (body mass index, waist circumference, waist-to-height ratio, waist-to-hip ratio, mid upper-arm circumference), blood pressure, and biochemical parameters (glycated haemoglobin).

Data collection tools, procedures, and operational definitions

A structured questionnaire was used to collect data on the sociodemographic, behavioural, and clinical factors. From medical records, we collected data on the duration of DM, type of DM treatment received, and the presence of chronic comorbid conditions including hypertension, HIV, and cardiovascular disease. Physical activity was assessed using the International Physical Activity Questionnaires (IPAQ) and categorised as < 600 (Low), 600–3 000 (Moderate), and > 3 000 (High) MET-minutes/week.¹⁴ Obstructive sleep apnoea was assessed using the Stop Bang scoring model and classified as high risk and low risk.¹⁵ Furthermore, data on anthropometric parameters (weight, height, waist circumference [WC], and hip circumference [HC]) and blood pressure (BP) were collected from the study participants by a well-trained nurse under the supervision of the principal investigators. In this study, blood pressure was measured using a digital sphygmomanometer, which was determined by taking the mean of two blood pressure readings that were collected five minutes apart. High blood pressure was defined as systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg.^{16,17} The weight and height of the participant was measured using a portable weight and height scale. Body mass index (kg/m^2) was calculated from weight and height and was categorised as normal ($< 25 \text{ kg}/\text{m}^2$), overweight ($25\text{--}29.9 \text{ kg}/\text{m}^2$), and obese ($\geq 30 \text{ kg}/\text{m}^2$).¹⁸ A non-stretchable Seca Ergonomic Circumference Measuring Tape (Seca GmbH, Hamburg, Germany) was used to measure the waist and hip circumferences. Two circumference readings were taken, and a third measurement was only done if the difference between first two was greater than 3 cm. Waist and hip circumferences were taken as the mean of two or three measurements. High waist circumference was defined as > 80 cm for females and > 94 cm for males.¹⁹ Waist-to-hip ratio was calculated from waist and hip circumferences and considered to be high if ≥ 0.85 for females and ≥ 0.9 for males.¹⁹ Low fruit and vegetable intake was defined as consuming less than five servings of fruit and/or vegetables per day.²⁰

For HbA1c analysis, capillary blood was collected from each participant into a capillary tube, then placed into a test cartridge that was inserted into an Afinion™ HbA1c analyser (Abbott Diagnostics Technologies AS, Oslo, Norway) at Nakaseke Hospital laboratory for glycated haemoglobin level determination. HbA1c was categorised as $\leq 7\%$ (good glycaemic control) and $> 7\%$ (poor glycaemic control).^{21,22} About 4 mL of venous blood sample was also collected from each of the study participant using red top vacutainers by the principal investigators, left for 15 minutes to clot, then centrifuged to obtain serum and put into cryovials. The serum samples in cryovials were properly packaged in dry ice and shipped on the day of

collection to the Uganda Cancer Institute laboratory, a SANAS-accredited facility compliant with International Standard ISO 15189:2022 (Accreditation No. M0921). Serum GGT levels were determined using the Cobas 6000 Roche analyser (Roche Diagnostics Basel, Switzerland), with GGT being one of the twenty accredited chemistry tests. Serum GGT levels were categorised as ≤ 50 U/L and > 50 U/L.²³ The study participants were also requested to provide a urine sample, which was analysed for urine microalbumin using a semi-quantitative urine dipstick method COMBINA 13, a product of Human Diagnostics (Wiesbaden, Germany). Results of a visual reading of COMBINA 13 compared with the fully quantitative immunoturbidimetry laboratory assay show agreement of 97.2% for normal and 95.7% for positive urine specimens. The overall agreement for the presence of microalbumin with a variation of $\pm$ one test pad is 98.6%.²⁴ COMBINA 13 strips were designed for the determination of up to 13 different analytes including microalbumin in human urine to provide diagnostic information on kidney disorders, liver diseases, urinary tract infections, haemolytic disorders, diabetes, metabolic abnormalities, and problems with the acid-base equilibrium. Test strips were immersed into the urine sample for approximately 2 seconds; excess liquid was stripped off on tissue paper. The developing colour of the microalbumin pad was read within 60 seconds and the pad colour was visually compared with a colour reference chart on the tube. The microalbumin parameter on the strip is designed to capture participants with 10, 30, 80, and 150 mg/L. Microalbuminuria is defined as urine albumin levels between 20 and 200 mg/L.^{25,26} A urine sample that resulted in a colour change on the COMBINA 13 strip corresponding to 30, 80, and 150 mg/L but negative for macroalbuminuria was considered to have microalbuminuria.

Statistical analysis

Microsoft Excel (Microsoft Corp, Redmond, WA, USA) was used to double-enter the gathered data, which were exported to STATA version 17 Software for analysis (StataCorp, College Station, TX, USA). Continuous variables were tested for normality using the Shapiro–Wilk normality test and were not normally distributed ($p < 0.05$) except for age. These were summarised using median (interquartile range: IQR) and a nonparametric test; a Mann–Whitney U test was used to compare their medians between participants with and without the outcome variable (microalbuminuria) to test whether there were any statistical differences between the two groups. A p -value < 0.05 was considered statistically significant. Age was summarised using mean $\pm$ standard deviation and the means in the two groups of the outcome were compared using Student's t -test. Categorical variables were summarised using frequencies and proportions (percentages).

The proportions of study participants with microalbuminuria and poor glycaemic control together with their 95% confidence intervals were determined by dividing the number of participants with each of the variables by the total number of study participants recruited and was expressed as a percentage and graphically presented using bar graphs. The distribution of microalbuminuria prevalence across the different levels of each of the categorical independent variables was compared using a chi-square test or Fisher's exact test. A p -value < 0.05 was considered to be statistically significant.

The studied factors were assessed using logistic regression. Microalbuminuria was the binary dependent variable (0 = absent, 1 = present). All independent variables, at bivariate

level, were compared with the dependent variable. The statistically significant prevalence ratios were identified by a p -value ≤ 0.2 at the bivariate level, and the associations were evaluated using odds ratios and their 95% CI. The multivariable model evaluated the factors that were statistically and/or clinically significant at this level. Precision, accuracy, and collinearity were adjusted for in the multivariate analysis by dropping some of the variables from the multivariate model without significant loss in the validity of the model. P -values ≤ 0.05 were deemed significant for relationships in the final multivariable model. We also used Spearman's rank correlation test to assess the correlation of serum GGT and HbA1c levels with urine microalbumin.

Results

Characteristics of the study participants stratified by albuminuria status

A total of 298 participants with a mean age of 54.66 ± 13.05 years were recruited for this study. There was a significant age difference between participants with and without microalbuminuria: 56.29 vs. 50.08, $p < 0.001$. The majority of the study participants were females: 193 (64.8%), married: 198 (66.4%), Catholic: 97 (32.6%), and resided in rural areas: 176 (59.1%). Significantly higher levels: 45.5 IU/L (IQR: 33.5–57) of GGT were observed in participants with microalbuminuria compared with those with normoalbuminuria: 39.5 IU/L (IQR: 29–50), $p = 0.011$. HbA1c levels, indicative of glycaemic control, were significantly higher in the microalbuminuria group: 8.2% (IQR: 7.2–9.65) as compared with those with normoalbuminuria: 7.6% (IQR: 6.9–9.1), $p = 0.012$. Additionally, participants with lower education levels and unemployment were observed to be significantly more common in the microalbuminuria group: 34.1% vs. 15.4%, $p < 0.001$ and 55.5% vs. 37.2% $p = 0.006$ respectively. The proportion of those with hypertension was significantly higher among participants with microalbuminuria: 119 (54.1%) compared with those with normoalbuminuria: 23 (29.5%), $p < 0.001$. High adherence to anti-diabetic medication was observed to be significantly higher in participants with microalbuminuria: 133 (60.5%) compared with those with normoalbuminuria: 44 (56.4%), $p = 0.010$. Further, significantly longer durations of diabetes and anti-diabetes medication were observed among participants with microalbuminuria (6 years vs. 5 years $p = 0.042$ and 6 years vs. 4.5 years, $p = 0.022$, respectively) compared with those with normoalbuminuria. Significantly higher systolic blood pressure and waist-to-height ratio were observed among participants with microalbuminuria ($p = 0.005$ and $p = 0.014$) respectively, as shown in Table 1. Other participant characteristics were evenly distributed in the two groups of albuminuria, $p > 0.05$ as indicated in Table 1.

Proportion of patients with diabetes who have microalbuminuria

Of the 298 participants who were recruited, 220 (73.8%) had microalbuminuria, giving an overall prevalence of 73.8% with a 95% CI of 68.52–78.52 as shown in Figure 1 and Table 2. The prevalence of microalbuminuria significantly increased with age, being highest among participants aged 60 years and above (81.0%), followed by those aged 50–59 years (76.7%), 40–49 years (71.8%), and lowest among those below 40 years (50.0%) ($p = 0.002$). The prevalence of microalbuminuria was also significantly higher among participants with elevated GGT levels (> 50 IU/L) compared with those with lower GGT levels (82.7% vs. 68.7%, $p = 0.007$). Educational attainment was

Table 1: Characteristics of the study participants stratified by albuminuria status

Variable	Total N = 298	Albuminuria status		Statistical test	p-value
		Normalalbuminuria <i>n</i> ₁ = 78	Microalbuminuria <i>n</i> ₂ = 220		
Age (years): mean (SD)	54.66 (13.05)	50.08 (13.39)	56.29 (12.57)	Student's <i>t</i> -test	< 0.001
Gender:				Chi-square test	0.68
Male	105 (35.2%)	26 (33.3%)	79 (35.9%)		
Female	193 (64.8%)	52 (66.7%)	141 (64.1%)		
Gamma glutamyl transferase: median (IQR)	44 (30–56)	39.5 (29–50)	45.5 (33.5–57)	Mann–Whitney <i>U</i>	0.011
Haemoglobin A1c: median (IQR)	8.2 (7.1–9.6)	7.6 (6.9–9.1)	8.2 (7.2–9.65)	Mann–Whitney <i>U</i>	0.012
Marital status:				Chi-square test	0.083
Single	18 (6.0%)	6 (7.7%)	12 (5.5%)		
Married/cohabiting	198 (66.4%)	58 (74.4%)	140 (63.6%)		
Separated/divorced	82 (27.5%)	14 (17.9%)	68 (30.9%)		
Education level:				Chi-square test	< 0.001
No education	87 (29.2%)	12 (15.4%)	75 (34.1%)		
Primary education	89 (29.9%)	24 (30.8%)	65 (29.5%)		
Secondary education	72 (24.2%)	19 (24.4%)	53 (24.1%)		
Tertiary education	50 (16.8%)	23 (29.5%)	27 (12.3%)		
Religion status:				Chi-square test	1.00
Catholic	97 (32.6%)	25 (32.1%)	72 (32.7%)		
Protestant	84 (28.2%)	22 (28.2%)	62 (28.2%)		
Moslem	46 (15.4%)	12 (15.4%)	34 (15.5%)		
Other	71 (23.8%)	19 (24.4%)	52 (23.6%)		
Employment status:				Chi-square test	0.006
Unemployed	151 (50.7%)	29 (37.2%)	122 (55.5%)		
Employed	147 (49.3%)	49 (62.8%)	98 (44.5%)		
Residence					0.10
Rural	176 (59.1%)	40 (51.3%)	136 (61.8%)	Chi-square test	
Urban	122 (40.9%)	38 (48.7%)	84 (38.2%)		
Smoking status:				Chi-square test	0.98
Never	231 (77.5%)	61 (78.2%)	170 (77.3%)		
Former	44 (14.8%)	11 (14.1%)	33 (15.0%)		
Current	23 (7.7%)	6 (7.7%)	17 (7.7%)		
Alcohol consumption:				Chi-square test	0.22
Never	167 (56.0%)	43 (55.1%)	124 (56.4%)		
Former	76 (25.5%)	16 (20.5%)	60 (27.3%)		
Current	55 (18.5%)	19 (24.4%)	36 (16.4%)		
IPAQ Total (MET min/week): Median (IQR)	4 823 (1 980–8 262)	5 617 (3 180–9 210)	4 617 (1 708.5–7 965)	Mann–Whitney <i>U</i>	0.081
Mean upper-arm circumference (cm): Median (IQR)	25.7 (24–27.8)	25 (24.1–26.7)	26 (24–28)	Mann–Whitney <i>U</i>	0.072
Vegetable fruit intake (days):				Chi-square test	0.87
< servings per day	231 (77.5%)	61 (78.2%)	170 (77.3%)		
≥ servings per day	67 (22.5%)	17 (21.8%)	50 (22.7%)		
Days vegetable consumption per week (days):				Chi-square test	0.37
≤ 4 days	238 (79.9%)	65 (83.3%)	173 (78.6%)		
> 4 days	60 (20.1%)	13 (16.7%)	47 (21.4%)		
Hypertension:				Chi-square test	< 0.001
No	156 (52.3%)	55 (70.5%)	101 (45.9%)		
Yes	142 (47.7%)	23 (29.5%)	119 (54.1%)		
HIV status				Chi-square test	0.059
Negative	256 (85.9%)	72 (92.3%)	184 (83.6%)		

(Continued)

Table 1: Continued.

Variable	Total N = 298	Albuminuria status		Statistical test	p-value
		Normalalbuminuria n ₁ = 78	Microalbuminuria n ₂ = 220		
Positive	42 (14.1%)	6 (7.7%)	36 (16.4%)		
Cardiovascular disease:				Chi-square test	0.22
No	205 (68.8%)	58 (74.4%)	147 (66.8%)		
Yes	93 (31.2%)	20 (25.6%)	73 (33.2%)		
Sleep duration (hours):				Chi-square test	0.10
< 5 h	35 (11.7%)	12 (15.4%)	23 (10.5%)		
5–7 h	190 (63.8%)	42 (53.8%)	148 (67.3%)		
> 7 h	73 (24.5%)	24 (30.8%)	49 (22.3%)		
Sleep quality:				Chi-square test	0.56
Poor	54 (18.1%)	16 (20.5%)	38 (17.3%)		
Moderate	126 (42.3%)	35 (44.9%)	91 (41.4%)		
Good	118 (39.6%)	27 (34.6%)	91 (41.4%)		
Obstructive sleep apnoea:				Chi-square test	0.26
Low risk of OSA	148 (49.7%)	43 (55.1%)	105 (47.7%)		
High risk of OSA	150 (50.3%)	35 (44.9%)	115 (52.3%)		
Family history of hypertension:				Chi-square test	0.17
No	148 (49.7%)	44 (56.4%)	104 (47.3%)		
Yes	150 (50.3%)	34 (43.6%)	116 (52.7%)		
Family history of cardiovascular disease:				Chi-square test	0.74
No	194 (65.1%)	52 (66.7%)	142 (64.5%)		
Yes	104 (34.9%)	26 (33.3%)	78 (35.5%)		
Family history of dyslipidaemia:				Chi-square test	0.094
Yes	103 (34.6%)	33 (42.3%)	70 (31.8%)		
No	195 (65.4%)	45 (57.7%)	150 (68.2%)		
Family history of kidney disease:				Chi-square test	0.85
No	239 (80.2%)	62 (79.5%)	177 (80.5%)		
Yes	59 (19.8%)	16 (20.5%)	43 (19.5%)		
Anti-diabetic medication adherence:				Chi-square test	0.010
Low adherence	53 (17.8%)	22 (28.2%)	31 (14.1%)		
Moderate adherence	68 (22.8%)	12 (15.4%)	56 (25.5%)		
High adherence	177 (59.4%)	44 (56.4%)	133 (60.5%)		
Duration with diabetes mellitus (years):	6 (4–10)	5 (2–8)	6 (4–10)	Mann–Whitney U	0.042
Duration on Diabetes mellitus medication (years): median (IQR)	5 (3–9)	4.5 (2–8)	6 (3–9.5)	Mann–Whitney U	0.022
Diabetes mellitus medication type:				Chi-square test	0.81
Insulin	15 (5.0%)	3 (3.8%)	12 (5.5%)		
Metformin	184 (61.7%)	48 (61.5%)	136 (61.8%)		
Oral hypoglycaemic agents	58 (19.5%)	14 (17.9%)	44 (20.0%)		
Mixed (insulin & metformin)	41 (13.8%)	13 (16.7%)	28 (12.7%)		
Systolic blood pressure (mmHg): Median (IQR)	124 (118–140)	120 (115–136)	126 (118.5–141)	Mann–Whitney U	0.005
Diastolic blood pressure (mmHg): Median (IQR)	80 (72–89)	80 (70–87)	80 (72–89)	Mann–Whitney U	0.62
Body mass index (kg/m ²): median (IQR)	26.00 (23.62–29.52)	25.67 (23.19–27.92)	26.28 (23.63–29.90)	Mann–Whitney U	0.24
Waist circumference (cm): median (IQR)	77.85 (69.20–82.20)	74.50 (68.50–80.20)	78.00 (70.25–82.60)	Mann–Whitney U	0.10
Waist-to-hip ratio: median (IQR)	0.93 (0.89–0.96)	0.93 (0.89–0.95)	0.93 (0.89–0.96)	Mann–Whitney U	0.44
Weight-to-height ratio: median (IQR)	0.47 (0.44–0.51)	0.46 (0.42–0.5)	0.48 (0.45–0.51)	Mann–Whitney U	0.014

P-values in bold indicate statistically significant findings.

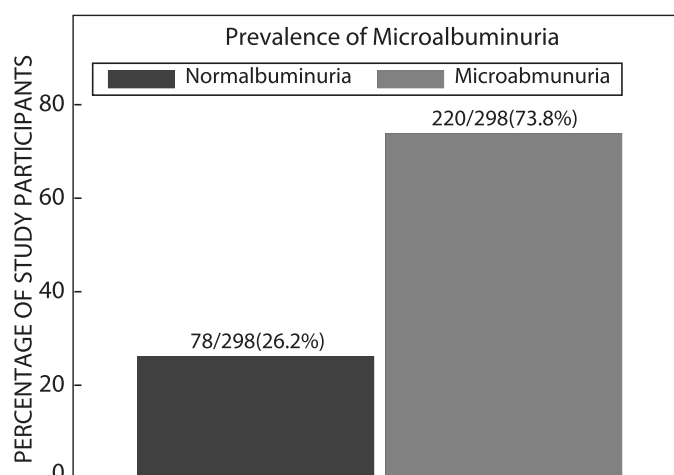


Figure 1: Bar graph showing proportion of diabetic patients with Microalbuminuria.

also associated with microalbuminuria prevalence, where individuals with no formal education showed the highest prevalence (86%, $p < 0.001$). Hypertensive individuals showed a higher prevalence of microalbuminuria (83.8%) compared with non-hypertensive participants (64.7%, $p < 0.001$). Anti-diabetic medication adherence also played a significant role, as those with moderate adherence displayed the highest prevalence of microalbuminuria (82.4%, $p = 0.010$), as shown in Table 2.

According to Spearman's rank correlation test, both GGT: $\rho = 0.2984$ $p < 0.001$, and HbA1c: $\rho = 0.3065$ $p < 0.001$ were significantly and positively correlated with urine microalbumin levels as indicated in Figures 2 and 3 respectively.

Following adjustment for confounders, HIV status, hypertension, and employment status were significantly associated with microalbuminuria (Table 3). HIV-positive individuals had significantly higher odds of developing microalbuminuria compared with their HIV-negative counterparts (aOR = 3.20, $p = 0.030$). Similarly, hypertension was strongly associated with microalbuminuria, with hypertensive participants demonstrating more than fourfold increased odds (aOR = 4.43, $p = 0.011$). Employment status also remained significant in the adjusted model, with unemployed individuals showing a more than twofold higher likelihood of microalbuminuria compared with those who were employed (aOR = 2.32, $p = 0.023$).

Discussion

The noted prevalence of microalbuminuria at 73.8% is significantly high, indicating a critical public health concern. This prevalence is notably higher than the overall pooled prevalence of 37.11% reported across various studies in Africa, indicating that diabetic nephropathy and its associated consequences may be more likely to occur in Ugandan patients with diabetes.^{9,27} In contrast, studies in Uganda have reported varying rates; for instance, a study at Mulago National Referral Hospital found a prevalence of 13.7% among newly diagnosed patients.²⁸ In East Africa, microalbuminuria rates vary greatly, with some studies reporting figures as low as 29%.²⁹ The high prevalence observed in this study could be attributed to several factors, encompassing poor glycaemic control (76.8%), and associated comorbidities such as hypertension (47.7%)

and HIV infection (14.1%), which, according to our analysis, are common in this demographic.

GGT levels were significantly higher in participants with microalbuminuria compared with those with normoalbuminuria. Clinically, elevated GGT, often with liver dysfunction, is also associated with oxidative stress, insulin resistance, and inflammation, all of which participate in renal dysfunction.^{30–32} This suggests that diabetic patients with elevated GGT are more likely to be associated with microalbuminuria, an early marker of diabetic nephropathy. Though no Ugandan or East African and sub-Saharan African studies were registered, global research supports the association between GGT and diabetes-related kidney disease complications.³³ The study also found that the participants with microalbuminuria had significantly higher HbA1c levels compared with those with normoalbuminuria, indicating poorer glycaemic control in the microalbuminuria group. This agrees with previous evidence of a positive association between high levels of HbA1c and the risk of microalbuminuria.³⁴ The study found that HIV positivity was significantly associated with microalbuminuria. The biological link between HIV and microalbuminuria is well supported, as HIV infection induces chronic inflammation, while some antiretrovirals contribute to nephrotoxicity, exacerbating renal impairment.^{35–38}

Additionally, insulin resistance and metabolic alterations seen in both diabetes and HIV further contribute to the increased risk of kidney dysfunction. Supporting evidence from existing literature consistently shows a higher prevalence of microalbuminuria among HIV-infected individuals compared with non-infected controls, with diabetes and HIV together significantly increasing the likelihood of albuminuria, reinforcing the study's findings.³⁵

Hypertension was strongly associated with microalbuminuria in our study. The biological link between hypertension and microalbuminuria is well established, as persistently high blood pressure can damage renal capillaries, leading to increased permeability and protein leakage into the urine.³⁹ This mechanism underscores the need for aggressive blood pressure control in individuals with diabetes to minimise renal complications. Supporting evidence from previous studies consistently identifies hypertension as a significant risk factor for microalbuminuria

Table 2: Distribution of the prevalence of microalbuminuria in the different levels of each independent variable

Variable	Total N = 298	Albuminuria status		Statistical test	p-value
		Normalalbuminuria <i>n</i> ₁ = 78	Microalbuminuria <i>n</i> ₂ = 220		
Age group (years):				Chi-square	0.002
< 40	38 (12.8%)	19 (50.0%)	19 (50.0%)		
40–49	71 (23.8%)	20 (28.2%)	51 (71.8%)		
50–59	73 (24.5%)	17 (23.3%)	56 (76.7%)		
≥ 60	116 (38.9%)	22 (19.0%)	94 (81.0%)		
Gender:				Chi-square	0.68
Male	105 (35.2%)	26 (24.8%)	79 (75.2%)		
Female	193 (64.8%)	52 (26.9%)	141 (73.1%)		
Gamma glutamyl transferase (U/L):				Chi-square	0.007
≤ 50	188 (63.1%)	59 (31.4%)	129 (68.6%)		
> 50	110 (36.9%)	19 (17.3%)	91 (82.7%)		
Haemoglobin A1c:				Chi-square	0.12
≤ 7%, Good	69 (23.2%)	23 (33.3%)	46 (66.7%)		
> 7, Poor	229 (76.8%)	55 (24.0%)	174 (76.0%)		
Marital status:				Chi-square	0.083
Single	18 (6.0%)	6 (33.3%)	12 (66.7%)		
Married/cohabiting	198 (66.4%)	58 (29.3%)	140 (70.7%)		
Separated/divorced	82 (27.5%)	14 (17.1%)	68 (82.9%)		
Education level:				Chi-square	< 0.001
No education	87 (29.2%)	12 (14%)	75 (86%)		
Primary education	89 (29.9%)	24 (27%)	65 (73%)		
Secondary education	72 (24.2%)	19 (26%)	53 (74%)		
Tertiary education	50 (16.8%)	23 (46%)	27 (54%)		
Religion status:				Chi-square	1.00
Catholic	97 (32.6%)	25 (26%)	72 (74%)		
Protestant	84 (28.2%)	22 (26%)	62 (74%)		
Moslem	46 (15.4%)	12 (26%)	34 (74%)		
Other	71 (23.8%)	19 (27%)	52 (73%)		
Employment:				Chi-square	0.006
Unemployed	151 (50.7%)	29 (19.2%)	122 (80.8%)		
Employed	147 (49.3%)	49 (33.3%)	98 (66.7%)		
Residence:				Chi-square	0.10
Rural	176 (59.1%)	40 (22.7%)	136 (77.3%)		
Urban	122 (40.9%)	38 (31.1%)	84 (68.9%)		
Smoking status:				Chi-square	0.98
Never	231 (77.5%)	61 (26.4%)	170 (73.6%)		
Former	44 (14.8%)	11 (25.0%)	33 (75.0%)		
Current	23 (7.7%)	6 (26.1%)	17 (73.9%)		
Alcohol consumption:				Chi-square	0.22
Never	167 (56.0%)	43 (25.7%)	124 (74.3%)		
Former	76 (25.5%)	16 (21.1%)	60 (78.9%)		
Current	55 (18.5%)	19 (34.5%)	36 (65.5%)		
Physical activity (MET min/week):				Chi-square	0.28
< 600	44 (14.8%)	9 (20.5%)	35 (79.5%)		
600–1 500	20 (6.7%)	3 (15.0%)	17 (85.0%)		
> 1 500	234 (78.5%)	66 (28.2%)	168 (71.8%)		
Vegetable fruit intake (per day):				Chi-square	0.87
< servings	231 (77.5%)	61 (26.4%)	170 (73.6%)		
≥ servings	67 (22.5%)	17 (25.4%)	50 (74.6%)		
Vegetable consumption per week (days):				Chi-square	0.37
≤ 4	238 (79.9%)	65 (27.3%)	173 (72.7%)		
> 4	60 (20.1%)	13 (21.7%)	47 (78.3%)		

(Continued)

Table 2: Continued.

Variable	Total N = 298	Albuminuria status		Statistical test	p-value
		Normalalbuminuria n ₁ = 78	Microalbuminuria n ₂ = 220		
Hypertension				Chi-square	< 0.001
No	156 (52.3%)	55 (35.3%)	101 (64.7%)		
Yes	142 (47.7%)	23 (16.2%)	119 (83.8%)		
HIV status:				Chi-square	0.059
Negative	256 (85.9%)	72 (28.1%)	184 (71.9%)		
Positive	42 (14.1%)	6 (14.3%)	36 (85.7%)		
Cardiovascular disease:				Chi-square	0.22
No	205 (68.8%)	58 (28.3%)	147 (71.7%)		
Yes	93 (31.2%)	20 (21.5%)	73 (78.5%)		
Sleep duration (hours):				Chi-square	0.10
< 5 h	35 (11.7%)	12 (34.3%)	23 (65.7%)		
5–7 h	190 (63.8%)	42 (22.1%)	148 (77.9%)		
> 7 h	73 (24.5%)	24 (32.9%)	49 (67.1%)		
Sleep quality:				Chi-square	0.56
Poor	54 (18.1%)	16 (29.6%)	38 (70.4%)		
Moderate	126 (42.3%)	35 (27.8%)	91 (72.2%)		
Good	118 (39.6%)	27 (22.9%)	91 (77.1%)		
Obstructive sleep apnoea:				Chi-square	0.26
Low risk of OSA	148 (49.7%)	43 (29.1%)	105 (70.9%)		
High risk of OSA	150 (50.3%)	35 (23.3%)	115 (76.7%)		
Family history of hypertension:				Chi-square	0.17
No	148 (49.7%)	44 (29.7%)	104 (70.3%)		
Yes	150 (50.3%)	34 (22.7%)	116 (77.3%)		
Family history of cardiovascular disease:				Chi-square	0.74
No	194 (65.1%)	52 (26.8%)	142 (73.2%)		
Yes	104 (34.9%)	26 (25.0%)	78 (75.0%)		
Family history of dyslipidaemia:				Chi-square	0.094
Yes	103 (34.6%)	33 (32.0%)	70 (68.0%)		
No	195 (65.4%)	45 (23.1%)	150 (76.9%)		
Family history of kidney disease:				Chi-square	0.85
No	239 (80.2%)	62 (25.9%)	177 (74.1%)		
Yes	59 (19.8%)	16 (27.1%)	43 (72.9%)		
Anti-diabetic medication adherence:				Chi-square	0.010
Low adherence	53 (17.8%)	22 (41.5%)	31 (58.5%)		
Moderate adherence	68 (22.8%)	12 (17.6%)	56 (82.4%)		
High adherence	177 (59.4%)	44 (24.9%)	133 (75.1%)		
Diabetes mellitus duration (years):				Chi-square	0.063
≤ 5	145 (48.7%)	45 (31.0%)	100 (69.0%)		
> 5	153 (51.3%)	33 (21.6%)	120 (78.4%)		
Diabetes mellitus medication duration (years):				Chi-square	0.068
≤ 5 years	157 (52.7%)	48 (30.6%)	109 (69.4%)		
> 5 years	141 (47.3%)	30 (21.3%)	111 (78.7%)		
Diabetes mellitus medication type:				Chi-square	0.81
Insulin	15 (5.0%)	3 (20.0%)	12 (80.0%)		
Metformin	184 (61.7%)	48 (26.1%)	136 (73.9%)		
Oral hypoglycaemic agents	58 (19.5%)	14 (24.1%)	44 (75.9%)		
Mixed (insulin & metformin)	41 (13.8%)	13 (31.7%)	28 (68.3%)		
Systolic blood pressure (mmHg):				Chi-square	0.16
< 140	219 (73.5%)	62 (28.3%)	157 (71.7%)		
≥ 140	79 (26.5%)	16 (20.3%)	63 (79.7%)		
Diastolic blood pressure (mmHg):				Chi-square	0.30

(Continued)

Table 2: Continued.

Variable	Total N = 298	Albuminuria status		Statistical test	p-value
		Normalalbuminuria $n_1 = 78$	Microalbuminuria $n_2 = 220$		
< 90	232 (77.9%)	64 (27.6%)	168 (72.4%)		
≥ 90	66 (22.1%)	14 (21.2%)	52 (78.8%)		
Body mass index (kg/m ²):				Chi-square	0.37
< 25	118 (39.6%)	31 (26.3%)	87 (73.7%)		
25–29	111 (37.2%)	33 (29.7%)	78 (70.3%)		
≥ 30	69 (23.2%)	14 (20.3%)	55 (79.7%)		
Waist circumference (cm):				Chi-square	0.47
Normal	232 (77.9%)	63 (27.2%)	169 (72.8%)		
High	66 (22.1%)	15 (22.7%)	51 (77.3%)		
Waist-to-hip ratio:				Chi-square	1.00
Normal	65 (21.8%)	17 (26.2%)	48 (73.8%)		
High	233 (78.2%)	61 (26.2%)	172 (73.8%)		
Waist-to-height ratio:				Chi-square	0.31
Normal	208 (69.8%)	58 (27.9%)	150 (72.1%)		
High	90 (30.2%)	20 (22.2%)	70 (77.8%)		

P-values in bold indicate statistically significant findings.

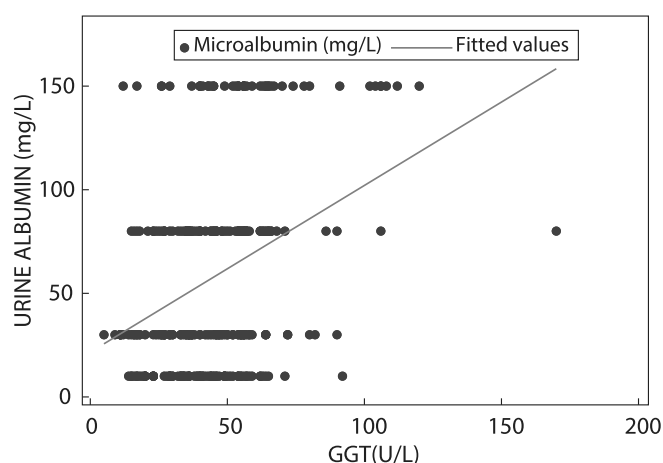


Figure 2: Correlation between GGT and urine albumin.

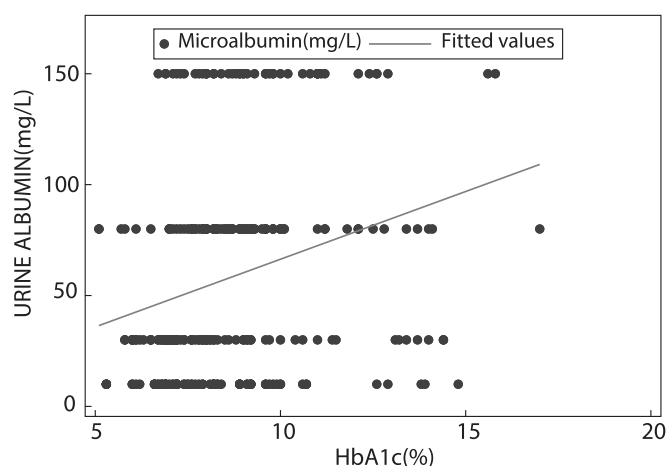


Figure 3: Correlation between HbA1c and urine albumin.

Table 3: Factors associated with microalbuminuria

Variable	Bivariate analysis		Multivariate analysis	
	cOR (95%CI)	p-value	aOR (95%CI)	p-value
Gamma glutamyl transferase (U/L):				
50	1.00		1.00	
> 50	2.19 (1.22–3.92)	0.008	1.60 (0.79–3.23)	0.191
Haemoglobin A1c:				
≤ 7%, Good	1.00		1.00	
> 7, Poor	1.58 (0.88–2.84)	0.125	1.42 (0.69–2.91)	0.341
Gender:				
Male	1.00		1.00	
Female	0.89 (0.52–1.54)	0.682	0.54 (0.22–1.37)	0.196
Age (years):				
< 40	1.00		1.00	
40–49	2.55 (1.12–5.79)	0.025	2.07 (0.77–5.61)	0.151
50–59	3.29 (1.43–7.60)	0.005	1.78 (0.62–5.07)	0.281
≥ 60	4.27 (1.92–9.39)	< 0.001	1.69 (0.54–5.34)	0.369
Marital status:				
Single	1.00			
Married/cohabiting	1.21 (0.43–3.37)	0.720		
Separated/divorced	2.43 (0.78–7.57)	0.126		
Education level:				
No education	1.00		1.00	
Primary education	0.43 (0.20–0.93)	0.033	0.60 (0.24–1.48)	0.270
Secondary education	0.45 (0.19–0.99)	0.049	0.81 (0.30–2.19)	0.678
Tertiary education	0.19 (0.08–0.43)	< 0.001	0.34 (0.11–1.02)	0.055
Religion:				
Catholic	1.00			
Protestant	0.98 (0.50–1.90)	0.949		
Moslem	0.98 (0.44–2.19)	0.968		
Other	0.95 (0.47–1.90)	0.886		
Employment status:				
Employed	1.00		1.00	
Unemployed	2.10 (1.24–3.58)	0.006	2.32 (1.12–4.81)	0.023
Residence:				
Rural	1.00			
Urban	0.65 (0.39–1.09)	0.105		
Smoking status:				
Never smoked	1.00		1.00	
Former smoker	1.08 (0.51–2.26)	0.846	0.78 (0.27–2.22)	0.638
Current smoker	1.02 (0.38–2.70)	0.974	0.72 (0.21–2.46)	0.605
Alcohol consumption:				
Never consumed	1.00		1.00	
Former drinker	1.30 (0.68–2.49)	0.429	1.17 (0.49–2.81)	0.726
Current drinker	0.66 (0.34–1.27)	0.209	0.64 (0.26–1.58)	0.335
Physical activity (MET min/week):				
> 1 500	1.00		1.00	
< 600	1.53 (0.70–3.35)	0.291	1.80 (0.31–10.43)	0.513
600–1 500	2.23 (0.63–7.85)	0.213	0.71 (0.27–1.88)	0.492
Vegetable fruit intake (per day):				
< servings	1.00			
≥ servings	1.06 (0.57–1.97)	0.865		
Vegetable consumption per week (days):				
≤ 4	1.00			
> 4	1.36 (0.69–2.67)	0.375		

(Continued)

Table 3: Continued.

Variable	Bivariate analysis		Multivariate analysis	
	cOR (95%CI)	p-value	aOR (95%CI)	p-value
Hypertension:				
No	1.00		1.00	
Yes	2.82 (1.62–4.90)	< 0.001	4.43 (1.40–14.00)	0.011
Cardiovascular disease:				
No	1.00		1.00	
Yes	1.44 (0.81–2.57)	0.218	0.48 (0.18–1.33)	0.159
HIV status:				
Negative	1.00		1.00	
Positive	2.35 (0.95–5.81)	0.065	3.20 (1.12–9.18)	0.030
Mid upper-arm circumference (cm)	1.12 (1.01–1.23)	0.028	1.06 (0.92–1.21)	0.421
Sleep duration (hours):				
< 5 h	1.00		1.00	
5–7 h	1.84 (0.84–4.00)	0.125	1.64 (0.62–4.34)	0.315
> 7 h	1.07 (0.45–2.50)	0.884	0.89 (0.31–2.57)	0.833
Obstructive sleep apnoea:				
Low risk of OSA	1.00			
High risk of OSA	1.35 (0.80–2.26)	0.262		
Sleep quality:				
Good	1.00			
Poor	0.70 (0.34–1.46)	0.344		
Moderate	0.77 (0.43–1.38)	0.381		
Family history of hypertension:				
No	1.00		1.00	
Yes	1.44 (0.86–2.43)	0.167	0.61 (0.25–1.47)	0.268
Family history of cardiovascular disease:				
No	1.00			
Yes	1.20 (0.64–1.89)	0.736		
Family history of dyslipidaemia:				
No	1.00			
Yes	1.57 (0.92–2.67)	0.095		
Family history of kidney disease:				
No	1.00			
Yes	0.94 (0.50–1.79)	0.854		
Anti-diabetic medication adherence:				
Low adherence	1.00		1.00	
Moderate adherence	3.31 (1.45–7.59)	0.005	2.60 (0.98–6.89)	0.055
High adherence	2.15 (1.13–4.08)	0.020	1.95 (0.87–4.36)	0.106
Diabetes mellitus duration (years):				
≤ 5	1.00		1.00	
> 5	1.64 (0.97–2.76)	0.064	0.94 (0.47–1.89)	0.860
Diabetes mellitus medication duration (years):				
< = 5 years	1.00			
> 5 years	1.63 (0.96–2.76)	0.070		
Diabetes mellitus medication type:				
Insulin	1.00		1.00	
Metformin	0.71 (0.19–2.62)	0.605	0.54 (0.11–2.64)	0.449
Oral hypoglycaemic agents	0.79 (0.10–3.19)	0.736	0.44 (0.08–2.36)	0.336
Mixed (insulin & metformin)	0.54 (0.13–2.24)	0.395	0.47 (0.09–2.55)	0.380
Systolic blood pressure (mmHg):				
< 140	1.00			
≥ 140	1.55 (0.83–2.90)	0.165		

(Continued)

Table 3: Continued.

Variable	Bivariate analysis		Multivariate analysis	
	cOR (95%CI)	p-value	aOR (95%CI)	p-value
Diastolic blood pressure (mmHg):				
< 90	1.00			
≥ 90	1.41 (0.73–2.73)	0.300		
Body mass index (kg/m ²):				
< 25	1.00		1.00	
25–29	0.84 (0.47–1.50)	0.560	0.68 (0.33–1.38)	0.286
≥ 30	1.40 (0.68–2.86)	0.357	1.00 (0.33–3.03)	0.990
Waist circumference (cm):				
Normal	1.00		1.00	
High	1.27 (0.67–2.41)	0.471	0.74 (0.27–2.05)	0.567
Waist-to-hip ratio:				
Normal	1.00		1.00	
High	1.00 (0.53–1.87)	0.997	1.67 (0.59–4.67)	0.331
Waist-to-height ratio:				
Normal	1.00		1.00	
High	1.35 (0.76–2.42)	0.308	1.14 (0.42–3.10)	0.804

P-values in bold indicate statistically significant findings.

and other kidney disease markers.^{39,40} Our findings align with these observations across diverse populations, reinforcing the critical need for integrating hypertension management into diabetes care to protect kidney function and prevent further complications.

The study identified a significant association between unemployment and microalbuminuria, suggesting that socioeconomic factors influence diabetes management and kidney health. Clinically, this underscores the need to address socioeconomic disparities to improve access to healthcare services essential for managing chronic conditions like diabetes. Biologically, while unemployment is not directly linked to microalbuminuria, it can introduce stressors that negatively impact health behaviours, such as diet quality and medication adherence, due to financial constraints and limited healthcare access. Although not directly linking unemployment to microalbuminuria, the literature indicates that lower socioeconomic status is associated with a higher prevalence of microalbuminuria.⁴¹ This highlights the broader impact of socioeconomic status on chronic disease management and kidney health.

Conclusion

Microalbuminuria is prevalent among diabetic patients. Microalbuminuria is associated with elevated GGT, and HbA1c levels, HIV positivity, hypertension, and unemployment. Screening, more stringent glycaemic and blood pressure control, and targeted interventions are warranted in high-risk groups to prevent the onset of diabetic nephropathy.

Acknowledgements – The authors would like to acknowledge the study participants who agreed to take part in the study.

Disclosure statement – No potential conflict of interest was reported by the authors.

Ethics considerations – This study was approved by the Faculty Research Committee (FRC) of Mbarara University of Science and Technology with approval number (MUST/MLS/24-16U).

Administrative clearance was also obtained from the Officer in Charge, Nakaseke Hospital before conducting the study.

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Received: 30-07-2025 Accepted: 10-12-2025



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** Refers to Ozempic® FlexTouch® Pen. Based on volume sales data: IQVIA-MIDAS database January 2018 – September 2025

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Evaluating red cell distribution width and kidney dysfunction in HIV-positive and HIV-negative adults with diabetes: insights from KwaZulu-Natal, South Africa

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Background: Red cell distribution width (RDW) is a prognostic marker in cardiovascular and kidney disease, but its significance in African populations with high burdens of diabetes and HIV is unclear.

Methods: 135 adults attending a diabetes clinic in South Africa were retrospectively analysed. Kidney dysfunction was defined as eGFR < 60 ml/min/1.73 m² or abnormal proteinuria defined as urine protein:creatinine ratio (uPCR) > 0.015 g/mmol or dipstick ≥ 1+ when uPCR was missing. Associations between RDW and kidney dysfunction were assessed using correlation tests and multivariable logistic regression in this cross-sectional analysis.

Results: Kidney dysfunction was present in 90/135 patients (66.7%): 29 by eGFR < 60 alone, 28 by abnormal proteinuria alone, and 33 by both. RDW did not differ significantly between those with and without kidney dysfunction (13.6 ± 1.7% vs. 13.2 ± 1.6%, *p* = 0.19). RDW was not correlated with eGFR (*p* = −0.10, *p* = 0.26) or uPCR (*p* = −0.04, *p* = 0.68) and showed only a weak trend with HbA1c (*p* = −0.15, *p* = 0.08). In multivariable regression, age (OR 1.10 per year, 95% CI 1.04–1.17, *p* = 0.001), and HIV-positive status (OR 4.36, 95% CI 1.06–17.98, *p* = 0.042) were independently associated with kidney dysfunction. RDW was not predictive (OR 1.23, 95% CI 0.90–1.67, *p* = 0.19).

Conclusion: RDW was not independently associated with kidney dysfunction in this cohort. Age and HIV infection remained independently associated with kidney dysfunction. Proteinuria was incorporated into the composite outcome definition and therefore was not treated as an independent predictor.

Keywords: APOL1, diabetic kidney disease, eGFR, HIV, kidney dysfunction, proteinuria, red cell distribution width, South Africa

Introduction

Diabetic kidney disease (DKD) is the leading cause of chronic kidney disease (CKD) worldwide, accounting for up to half of all cases of end-stage kidney disease (ESKD).¹ CKD affects between 8% and 16% of the global population, and nearly half of individuals with type 2 diabetes and one-third with type 1 diabetes develop some degree of kidney impairment during their lifetime.^{2–4} In sub-Saharan Africa, the growing diabetes epidemic intersects with a high burden of HIV, compounding risks for kidney disease.⁵

HIV-associated nephropathy (HIVAN) remains one of the most important causes of CKD in African populations living with HIV, particularly among individuals carrying APOL1 risk variants, which confer odds ratios as high as 89 for developing kidney disease.^{6,7} Even in the era of antiretroviral therapy, CKD prevalence among people living with HIV remains high in Africa, estimated at between 6% and 15%.^{8,9}

Red cell distribution width (RDW), routinely reported in full blood counts, measures the variation in size of circulating red cells (anisocytosis). Beyond its traditional use in differentiating anaemias, RDW has been identified as a prognostic marker in cardiovascular disease, CKD, and acute illness.^{10–13} Elevated RDW is linked to inflammation, oxidative stress, and nutritional deficiencies.^{14,15} In diabetes, chronic low-grade inflammation, oxidative stress, and endothelial dysfunction contribute to glomerular injury, microvascular damage, and the development of proteinuria. These same processes

influence erythropoiesis and red cell heterogeneity, providing biological plausibility for a potential association between RDW and diabetic kidney disease. In Asian and European cohorts with diabetes, higher RDW values have been associated with greater proteinuria, faster eGFR decline, and increased risk of ESKD.^{16,17} Meta-analyses of CKD cohorts have confirmed RDW as a predictor of adverse kidney outcomes and mortality.^{18–20} However, evidence from African populations remains scarce, despite the dual burden of diabetes and HIV.

This study aimed to investigate whether RDW is independently associated with kidney dysfunction in a real-world cohort of South African adults with diabetes, while accounting for HIV as an important comorbidity in this setting.

Methods

Study design and population

We performed a retrospective cross-sectional chart review study of adult diabetic patients attending the Victoria Mxenge Hospital outpatient diabetes clinic, KwaZulu-Natal, between 1 January 2018 and 31 December 2024. This cross-sectional design permits assessment of associations only and does not allow inference regarding temporality or causality. Patients aged ≥ 18 years with type 1 or type 2 diabetes were eligible if they had complete data for eGFR, RDW, and HbA1c, and either uPCR or dipstick proteinuria, obtained at the same

clinic visit or within a three-month interval as part of routine clinical care.

Outcome definition

Kidney dysfunction was compositely defined as $\text{eGFR} < 60 \text{ ml/min/1.73 m}^2$ or the presence of abnormal proteinuria. Abnormal proteinuria was defined as $\text{uPCR} > 0.015 \text{ g/mmol}$ (15 mg/mmol) when available. Where uPCR was missing, dipstick proteinuria $\geq 1+$ was used. uPCR values were prioritised over dipstick readings whenever both were available.

Data analysis

Continuous variables were summarised as means $\pm$ standard deviation or medians (IQR), categorical variables as counts and percentages. Group comparisons were assessed using t -tests or Mann–Whitney U tests for continuous data and chi-square/Fisher's exact tests for categorical data. Correlations were analysed with Spearman's rank tests. Logistic regression was used to identify independent predictors of kidney dysfunction, adjusting for age, HbA1c, hypertension, HIV status, gender, and RDW. Statistical significance was set at $p < 0.05$. Hypertension was defined as a documented clinical diagnosis, current use of antihypertensive medication, or repeated clinic blood pressure measurements $\geq 140/90 \text{ mmHg}$.

Ethical considerations

Ethical approval for this study was obtained from the University of KwaZulu-Natal Biomedical Research and Ethics Committee (BREC 8975/25). The requirement for individual informed consent was waived, as only routinely collected clinical data were analysed anonymously.

Results

Study population

A total of 135 adults with diabetes met the inclusion criteria, with complete data available for RDW, HbA1c, eGFR , and either uPCR or dipstick proteinuria. The mean age was 57.4 ± 10.2 years, and 63.7% were female. Type 2 diabetes was the predominant diagnosis, and the mean HbA1c was $9.3 \pm 2.9\%$. Hypertension was present in 67 patients (49.6%), and 23.7% were HIV-positive. Compared with patients with preserved kidney function ($n = 45$), those with kidney dysfunction ($n = 90$) were older (59.2 ± 9.3 vs. 52.9 ± 10.1 years, $p = 0.001$), more likely to be hypertensive (60% vs. 28.9%, $p = 0.002$), and more frequently HIV-positive (30% vs. 11.1%, $p = 0.015$).

The mean HbA1c did not differ significantly between groups ($9.2 \pm 2.6\%$ vs. $9.5 \pm 3.3\%$, $p = 0.54$). RDW values were also comparable ($13.6 \pm 1.7\%$ vs. $13.2 \pm 1.6\%$, $p = 0.19$). As expected, eGFR was significantly lower in the kidney dysfunction group (57.4 ± 23.9 vs. $89.2 \pm 18.0 \text{ ml/min/1.73 m}^2$, $p < 0.001$). Median uPCR values were higher in patients with kidney dysfunction ($0.29 [0.09–0.86]$ vs. $0.14 [0.05–0.32] \text{ g/mmol}$, $p = 0.03$). Table 1.

Prevalence of kidney dysfunction

Kidney dysfunction was identified in 90 patients (66.7%). Among these, 29 (21.5%) qualified on the basis of reduced eGFR alone, 28 (20.7%) by abnormal proteinuria alone, and 33 (24.4%) by both criteria. uPCR was available for 97 patients (71.9%), of whom 57 (58.8%) had abnormal values ($> 0.015 \text{ g/mmol}$). Dipstick proteinuria was used in 38 patients where uPCR was missing, and 4 of these (10.5%) were abnormal (Figure 1).

Table 1: Baseline characteristics by kidney dysfunction status

Variable	Kidney dysfunction ($n = 90$)	Preserved function ($n = 45$)	p -value
Age (years), mean $\pm$ SD	59.2 ± 9.3	52.9 ± 10.1	0.001
Female, n (%)	58 (64.4)	28 (62.2)	0.81
Hypertension, n (%)	54 (60.0)	13 (28.9)	0.002
HIV-positive, n (%)	27 (30.0)	5 (11.1)	0.015
HbA1c (%), mean $\pm$ SD	9.2 ± 2.6	9.5 ± 3.3	0.54
RDW (%), mean $\pm$ SD	13.6 ± 1.7	13.2 ± 1.6	0.19
eGFR (ml/min/1.73 m^2), mean $\pm$ SD	57.4 ± 23.9	89.2 ± 18.0	<0.001
uPCR (g/mmol), median (IQR) [†]	0.29 (0.09–0.86)	0.14 (0.05–0.32)	0.03

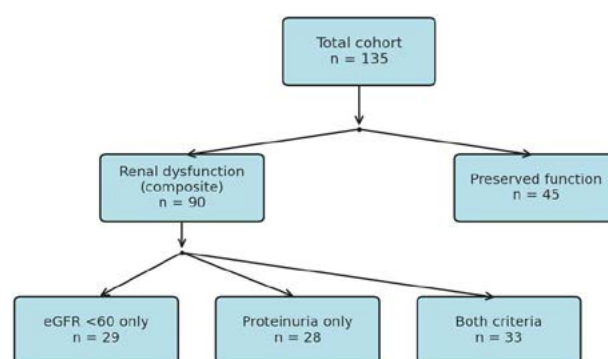


Figure 1: Patient classification flow diagram.

Correlations of RDW

Spearman correlation analyses demonstrated no significant association between RDW and eGFR ($\rho = -0.10$, $p = 0.26$), RDW and uPCR ($\rho = -0.04$, $p = 0.68$), or RDW and HbA1c ($\rho = -0.15$, $p = 0.08$). See Figures 2–4 respectively.

Predictors of kidney dysfunction

In unadjusted analyses, hypertension was significantly more frequent among patients with kidney dysfunction (OR 2.63, 95% CI 1.22–5.65, $p = 0.015$).

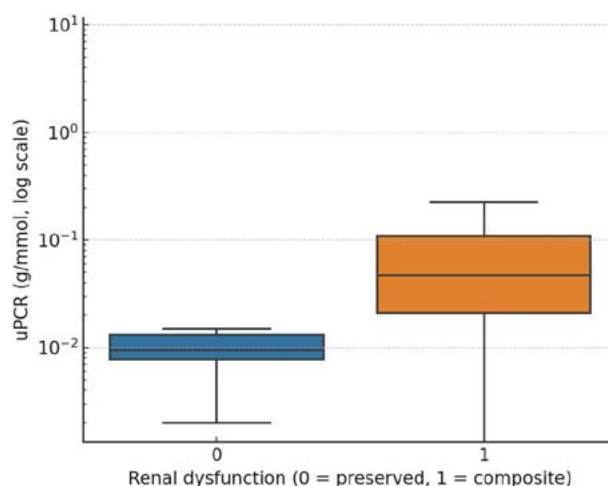


Figure 2: Distribution of uPCR by kidney dysfunction.

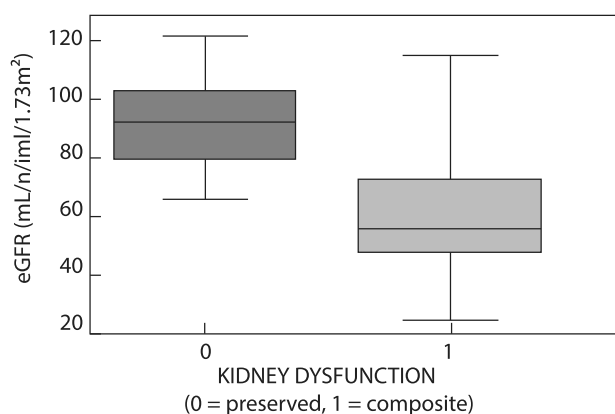


Figure 3: Distribution of eGFR by kidney dysfunction.

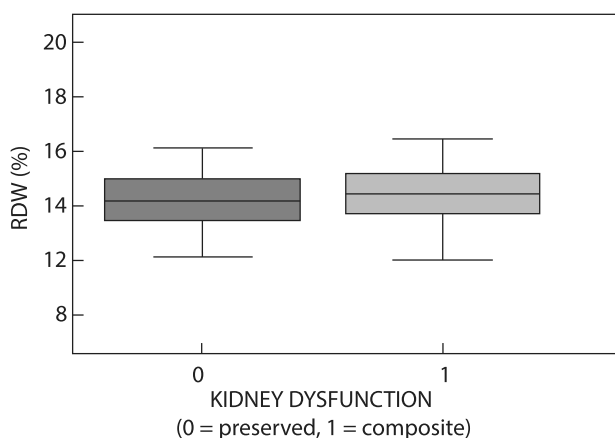


Figure 4: Distribution of RDW by kidney dysfunction.

Table 2: Logistic regression for predictors of kidney dysfunction (composite definition)

Variable	OR	95% CI	p-value
Age (per year)	1.10	1.04–1.17	0.001
RDW (per 1%)	1.23	0.90–1.67	0.19
HbA1c (per 1%)	0.95	0.79–1.13	0.55
Hypertension	2.42	0.79–7.36	0.12
HIV-positive	4.36	1.06–17.98	0.042
Male sex	0.45	0.16–1.25	0.13

In the multivariable logistic regression model adjusting for age, HbA1c, hypertension, HIV status, gender, and RDW (Table 2), age was independently associated with kidney dysfunction (OR 1.10 per year, 95% CI 1.04–1.17, $p=0.001$). HIV-positive status was also independently predictive (OR 4.36, 95% CI 1.06–17.98, $p=0.042$). Hypertension showed a non-significant trend (OR 2.42, 95% CI 0.79–7.36, $p=0.12$). RDW was not independently associated (OR 1.23, 95% CI 0.90–1.67, $p=0.19$), nor was HbA1c (OR 0.95, 95% CI 0.79–1.13, $p=0.55$). Interpretation of these findings should consider the high prevalence of kidney dysfunction in the cohort, the composite outcome definition incorporating proteinuria, limited variability in RDW values, and wide confidence intervals for some estimates.

Discussion

In this study of 135 South African adults with diabetes, RDW was not independently associated with kidney dysfunction when defined by a composite outcome incorporating both eGFR and proteinuria. While RDW showed a weak trend, age and HIV-positive status emerged as the only independent predictors of kidney dysfunction. These findings highlight age and HIV status as independent correlates of kidney dysfunction, while proteinuria represents a major contributor to the composite outcome definition.

Our results diverge from studies in Asian and European cohorts where RDW has consistently been linked to adverse kidney outcomes. Chen et al.¹⁶ demonstrated that higher RDW values were associated with greater proteinuria and risk of progression to ESKD in Chinese patients with biopsy-proven diabetic nephropathy. Wang et al.¹⁷ similarly reported that RDW predicted kidney function decline in type 2 diabetes. Meta-analyses of CKD cohorts have further confirmed RDW as a prognostic marker for progression and mortality.^{18–20}

Several factors may explain why RDW did not perform as a useful biomarker in this setting. Anaemia, nutritional deficiencies, chronic inflammation, and HIV-related immune activation are common in South African populations and may influence RDW independently of kidney injury. This heterogeneity may obscure kidney-specific signals and reduce the discriminatory value of RDW. Additionally, single time-point RDW measurements may fail to capture longitudinal changes that could be more relevant to kidney disease progression.

The absence of an association in our cohort may reflect important differences. Anaemia, malnutrition, and inflammatory conditions are common in African populations with diabetes and HIV, potentially obscuring specific links between RDW and kidney injury. Furthermore, our cross-sectional design may underestimate longitudinal changes in RDW that could predict progression.

HIV emerged as an independent predictor of kidney dysfunction in our cohort. This aligns with established evidence that HIV infection contributes to CKD in sub-Saharan Africa, often through HIV-associated nephropathy (HIVAN).^{6,8,9} APOL1 risk variants confer up to 89-fold higher odds of HIVAN in South African populations, and although we lacked genotyping data, the presence of HIV in one-quarter of our cohort likely contributed significantly to the observed kidney burden.^{6,7} Interestingly, RDW did not differ by HIV status, suggesting that RDW is not sensitive to HIV-related effects in this setting.

Age remained the strongest predictor of kidney dysfunction, consistent with the well-established age-related decline in kidney function and the cumulative effects of long-standing diabetes.^{1,4} Hypertension was significantly more common among patients with kidney dysfunction in crude analysis, but this association was attenuated in multivariable models. This may reflect collinearity with age and HIV status, both of which are highly prevalent in our population.

The lack of association between RDW and kidney dysfunction in our cohort suggests that RDW may not be a reliable surrogate marker in African diabetic populations. RDW is influenced by multiple haematological and nutritional factors – iron deficiency, vitamin B12 or folate deficiency, chronic inflammation – that are common in resource-limited settings.^{14,15}

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These background influences may dilute its specificity for kidney outcomes. Furthermore, RDW was measured at a single time point; longitudinal monitoring may better capture its prognostic potential.

Clinical implications

Our findings reinforce age and HIV status as key independent correlates of kidney dysfunction. Proteinuria remains clinically important as a defining component of kidney disease rather than as a predictive factor in this analysis. In settings with high HIV prevalence, routine HIV testing and monitoring remain crucial, as HIV was an independent predictor of kidney dysfunction in our cohort. While RDW is easily available from full blood counts, its utility as a prognostic marker for kidney dysfunction in African populations appears limited.

Limitations

This was a single-centre cross-sectional study, limiting generalisability and precluding assessment of temporality or causality. Inclusion required complete laboratory data, introducing potential selection bias toward patients receiving more comprehensive testing. The modest sample size resulted in imprecision for some estimates, as reflected by wide confidence intervals. Residual confounding from nutritional status, inflammation, and unmeasured anaemia aetiologies cannot be excluded.

Future directions

Future research should adopt prospective designs with serial RDW measurements to assess whether temporal changes predict kidney outcomes. Inclusion of APOL1 genotyping and inflammatory markers would clarify mechanisms underlying HIV-associated kidney dysfunction and the potential modifying role of RDW. Larger multicentre studies across Africa are warranted to validate these findings and explore whether RDW has prognostic value in specific subgroups, such as those with advanced proteinuria or anaemia.

Conclusion

RDW was not independently associated with kidney dysfunction in this cohort, even when a composite outcome prioritising quantitative uPCR was applied. These findings suggest that RDW does not add incremental clinical value beyond age and HIV status, while proteinuria contributes to the composite definition of kidney dysfunction. Age and HIV infection were the strongest predictors, reinforcing the primacy of traditional and region-specific risk factors. Larger prospective African studies incorporating RDW, HIV, and genetic risk markers are warranted to clarify RDW's role.

Disclosure statement – No potential conflict of interest was reported by the author.

Ethical considerations – Ethical approval for this study was obtained from the University of KwaZulu-Natal Biomedical Research and Ethics Committee (BREC 8975/25).

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Received: 13-10-2025 Accepted: 24-04-2026

Prediabetes as the reversible window: academic reflections on a breakfast symposium at SEMDSA Congress 2026

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At the 58th Annual Congress of the Society for Endocrinology, Metabolism and Diabetes of South Africa (SEMDSA), a breakfast symposium delivered by Professor Peter E. H. Schwarz revisited prediabetes as a biologically active and potentially reversible stage in the trajectory towards type 2 diabetes. This opinion paper reflects on the symposium through three deliberately signposted questions: why prediabetes matters, what may still be reversible, and how clinicians and health systems can act in practice. The central message - that prediabetes should prompt active pursuit of normoglycaemia rather than passive risk recognition - aligns with evidence supporting structured lifestyle intervention, regression from prediabetes to normal glucose regulation, and selective metformin use in high-risk individuals.¹⁻⁴ The paper also considers environmental determinants, including air pollution, and uses a South African clinical vignette and practical box to translate the lecture's scientific themes into non-promotional, patient-centred prevention steps. For South African practice, the symposium's value lies in reframing prediabetes as a reversible clinical opportunity that requires structured prevention pathways, patient-centred communication, careful risk stratification, and system-level support.

Keywords: Prediabetes, remission, diabetes prevention, lifestyle intervention, metformin

Introduction

Professor Peter E. H. Schwarz, President of the International Diabetes Federation (IDF), presented the Merck Breakfast Symposium entitled "Prediabetes: The Reversible Window" on 17 April 2026 during the 58th SEMDSA Congress in Cape Town. Figure 1 shows Professor Schwarz delivering the symposium.

This reflection is organised around three practice-facing questions: why prediabetes matters, what may still be reversible, and how South African clinicians and health systems can act.

At its core, the session repositioned prediabetes as a clinically meaningful and potentially reversible condition, rather than a vague precursor of future disease. This matters because prediabetes is often diagnosed but not always acted on with sufficient intensity. The lecture proposed restoration of normoglycaemia as a realistic treatment goal and encouraged earlier, more deliberate intervention within the reversible window.¹

Why prediabetes matters

The prevention window is epidemiologically important. Global estimates project substantial increases in both impaired glucose tolerance (IGT) and impaired fasting glucose (IFG), while the IDF Diabetes Atlas 11th edition estimates that 589 million adults aged 20-79 years were living with diabetes in 2024, with a projected rise to 853 million by 2050.^{5,6} Approximately 252 million adults with diabetes were estimated to be undiagnosed in 2024, underscoring the importance of earlier detection and prevention.⁶ For South African clinicians, this global picture is not abstract: it intersects with a local non-communicable disease (NCD) burden in which earlier detection, risk stratification and prevention are central health-system priorities.^{18,19}



Figure 1: Professor Peter E. H. Schwarz presenting "Prediabetes: The Reversible Window" at the Merck Breakfast Symposium, SEMDSA Congress 2026, Cape Town, 17 April 2026. Photograph supplied by the author.

Prediabetes matters because it is not merely a laboratory label. It finds a point on the dysglycaemic continuum where insulin resistance, β -cell stress, visceral adiposity, hepatic fat accumulation, and cardiovascular risk may already be present, but where the trajectory may still be altered. The term "reversible window" is therefore clinically useful if it changes behaviour: it should prompt structured intervention, planned review, and an explicit attempt to move the person back towards normal glucose regulation, rather than simply documenting risk.

The South African relevance of this message lies in its pragmatism. A clinician in a busy primary-care or private-practice setting does not need to turn every person with prediabetes into a specialist referral. However, the diagnosis should trigger a prevention pathway: confirm dysglycaemia, assess

overall cardiometabolic risk, communicate hope without minimising risk, start structured lifestyle support, and consider pharmacological prevention only for carefully selected high-risk individuals.^{1,15,19,20}

What is reversible?

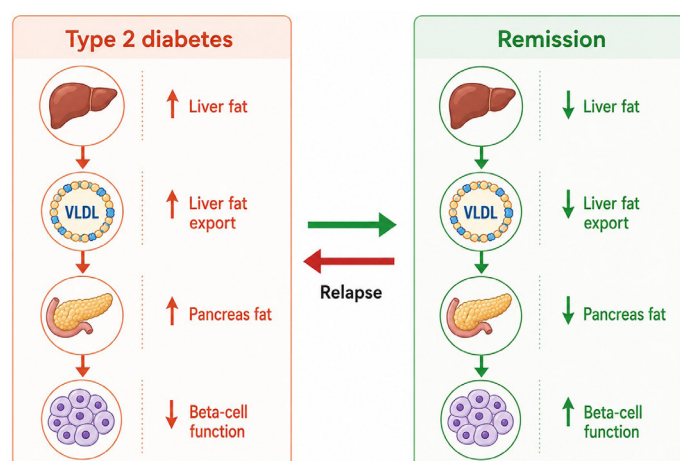
The lecture positioned prediabetes as active pathophysiology rather than a mild biochemical abnormality. Glucose variability, visceral adiposity, hepatic fat accumulation, and β -cell stress were presented within a broader narrative of reversibility. This framework aligns with the twin-cycle model, in which ectopic fat accumulation in the liver and pancreas contributes to insulin resistance and impaired insulin secretion, but can improve when metabolic load is reduced.⁷ This reversible sequence is summarised schematically in Figure 2.

The symposium also situated reversibility within a wider environmental context. Large-scale burden estimates suggest that exposure to fine particulate matter of 2.5 micrometres or less in diameter (PM_{2.5}) accounts for one fifth of the global type 2 diabetes burden. More recent evidence syntheses support associations between long-term exposure to PM_{2.5}, particulate matter of 10 micrometres or less in diameter (PM₁₀), nitrogen dioxide and ozone and incident type 2 diabetes.^{8,9} These findings reinforce that diabetes prevention cannot be reduced to individual willpower; clinical prevention must be complemented by policy action on environments that shape metabolic risk.

Prediabetes remission as a clinical target

A key scientific message was that prediabetes remission should be considered an explicit prevention endpoint. Prevention-trial evidence supports this position. In the original Diabetes Prevention Program (DPP), intensive lifestyle intervention reduced incident type 2 diabetes by 58%, while metformin reduced it by 31% compared with placebo.² Long-term follow-up in the Diabetes Prevention Program Outcomes Study (DPPOS) confirmed durable prevention effects over 15 years.³ DPP/DPPOS analyses further showed that regression from prediabetes to normal glucose regulation was associated with substantially lower future diabetes risk, including an approximately 56% reduction over 10 years in one analysis.⁴ Additional work linked regression to normoglycaemia with lower estimated cardiovascular risk and lower microvascular disease burden than persistent dysglycaemia.^{10,11}

Recent literature extends this concept. A 2025 study in *Nature Medicine* reported that prediabetes remission, even without overall weight loss, was associated with markedly lower subsequent type 2 diabetes risk, highlighting the importance of improved insulin sensitivity and favourable fat redistribution rather than body weight alone.¹² This evolving evidence base has been accompanied by an editorial call to define prediabetes remission as a distinct prevention endpoint, and by post-hoc analyses suggesting that remission may translate into lower cardiovascular morbidity and mortality over time.^{13,14} The



Adapted conceptually from Taylor R, Ramachandran A, Yancy WS Jr, Forouhi NG. Nutritional basis of type 2 diabetes remission. *BMJ*. 2021;374:n1449.

VLDL, very low-density lipoprotein.

Figure 2: Author-created schematic of the twin-cycle model showing ectopic fat and VLDL-mediated pathways in type 2 diabetes risk and remission. VLDL, very low-density lipoprotein.⁷

symposium's emphasis on remission was therefore forward-looking, but grounded in an emerging evidence base.

Metformin: evidence-based adjunct, not a substitute for prevention care

The symposium also addressed metformin. Its central message was selective and evidence-aligned: metformin may have a role as an adjunctive option in selected adults with prediabetes who are at particularly elevated risk of progression. Current American Diabetes Association (ADA) standards state that metformin should be considered for prevention of type 2 diabetes in adults at high risk, as typified by the DPP, while the 2025 IDF recommendations include prevention and risk-reduction strategies within an adaptable framework for diverse care settings.^{1,15} This position is consistent with DPP evidence and pragmatic international practice, especially for younger adults with severe obesity, higher fasting glucose or glycated haemoglobin (HbA_{1c}) values, and women with a history of gestational diabetes.^{1–3}

Lifestyle intervention remains foundational, metformin is adjunctive in selected high-risk individuals, and the two approaches should not be framed as interchangeable.^{1–3,15} Metformin should be discussed as part of shared decision-making that includes renal function, gastrointestinal tolerability, the possibility of vitamin B12 deficiency with long-term use, pregnancy intentions where relevant, patient preference and the availability of ongoing lifestyle support.^{1,19,20}

Fasting-based dietary strategies and insulin sensitivity

The symposium highlighted fasting-based dietary strategies as a potential means of improving insulin sensitivity, reducing hepatic fat, and supporting movement towards remission. This is biologically plausible, given the roles of energy balance, visceral adiposity, hepatic fat accumulation and β -cell workload in the dysglycaemic continuum.⁷ Current evidence suggests that intermittent fasting may offer cardiometabolic benefits broadly

comparable to continuous energy restriction, while some data in steatotic liver disease suggest possible improvements in hepatic steatosis and insulin sensitivity.^{16,17}

Clinicians may consider fasting as one part of broader nutritional care, provided the approach is individualised, appropriately supervised, and tailored to the patient's clinical context. The approach should remain patient-centred and guided by safety, feasibility, cultural acceptability, food security, work patterns, co-morbidities, medicines, and available support. For most people with prediabetes, fasting may be best positioned as complementary to - not a replacement for - structured lifestyle intervention, physical activity, and sustained weight-management support. Fasting-based approaches should be avoided or used only with specialist guidance in individuals who are pregnant, frail, at risk of disordered eating, or using medicines that increase hypoglycaemia risk.^{1-3,13}

How to act in practice

In practice, the lecture suggests turning "prediabetes" into a practical, hopeful plan with clear follow-up. The message should neither alarm nor falsely reassure. A useful patient-facing phrasing is: "Your glucose is high enough for us to take seriously, but early enough for us to improve. Our goal is to help you return to normal glucose levels if possible." This reflects the symposium's central theme while keeping the conversation respectful, non-stigmatising and action oriented.

Local clinical vignette

The following vignette is fictional and holds no patient-identifiable information.

A 49-year-old woman from Tshwane attends a primary-care clinic for routine blood pressure follow-up. Her body mass index is 33 kg/m². She has a family history of type 2 diabetes and had gestational diabetes 14 years ago. Screening shows an HbA1c of 6.2% and a fasting plasma glucose of 6.3 mmol/L, both confirmed on repeat testing.

The clinician frames the consultation around reversibility rather than blame, explaining that the results are an early metabolic warning sign rather than inevitable progression to type 2 diabetes. Together, they agree on a practical three-month prevention plan that includes modest weight loss where possible, 150 minutes of brisk walking per week in manageable sessions, reducing sugar-sweetened beverages, culturally selected meal planning, and addressing sleep and stress-related factors. They plan repeat HbA1c and fasting plasma glucose testing to assess progress.

Because she has high-risk features, including obesity, a family history of type 2 diabetes, and a history of gestational diabetes, metformin is discussed as an adjunct to lifestyle intervention after renal function assessment and shared decision-making. The clinical goal is framed not only as delaying future diabetes but also as actively trying to restore normal glucose regulation where possible.^{1-4,15}

The practical approach in Table 1 is offered as the author's synthesis for South African practice and should not be read as a protocol specifically proposed by the symposium speaker.

Strengths of the symposium

The symposium had three notable strengths. First, it communicated urgency without fatalism, avoiding the passivity often associated with terms such as "borderline diabetes." Secondly, it used pathophysiology to support clinical communication: visceral fat, hepatic insulin resistance and β -cell stress were presented as practical explanatory tools rather than abstract concepts.⁷ Thirdly, it linked individual care to system-level priorities, including earlier detection, structured prevention

Table 1: Author's pragmatic "how-to" synthesis for South African practice

Step	Practical action	Clinical note
1. Confirm and contextualise	Confirm dysglycaemia using locally accepted testing pathways; review symptoms, medicines, pregnancy status where relevant, family history, adiposity, blood pressure, lipids, and cardiovascular risk.	Prediabetes is a risk marker and a prevention trigger; interpret it within cardiometabolic risk. ^{1,19,20}
2. Name the goal	Use hopeful, concrete language: "The goal is to move your glucose back into the normal range where possible."	Normoglycaemia predicts lower diabetes risk and more favourable vascular outcomes. ^{4,10,11,13,14}
3. Start structured lifestyle support	Offer a DPP-style plan: realistic weight reduction where needed, at least 150 minutes/week of moderate activity, resistance exercise where possible, nutritional counselling, sleep/stress review, and planned follow-up.	Structured, measurable, culturally acceptable and reviewable. ^{1-3,15}
4. Consider metformin selectively	Discuss metformin for high-risk adults, especially those with multiple risk features such as severe obesity, higher HbA1c or fasting plasma glucose (FPG) values, younger age, or a history of gestational diabetes; check renal function and tolerability.	Adjunct only in selected high-risk patients after safety review. ^{1-3,15}
5. Review and intensify	Reassess after approximately three months, repeat glycaemic measures according to clinical judgement, and refer or intensify if values progress, symptoms develop or risk is complex.	Avoid "diagnose and discharge"; review, escalate or refer.
6. Build the pathway	Use nurses, diabetes educators, group sessions, digital reminders, community resources, and clear referral criteria to make prevention repeatable rather than dependent on one enthusiastic clinician.	A repeatable pathway is needed; prevention cannot depend on one clinician. ^{18,19}

pathways, primary-care support and policy commitment. This systems perspective is particularly relevant in low- and middle-income settings, where fragmented care pathways may undermine sound prevention advice.^{15,18,19}

A further strength was the ethical positioning of the lecture. The emphasis fell on lifestyle support, careful selection for metformin and avoidance of product-specific promotion. That approach is important in an industry-sponsored symposium: it allows the scientific and public health argument to stand on its own merits while supporting credibility with clinicians and readers.

Limitations and points requiring caution

Prediabetes remission is increasingly relevant, but it still requires standardisation regarding duration, biochemical criteria, and interpretation in relation to medication exposure.¹³ Prevention strategies should therefore be individualised rather than applied uniformly to all people with prediabetes. The 2025 IDF recommendations and ADA standards appropriately position structured lifestyle intervention as the foundation of prevention, with metformin considered as an added possibility for selected high-risk individuals.^{1,15}

Clinicians and health systems should interpret the symposium's forward-looking messages as clinically useful guidance for more proactive prevention, while ensuring that implementation is guided by the strength of the evidence, individual patient characteristics, safety considerations, feasibility, and local implementation capacity. Readers should therefore approach this article as a reflective opinion paper, rather than as a systematic review of all prediabetes interventions or as a substitute for local clinical guidelines.

Implications for South African clinical practice

For South African clinicians, the practical message is that prediabetes should trigger action, not observation alone. Clinicians can communicate risk in concrete but hopeful terms, support nutritional and physical-activity change, and review progress with the explicit aim of restoring normoglycaemia where possible. Structured lifestyle intervention is still the most effective first-line strategy, while metformin has a role in carefully selected high-risk individuals, especially where risk is high, lifestyle response is inadequate or prevention infrastructure is limited.^{1-3,15}

The broader challenge is implementation. Earlier case-finding, usable risk stratification tools, referral pathways, nurse- and diabetes-educator-led support, community-based programmes and digital or hybrid prevention models are needed if the reversible window is to become more than a compelling metaphor. This is consistent with South Africa's NCD policy direction, which emphasises prevention, people-centred care and strengthened care cascades for diabetes and other chronic diseases.^{18,19}

Call to action

- For individual clinicians: do not leave prediabetes as a passive label; confirm the result, explain reversibility, set

normoglycaemia as the aspiration where possible, and schedule follow-up.^{1,4,13}

- For practices, academic societies, and SEMDSA-level implementation: develop simple prediabetes pathways that specify risk stratification, referral criteria, lifestyle support, metformin use, and repeat testing intervals.^{1,15,19,20}
- For health systems: invest in prevention infrastructure that can be delivered by multidisciplinary teams, including nurses, diabetes educators, dietitians, pharmacists, community health workers, and digital support tools.^{18,19}
- For policy and environmental action: treat diabetes prevention as more than individual counselling by addressing food environments, safe spaces for activity and air-pollution exposure as determinants of metabolic risk.^{8,9,18}

Conclusion

Overall, "Prediabetes: The Reversible Window" was a clinically relevant symposium that reframed prediabetes as an active prevention opportunity. Its strongest contribution was the insistence that normoglycaemia matters and that reversibility should be pursued deliberately, safely, and equitably. For South African practice, the symposium offered a constructive provocation: if prediabetes can be reversible in selected individuals, clinical systems should be designed to support early, structured, and equitable prevention. The next step is therefore clear: move from awareness to structured prevention, from risk labelling to regression- or remission-oriented prevention care, and from individual advice to pathways that make healthier metabolic trajectories achievable for patients in real-world South African settings.

Acknowledgements

This reflection was informed by the symposium presentation and supporting public literature. The author acknowledges Professor Peter E. H. Schwarz for reviewing the draft and providing constructive scholarly comments; the final interpretation and content remain the responsibility of the author.

Conflicts of interest

The author received support from Merck (Pty) Ltd, South Africa for congress attendance, including support for travel and registration. No honorarium was provided. This article reflects on an industry-sponsored breakfast symposium and is presented as a non-promotional academic commentary. No other conflicts of interest are declared.

Funding source

None declared.

Ethical approval

Not applicable. This is an opinion/reflection article and did not involve human participants, patient records, or patient-identifiable data.

Data availability

Not applicable.

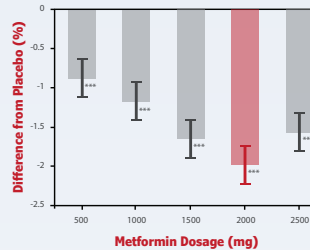


Facets of Metformin – Beneficial effects on Glycaemia and insulin requirement¹⁻⁵

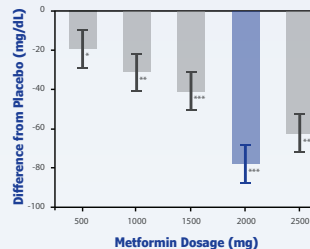
Anti-hyperglycaemic effect¹



Dose-dependent HbA1c reduction – optimum at 2000 mg¹



Dose-dependent Fasting Plasma Glucose (FPG) reduction – optimum at 2000 mg¹



No hypoglycaemic events when used alone³

Reduced insulin requirement⁵



Metformin is a biguanide with **antihyperglycaemic** effects, on both **basal** and **postprandial** hyperglycaemia.^{2,3}



Metformin alone does not stimulate insulin secretion and therefore **does not cause hypoglycaemia**.^{2,4}



Metformin reduces **basal hyperinsulinemia**, and in combination with insulin, reduces insulin requirement.^{4,5}



Glucophage® XR dosing schedule⁶

Initiate Glucophage® XR 500 mg and titrate up to 2 Glucophage® XR 1000 mg tablets once-daily with the evening meal



500 mg

1 x 1000 mg

3 x 500 mg

2 x 1000 mg



	SEP (Incl. VAT) ⁷	Pack Size
Glucophage XR 500 mg	R27.25	30
Glucophage XR 1000 mg	R150.36	60

References: 1. Garber AJ et al. 1997, DOI 10.1016/S0002-9343(97)00254-4. 2. DeFronzo RA, Barzilai N, Simonson DC 1991, DOI 10.1210/jcem-73-6-1294. 3. Harada N 2020, DOI 10.1111/jdi.13301. 4. Wiernsperger NF, Bailey CJ, *Drugs* 1999; 58 Suppl 1: 31-9. 5. Sanchez-Rangel E, Inzucchi SE, DOI 10.1007/s00125-017-4336-x. 6. Glucophage® XR Professional Information. 12 Apr 2021. 7. Database-Of-Medicine-Prices_01-September-2025

Proprietary Name (and dosage form): [S3] Glucophage XR 500 mg: **Composition:** Each tablet contains metformin hydrochloride 500 mg. **Reg. No.:** A39/21.2/0027. **Proprietary Name (and dosage form):** [S3] Glucophage XR 1000 mg: **Composition:** Each tablet contains metformin hydrochloride 1000 mg. **Reg. No.:** 45/21.2/0066. For full prescribing information please refer to the package insert approved by the Medicines Regulatory Authority. MERCK (Pty) Ltd. Reg. No.1970/004059/07. 1 Friesland Drive, Longmeadow Business Estate South, Modderfontein, 1645. Tel. (011) 372-5000. Report adverse events to drug.safety.southeastafrica@merckgroup.com. ZA-GLUX-00147 July 2026

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A rare case of hypokalaemic thyrotoxic periodic paralysis in a young African woman

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Background: Thyrotoxic periodic paralysis (TPP) is a rare, potentially life-threatening complication of thyrotoxicosis, presenting with acute flaccid weakness and hypokalaemia. Typically presenting in young Asian males, TPP can affect all ethnicities. The diagnosis can be challenging in people with HIV (human immunodeficiency virus) on tenofovir disoproxil fumarate (TDF), where hypokalaemia may be misattributed to drug-induced renal potassium wasting.

Case: A 31-year-old African woman on a TDF-based treatment regimen for HIV infection presented with acute generalised weakness and severe hypokalaemia (1.9 mmol/l). Clinically she displayed subtle thyrotoxic symptoms, most notably loss of weight. Investigations showed suppressed TSH (0.005 mIU/l) and elevated FT₄ (32 pmol/l). Low urinary potassium excluded TDF-related renal wasting. She was treated with intravenous potassium chloride, propranolol, and carbimazole, with rapid recovery. Thyroid scintigraphy confirmed toxic multinodular goitre, and she was referred for radioactive ablation.

Discussion: TPP should be considered in patients with acute hypokalaemic paralysis, even without the classical features of hyperthyroidism. In high HIV-burden settings, distinguishing TPP from TDF-induced proximal tubulopathy is critical. Management includes correction of hypokalaemia, control of sympathetic symptoms, and definitive treatment of hyperthyroidism.

Conclusion: This case highlights TPP as the initial manifestation of thyrotoxicosis in an African woman living with HIV on TDF-based ART. Awareness of this rare presentation is key for prompt diagnosis and timely management to prevent complications.

Keywords: thyrotoxicosis, hypokalaemia, paralysis, African, HIV

Introduction

Thyroid hormones are essential for the metabolic functioning of virtually all cells in the body. Elevated levels of thyroid hormone can cause severe dysfunction of multiple body systems including the cardiovascular, central nervous, and musculoskeletal systems.¹ Thyrotoxic periodic paralysis (TPP) is a rare but important manifestation of thyrotoxicosis. It is characterised by recurrent episodes of muscle weakness due to the intracellular shift of potassium and a resultant hypokalaemia.² The mainstay of treatment includes prompt correction of the hypokalaemia and the restoration of a euthyroid state to prevent further attacks.³

TPP is most often reported in Asian males, affecting approximately 2% of thyrotoxic patients in Asia.⁴ In contrast, it is rarely documented in sub-Saharan Africans, with an incidence rate of less than 0.2% in non-Asian populations.^{2,5,6}

Many patients with TPP do not exhibit overt clinical signs or symptoms of thyrotoxicosis, leading to frequent under-recognition and underdiagnosis.^{7,8} Furthermore, one study reported that 80% of patients with thyrotoxicosis initially presented with TPP.⁹ This creates a diagnostic challenge, particularly in people living with human immunodeficiency virus (HIV) in high-burden regions who are on tenofovir disoproxil fumarate (TDF)-based antiretroviral therapy (ART), where hypokalaemia

and paralysis may be misattributed to TDF-associated proximal tubulopathy and renal potassium wasting. A careful and thorough evaluation of patients presenting with acute-onset paralysis and hypokalaemia is essential, with emphasis on identifying and treating the correct underlying cause to prevent potentially serious complications such as cardiac arrhythmias and death.

Herein, we present a rare case of TPP as the initial manifestation of thyrotoxicosis in an African woman living with HIV on TDF-based ART.

Case description

A 31-year-old female of African descent, with a history of HIV on ART (TDF based regimen – tenofovir disoproxil fumarate 300 mg, lamivudine 300 mg and dolutegravir 50 mg fixed dose combination [TLD]). Her HIV viral load was lower than detectable limits and her CD4 count was 893 cells/mm³.

She presented to the emergency department of a tertiary academic hospital with a two-day history of generalised muscle weakness with no identifiable precipitants such as a high carbohydrate diet, steroid use, or strenuous exercise. She reported no history of a similar presentation and no previous trauma. On further enquiry, the patient reported a two-month history of intermittent vomiting, dysphagia, fatigue, and significant

unintentional weight loss of 21 kg. She denied any history of palpitations, heat intolerance, dyspnoea, or changes in bowel or menstrual function. She was of sober habits and had no use of over-the-counter medications or any other prescription medications except for her ART. There was no family history of periodic paralysis or thyroid disorders.

Physical examination was notable for a cachectic female weighing 42 kg. She was afebrile, normotensive, and normoglycaemic; however, she had a regular tachycardia of 113 bpm. Clinically, no lower limb oedema or skin changes were observed. Her neurological examination revealed normal higher mental function, intact cranial nerves, and normal sensory parameters. She had bilateral symmetrical reduced muscle bulk, reduced tone with reduced muscle power in all four limbs graded 1/5 both proximally and distally (tetraparesis), and an inability to perform neck flexion and extension. In addition, reflexes were diminished globally. There was no palpable goitre, ophthalmopathy, or other features of Graves' disease clinically. Pulmonary examination yielded marked tachypnoea on initial presentation. Cardiovascular and abdominal examinations were unremarkable.

On presentation her potassium level was 1.9 mmol/l (3.5–5.5 mmol/l) measured on a Nova Biomedical arterial blood gas analyser (Nova Biomedical, Waltham, MA, USA). An electrocardiogram (Figure 1) revealed a sinus tachycardia with features in keeping with the hypokalaemia, with the presence of U-waves.

Further biochemical investigations revealed an elevated free thyroxine (FT₄) level of 32 pmol/l (11.9–21.6 pmol/l) with a suppressed thyroid stimulating hormone (TSH) of 0.005 mIU/l (0.27–4.20 mIU/l) (Table I).

Urine analysis was done including a urine dipstick, which was normal, and urinary electrolytes yielded a reduced potassium of 3.83 mmol/l (20–80 mmol/l). Furthermore, a urine pregnancy test was negative.

Given the presentation of an acute reversible flaccid paralysis syndrome, a lumbar puncture was performed. The cell count findings were non-contributory with glucose and protein within normal limits. In addition, a negative viral panel and bacterial culture were noted. Initial concern for any central nervous system abnormalities was excluded following a normal computed tomography (CT) scan of the brain.

She was treated with an intravenous potassium chloride infusion in the emergency department overnight. After 12 hours, her potassium level was 3.8 mmol/l and her weakness resolved within 24 hours of admission.

Factoring in her medication use of a TDF-based ART regimen, there was an initial concern for a TDF proximal tubulopathy causing her severe hypokalaemia and renal dysfunction. However, given her low urinary potassium value, TDF-associated renal potassium wasting was deemed unlikely. A decision to omit TDF was taken and it was replaced with an abacavir (ABC)-containing ART regimen to mitigate any possible superimposed hypokalaemia caused by TDF.

The patient was initiated on carbimazole 15 mg and propranolol 10 mg each twice daily. Her clinical condition improved markedly, and she was discharged one week after admission

with scheduled follow-up with the endocrinology department. On her subsequent check-up, the results for her TSH receptor antibodies (TRAB) were negative at 1.32 U/l (< 1.8 U/l). Thyroid scintigraphy was performed, which yielded findings of hyperfunctioning 'hot' nodules in keeping with a toxic multinodular goitre. She is currently on carbimazole and is awaiting radioactive ablation therapy. She reported no further episodes of weakness.

Discussion

TPP is a rare endocrine emergency characterised by a triad of sudden reversible flaccid paralysis in the setting of thyrotoxicosis and hypokalaemia.¹⁰ TPP may occur in the context of thyrotoxicosis of any aetiology. While Graves' disease is the most frequent underlying cause, cases associated with toxic multinodular goitre, thyroiditis, and thyroid adenomas have also been reported.⁸ TPP is differentiated biochemically from familial hypokalaemic periodic paralysis (FHPP) by the presence of elevated thyroid hormones.¹

TPP most commonly presents in young to middle-aged men, particularly of East Asian or Latin American descent. It is infrequent in populations with black ancestry, with only a few cases reported in Africa.¹¹ The under-recognition and paucity of data regarding TPP in African settings may be due to under-reporting, diagnostic resource limitations or true genetic variability. Contributing genetic variants such as mutations in the KCNJ18 gene, encoding Kir 2.6 potassium channels, have been described, more frequently in Asian populations.¹² While hyperthyroidism is more commonly seen in females, TPP predominates in men at a ratio of 26:1.^{8,13}

The pathophysiological mechanisms underlying TPP are not well understood but current evidence suggests that the condition is precipitated by a combination of thyrotoxicosis, environmental stressors, and underlying genetic mutations, resulting in increased Na-K-ATPase pump activity in skeletal muscle and subsequent hypokalaemia.¹⁰

In this context, hypokalaemia results from transcellular potassium shift rather than a true potassium deficit.¹⁴

Potassium is the predominant intracellular cation and is regulated by the Na-K-ATPase pump and the inward-rectifying potassium channels (Kir).¹⁵ Skeletal muscle contains the largest proportion of total body potassium stores.¹⁶

Thyroid hormone upregulates the Na-K-ATPase pump by binding to the thyroid response elements and subsequently upregulating gene transcription of the Na-K-ATPase pump.¹⁵

This effect is further amplified by catecholamines and insulin. Catecholamines stimulate the Na-K-ATPase pump through beta-adrenergic receptors, whilst insulin, which is often elevated after a high-carbohydrate meal, stimulates membrane insertion of the Na-K-ATPase pump and elevated intrinsic activity.¹⁶

Collectively, these mechanisms result in an increased potassium influx to the cell with a decreased extracellular level of potassium leading to paradoxical depolarisation of the skeletal muscle membrane, thus, rendering them inexcitable and paralysed.^{1,16,17}

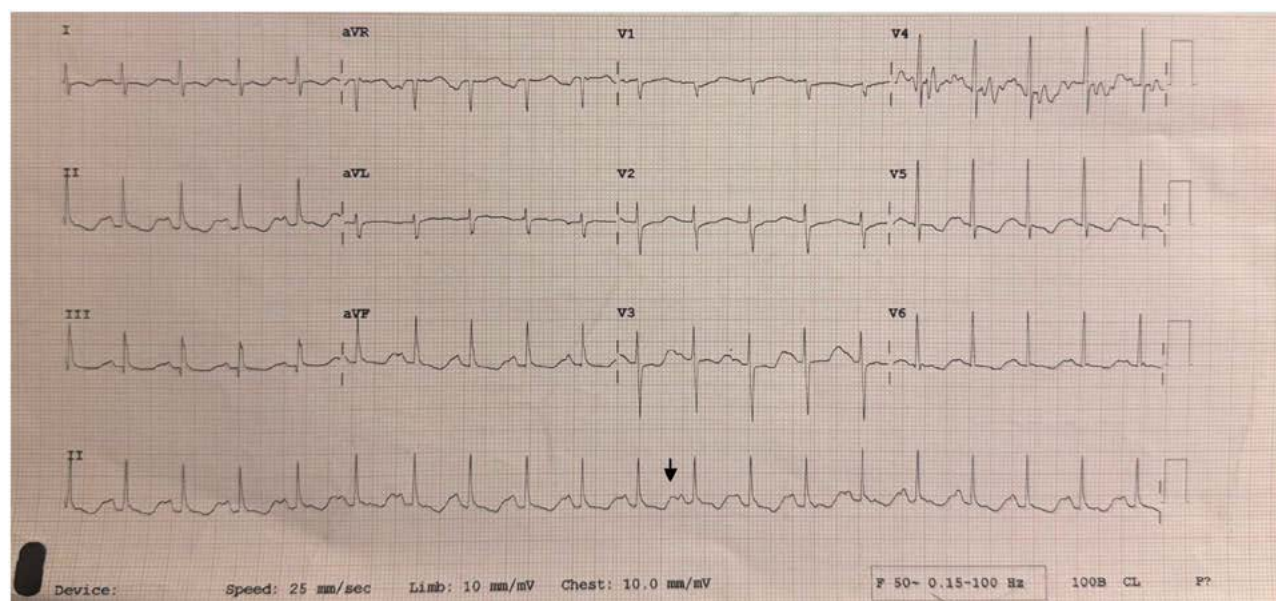


Figure 1: ECG displaying a sinus tachycardia with U-waves (arrow).

Clinically, patients with TPP present with acute onset of muscle weakness, beginning proximally, and ranging from mild self-limiting weakness to severe tetraplegia. There may be associated cardiac arrhythmias. Deep tendon reflexes are often diminished. Respiratory, swallowing, bladder, and bowel function are generally preserved.^{13,16} It is also important to consider that classic features of thyrotoxicosis such as warm skin, tachycardia, or a goitre are often subtle and may not be the initial presentation of thyrotoxicosis.⁷ A study by Chang *et al.* found that

only 17% of TPP patients had overt signs and symptoms of thyrotoxicosis.⁸

Previously documented rare initial presentations included respiratory muscle involvement and ventricular fibrillation.^{18,19} Common environmental precipitants include stress, high-carbohydrate meals, alcohol, and strenuous exercise.¹⁷ However, a prior study showed only 34% of TPP patients had an identifiable precipitant.⁸ In our patient's case, no precipitating factor could be identified.

Table 1: Biochemical investigations

Item	Day 0	Discharge	One-month follow-up	Reference range
Potassium	1.9	3.8	3.5	3.5–5.5 (mmol/l)
Magnesium	1.19	0.66	0.90	0.63–1.05 (mmol/l)
Inorganic phosphate	0.55	0.65	0.96	0.78–1.42 (mmol/l)
TSH	0.01			0.27–4.20 (mIU/l)
FT ₄	32		14.7	11.9–21.6 (pmol/l)
T ₃	17.1		5.3	3.1–6.8 (pmol/l)
TRAB	1.32			< 1.8 (U/l)
Urea	7.2	4.4	3.9	2.1–7.1 (mmol/l)
Creatinine	142	107	99	49–90 (mmol/l)
Estimated GFR	42	60	65	ml/min/1.73 m ²
Urine dipstick	No abnormalities detected			
Urine potassium	3.83			20–80 (mmol/l)
Urine pregnancy test		Negative		

TSH: thyroid stimulating hormone, FT₄: thyroxine, TRAB: TSH receptor antibody.

TPP should be considered in any patient presenting with acute onset paralysis in the presence of hypokalaemia. Confirmation requires a thyroid panel showing suppressed TSH with elevated FT₄ levels and triiodothyronine (T₃) levels.⁸ It is differentiated clinically from FHPP by a later age of onset, the absence of a family history of paralysis and the presence of thyrotoxicosis symptoms.¹⁹ Other acquired causes of hypokalaemic periodic paralysis such as renal potassium loss and medications such as insulin and steroid use need to be excluded.

The prevalence of HIV in South Africa is estimated to be 12.7% as of 2022.²⁰ In a country with a significant HIV burden, where TDF-based regimens are first-line treatment, it is crucial to exclude potential confounders such as TDF tubulopathy and to consider TPP in the differential diagnosis, as in our case.

TDF, a nucleotide reverse transcriptase inhibitor (NRTI), is a mitochondrial toxin that inhibits the enzyme responsible for replication of mitochondrial DNA. This affects the proximal renal tubule and can result in a renal tubular acidosis (RTA) or Fanconi syndrome.²¹

A proximal RTA (type 2) is an isolated defect in the tubular transport of bicarbonate and is characterised by a decreased rate of bicarbonate absorption. Fanconi syndrome is a more generalised defect in the resorptive capacity of the proximal convoluted tubule resulting in a loss of potassium, phosphate, uric acid, glucose, amino acids, and bicarbonate.²² Drug-induced nephrotoxicity, including TDF, is the most common acquired cause of Fanconi syndrome.²² Although hypophosphataemia

was present in our patient on admission, this was considered secondary to the redistribution of phosphate intracellularly under the similar mechanism of hypokalaemia described in TPP.⁵ In addition, the weakness resolved rapidly with potassium supplementation only and the phosphate levels normalised on follow-up once the patient was biochemically euthyroid. The clinical presentation is similar; however, the management between renal tubular wasting and TPP differs. As such, evaluating the patient's urinary studies and acid-base status is crucial for establishing the correct diagnosis.

Management of thyrotoxic periodic paralysis

Recommended therapies involve the correction of the hypokalaemia in the acute setting. Due to the low potassium attributed to a transcellular shift, it is essential to monitor for rebound hyperkalaemia whilst administering aggressive potassium supplementation. The use of non-selective beta-adrenergic blockers such as propranolol is recommended as they blunt the adrenergic stimulation of the Na-K-ATPase pump, thus preventing the intracellular shift of potassium. In addition, this also reduces the peripheral conversion of FT₄ to T₃, which attenuates the stimulation of the Na-K-ATPase pump and lessens the hypokalaemia.

Definitive management, however, entails maintaining a euthyroid state and treating the underlying aetiology for the hyperthyroidism. There are various options such as antithyroid medication, radioactive iodine ablation, or surgical thyroidectomy.²³

Conclusion

This case illustrates a rare presentation of TPP in an African woman living with HIV on TDF-based ART, in whom TPP was the first clinical manifestation of thyrotoxicosis. Given the diagnostic challenge presented by overlapping clinical features and potential confounders such as TDF-induced proximal tubulopathy, this case underscores the importance of a comprehensive evaluation, early identification, and close monitoring in patients presenting with acute hypokalaemic paralysis. Given the scarcity of reported cases of TPP in the African population, further research is warranted to raise awareness and allow clinicians to have a high index of suspicion to support a timely diagnosis. This case reinforces that this condition is no longer confined to the Asian population.

Disclosure statement – No potential conflict of interest was reported by the authors.

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Received: 04-12-2025 Accepted: 12-02-2026



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Monogenic diabetes in South Africa: clinical clues and lessons from seven cases

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Monogenic diabetes is an important but under-recognised cause of diabetes mellitus, particularly in settings with limited access to genetic testing. A retrospective case series of seven individuals with genetically confirmed monogenic diabetes managed at tertiary academic centres in Cape Town is described to emphasise that these conditions occur in South Africa. Patients with mutations associated with maturity-onset diabetes of the young, neonatal diabetes, mitochondrial diabetes, and syndromic insulin resistance were identified. Diagnostic reassessment was prompted by early-onset diabetes, preserved endogenous insulin secretion, negative islet autoantibodies, syndromic features, or unexpected treatment responses. Genetic confirmation had important implications for treatment, prognosis, and family screening. This case series demonstrates that monogenic diabetes occurs across a broad phenotypic spectrum in South Africa and that recognition in routine clinical practice leads to meaningful changes in management, surveillance, and family counselling.

Keywords: Africa, mitochondrial diabetes, monogenic diabetes, MODY, neonatal diabetes

Introduction

Monogenic diabetes comprises a heterogeneous group of single-gene disorders affecting pancreatic β -cell development, insulin secretion, or insulin action. It accounts for an estimated 1–2% of all diabetes globally, although the proportion is likely higher due to persistent underdiagnosis.^{1–4} Landmark advances in molecular genetics over the past three decades have clarified the pathophysiology and clinical features of maturity-onset diabetes of the young (MODY), neonatal diabetes, mitochondrial diabetes, and syndromic insulin-resistance disorders. Yet, despite this progress, monogenic diabetes remains under-recognised: studies from high-income countries indicate that up to 80–95% of individuals with monogenic diabetes are misclassified as having either type 1 or type 2 diabetes.^{4–6}

Underdiagnosis is likely even more profound in low- and middle-income countries, where limited access to molecular diagnostics intersects with a high burden of autoimmune and type 2 diabetes.⁷ Case reports and small series from Africa confirm that monogenic diabetes does occur on the African continent, although the cases are dominated by neonatal and syndromic forms with very limited representation of classical MODY phenotypes.^{7–12} However, systematic screening programmes are absent, and testing capacity remains extremely limited.

South African data mirror this situation. Publications describing monogenic diabetes in South Africa remain sparse and are largely limited to isolated cases presented as abstracts.^{13,14}

Accurate diagnosis has major therapeutic implications. Individuals with GCK-MODY exhibit stable, mild hyperglycaemia and typically require no glucose-lowering therapy.¹⁵ Conversely, patients with HNF1A- or HNF4A-MODY are highly sensitive to sulfonylureas and often transition off insulin with improved glycaemic control.¹⁶ HNF1B-MODY is a multisystem disorder requiring dedicated renal, hepatic, and endocrine surveillance.¹⁷ Mitochondrial diabetes, especially the m.3243A>G

mutation associated with maternally inherited diabetes and deafness (MIDD), carries risks of cardiomyopathy, neurological involvement, and lactic acidosis, and metformin must be used cautiously.¹⁸ Neonatal diabetes demonstrates one of the most dramatic examples of genotype-directed therapy: activating KCNJ11 mutations can be treated with high-dose sulfonylureas, improving glycaemia and neurodevelopment.^{19–21} Similarly, PPARG-related familial partial lipodystrophy confers severe metabolic risk and requires targeted management.²²

In resource-constrained environments such as South Africa, careful clinical phenotyping is essential for selecting patients for genetic testing. Features that raise suspicion include early-onset diabetes, preserved C-peptide, absence of obesity or insulin resistance, negative pancreatic autoantibodies, a strong multigenerational autosomal-dominant pattern, atypical clinical features (renal cysts, deafness, lipodystrophy), or unusual drug responses.^{4,5} Tools such as the MODY probability calculator can support rational triage where testing resources are limited.²³

In this context, we present seven genetically confirmed cases of monogenic diabetes identified during routine clinical practice, illustrating phenotypic diversity, diagnostic challenges, and the clinical consequences of molecular diagnosis in a resource-constrained setting. This report is not intended as a comprehensive review of monogenic diabetes, but rather as an illustrative case series highlighting practical clinical clues and management implications relevant to routine practice in resource-constrained settings.

Methods

This study is a retrospective descriptive case series of seven patients with genetically confirmed monogenic diabetes mellitus managed at Groote Schuur Hospital and Red Cross War Memorial Children's Hospital in Cape Town, South Africa. Cases were identified through specialist diabetes clinics and departmental clinical records, based on clinical suspicion of

monogenic diabetes followed by confirmatory genetic testing performed as part of routine clinical care.

Clinical data were extracted from medical records, including age at diagnosis, family history, clinical phenotype, biochemical features (including C-peptide and pancreatic autoantibodies where available), genetic results, and management before and after molecular diagnosis. Genetic testing was performed using targeted single-gene sequencing, gene panels, or deletion analysis, selected according to clinical phenotype and availability at the time of testing. Variants were classified by the reporting laboratories using standard pathogenicity frameworks, including established disease associations and, where applicable, segregation within families.

Ethical approval for this case series was obtained from the University of Cape Town Human Research Ethics Committee (HREC Ref: 842/2025). The requirement for written informed consent was waived by the Committee. All data were anonymised, and no identifying images or personal identifiers are included. The authors declare no conflicts of interest.

Case reports

Case 1: *HNF1A-MODY*

A 29-year-old woman was referred for evaluation of atypical diabetes that had been diagnosed at the age of 24 years. There was a strong multigenerational family history of diabetes consistent with autosomal dominant inheritance. Her mother was diagnosed with diabetes at the age of 29 years following pregnancy and had been well controlled on glibenclamide since diagnosis. The patient's sister was diagnosed with diabetes at age 29 years and had had documented glycosuria from the age of 18 years, with subsequent deterioration in glycaemic control despite dietary management. The maternal grandfather also had diabetes. No family members were known to have been obese.

At the time of diagnosis, the patient was lean, with a body mass index of 19 kg/m² and exhibited predominantly post-prandial hyperglycaemia during an oral glucose tolerance test. The fasting plasma glucose was 8.0 mmol/l rising to 18.0 mmol/l at 2 hours, consistent with marked post-challenge hyperglycaemia. There were no clinical features of insulin resistance, including no acanthosis nigricans, dyslipidaemia suggestive of metabolic syndrome, or central obesity. She did not present with ketosis or diabetic ketoacidosis, and no syndromic features were identified.

HbA1c at diagnosis was 6.6% and rose progressively to 7.4% and later 8.2% over four years despite dietary therapy. At the time of specialist referral, approximately five years after diagnosis, non-fasting C-peptide remained preserved at 526 pmol/l, indicating ongoing endogenous insulin secretion. Lipid profile showed triglycerides of 1.96 mmol/l, HDL-cholesterol of 2.19 mmol/l, and LDL-cholesterol of 2.19 mmol/l. Islet autoantibodies (anti-GAD and anti-IA2) were negative.

The patient was initially presumed to have type 2 diabetes despite her lean phenotype. She was unable to tolerate metformin and was managed with dietary modification alone for approximately four years; however, progressive deterioration in glycaemic control despite appropriate lifestyle measures prompted diagnostic reassessment. Given the young age at diagnosis, strong autosomal dominant family history, absence of clinical features of insulin resistance, preserved C-peptide

several years after diagnosis, and negative autoantibodies, monogenic diabetes was suspected. A MODY probability calculator indicated a greater than 75% likelihood of MODY, and genetic testing was undertaken.

Genetic testing confirmed a pathogenic duplication in the *HNF1A* gene (c.375_377dup), consistent with *HNF1A-MODY*. The same variant was identified in the patient's sister, confirming familial segregation and autosomal dominant inheritance. Following genetic confirmation, insulin therapy was avoided and the patient was commenced on low-dose sulfonylurea therapy, resulting in significant improvement in glycaemic control. Her sister was treated with low-dose gliclazide with similar benefit, and both achieved better glycaemic control on oral agents than previously on diet alone. This case highlights the importance of considering *HNF1A-MODY* in young individuals with preserved C-peptide, negative autoantibodies, and a strong autosomal dominant family history, as correct diagnosis allows effective treatment with low-dose sulfonylureas and avoidance of unnecessary insulin therapy.

Case 2: *glucokinase-MODY (GCK-MODY)*

A 28-year-old woman was referred to the diabetes clinic for post-partum assessment three months after delivery. Diabetes was first identified during pregnancy at the age of 26 years. There was a strong family history of diabetes affecting three generations in a pattern consistent with autosomal dominant inheritance. Her brother, mother, maternal grandmother, and maternal aunt had all been diagnosed with diabetes in adulthood and were treated with oral hypoglycaemic agents. No family members were known to be obese.

The patient had always been of normal bodyweight, and at post-partum assessment her body mass index remained within the normal range. There were no clinical features of insulin resistance, including no acanthosis nigricans or central obesity. She had never presented with ketosis or diabetic ketoacidosis, and no syndromic features were present.

During pregnancy, she was diagnosed with gestational diabetes at 26 weeks' gestation and was treated with insulin for the remainder of the pregnancy. Post-partum biochemical assessment demonstrated stable, mild hyperglycaemia. A 75-g oral glucose tolerance test performed after pregnancy showed a fasting plasma glucose of 7.2 mmol/l and a 2-hour plasma glucose of 9.1 mmol/l. HbA1c was 6.3%. Islet autoantibodies (anti-GAD and anti-IA2) were negative, and a fasting C-peptide level demonstrated preserved endogenous insulin secretion at 860 pmol/l. Glycaemic values remained stable over time without progression.

The patient was initially diagnosed with gestational diabetes during pregnancy and treated with insulin to achieve glycaemic targets for foetal safety. Insulin therapy was discontinued following delivery; however, the persistence of mild fasting hyperglycaemia post-partum raised consideration of underlying diabetes rather than transient gestational dysglycaemia. Given the combination of mild, stable hyperglycaemia, preserved beta-cell function, negative islet autoantibodies, absence of insulin resistance, and a strong autosomal dominant family history across three generations, monogenic diabetes was suspected and genetic testing was undertaken.

Genetic testing identified a likely pathogenic heterozygous missense variant in the glucokinase gene, *GCK* (c.127C>T;

p.Arg43Cys), consistent with a diagnosis of GCK-MODY and autosomal dominant inheritance. Following confirmation of the diagnosis, no pharmacological treatment was initiated, as treatment is not indicated for this condition outside of specific pregnancy contexts. The patient was counselled regarding the benign nature of her hyperglycaemia and the implications for future pregnancies, including the need for individualised foetal growth-guided management. Genetic testing of her son was not undertaken, with the plan to assess fasting glucose levels if clinically indicated. This case illustrates that mild, stable fasting hyperglycaemia with preserved insulin secretion and strong autosomal dominant inheritance should prompt consideration of GCK-MODY, as correct diagnosis avoids unnecessary lifelong treatment and informs management of future pregnancies.

Case 3: HNF1B-MODY (Renal cysts and diabetes syndrome)

A 14-year-old boy presented to the emergency department of a regional hospital with acute onset severe dystonic movements and altered sensorium. Initial investigations revealed severe non-ketotic hyperglycaemia with a plasma glucose of 71 mmol/l, negative serum and urinary ketones, and profound hyponatraemia with a plasma sodium of 119 mmol/l. There was no family history of diabetes. As a neonate, he was noted to have a small, non-functioning right kidney containing multiple cysts and underwent pyeloplasty in infancy for a congenital left mid-ureteric obstruction.

On examination, he was lean with a normal body mass index and was prepubertal (Tanner stage I). There were no clinical features of insulin resistance, including no acanthosis nigricans or lipodystrophy. Fasting plasma glucose on day five was 11.9 mmol/l with a simultaneous fasting C-peptide of 200 pmol/l, rising to 330 pmol/l following glucagon stimulation, indicating impaired but preserved endogenous insulin secretion. Islet autoantibodies (anti-GAD and anti-IA2) were negative. Lipid profile showed triglycerides of 1.7 mmol/l, total cholesterol of 3.7 mmol/l, and HDL-cholesterol of 1.0 mmol/l. HbA1c at presentation was 11%.

The association of atypical diabetes with renal and urogenital malformations strongly suggested HNF1B-related disease, prompting targeted genetic testing. Multiplex ligation-dependent probe amplification identified a heterozygous deletion of the entire HNF1B gene (p.Met1_Trp557del), confirming a diagnosis of HNF1B-MODY, also known as renal cysts and diabetes syndrome. Parental testing did not identify the variant, consistent with a de novo mutation. Following genetic confirmation, the patient continued long-term insulin therapy due to progressive beta-cell dysfunction, with ongoing multidisciplinary follow-up for renal function, electrolyte abnormalities, and diabetes control. This case demonstrates that the combination of early-onset diabetes and congenital renal abnormalities should prompt consideration of HNF1B-MODY, as recognition of the syndromic phenotype directs appropriate genetic testing and long-term multisystem surveillance.

Case 4: maternally inherited diabetes and deafness (MIDD)

A 40-year-old man was referred to specialist medical outpatient services following presentation with new-onset heart failure. Diabetes had been diagnosed eight years earlier, at the age of 32 years. There was a strong maternal family history of diabetes affecting three generations, with multiple maternal relatives

diagnosed between the ages of 30 and 40 years. Several affected family members also had progressive sensorineural hearing loss, which appeared to precede the diagnosis of diabetes, consistent with maternal inheritance.

The patient was lean with a body mass index of 21 kg/m² and had no clinical features of insulin resistance, including no acanthosis nigricans. He reported progressive bilateral sensorineural hearing loss since the age of 19 years. Six months prior to referral, he had suffered an ischaemic stroke, followed by focal epilepsy and cognitive decline. At presentation, he had symptoms of heart failure for approximately three months. Previous cardiac investigations demonstrated normal coronary arteries and an echocardiogram showing global left ventricular dysfunction with an ejection fraction of 40%. On examination, there was evidence of a previous stroke with a mild hemiplegia and a visual field defect. Cognitive assessment revealed mild impairment, with a Mini-Mental State Examination score of 25/30, reduced attention, and impaired working memory.

At the time of review, HbA1c was 6.8% while on insulin therapy. Fasting C-peptide was relatively preserved at 530 pmol/l, indicating residual endogenous insulin secretion many years after diagnosis. Islet autoantibodies (anti-GAD and anti-IA2) were negative. Resting plasma lactate was elevated at 3.2 mmol/l.

The patient had initially been diagnosed with type 2 diabetes at the age of 32 years and treated with oral hypoglycaemic agents, with insulin therapy introduced approximately seven years later due to progressive hyperglycaemia. The subsequent development of neurological and cardiac complications prompted reassessment of the underlying diagnosis. Given the combination of young-onset diabetes in a lean individual, preserved C-peptide, negative islet autoantibodies, progressive sensorineural deafness, neurological features, cardiomyopathy, elevated lactate, and a strong maternal pattern of inheritance, mitochondrial diabetes was suspected and targeted genetic testing was undertaken.

Molecular analysis using polymerase chain reaction followed by restriction fragment length polymorphism analysis confirmed the presence of the A3243G mitochondrial DNA mutation, consistent with a diagnosis of maternally inherited diabetes and deafness. Following genetic confirmation, management focused on multidisciplinary care, including optimisation of insulin therapy, cardiology follow-up for cardiomyopathy, neurological management for epilepsy and cognitive impairment, and audiological support for progressive hearing loss. Metformin was avoided due to the risk of lactic acidosis, and family members on the maternal side were advised to undergo clinical screening and genetic counselling. This case highlights that young-onset diabetes with maternal inheritance, sensorineural deafness, preserved C-peptide, and multisystem involvement should prompt consideration of MIDD, as recognition of the mitochondrial aetiology has important implications for treatment choice and family counselling.

Case 5: permanent neonatal diabetes mellitus due to a KCNJ11 mutation

A male infant was born prematurely at 34 weeks' gestation with a birthweight of 2.45 kg. Diabetes was diagnosed in the neonatal period shortly after birth. There was no known family history of diabetes.

The infant presented with persistent hyperglycaemia soon after birth that was difficult to control. Growth was poor, with a weight of 3.55 kg at 5 months of age. His clinical course was complicated by recurrent episodes of sepsis caused by multiple organisms, developmental delay with hypertonia, and a small bowel obstruction secondary to a focal area of intestinal atresia. Additional findings included an enlarged interventricular septum with a small pericardial effusion. Overall, the phenotype was suggestive of a syndromic form of neonatal diabetes with neurological involvement.

Biochemical investigations demonstrated severe hyperglycaemia with very low endogenous insulin secretion. C-peptide levels were markedly low (< 20 pmol/l), consistent with severe beta-cell dysfunction.

The patient was initially treated as having neonatal diabetes and commenced on insulin therapy. Glycaemic control remained challenging despite insulin treatment, in the context of recurrent infections and multisystem disease. Given the neonatal onset of diabetes, profound insulin deficiency, and the presence of neurological and systemic features, monogenic neonatal diabetes was strongly suspected and genetic testing was undertaken.

Genetic analysis identified a heterozygous pathogenic missense variant in the *KCNJ11* gene (c.878C > A; p.Thr293Asn), consistent with permanent neonatal diabetes with associated neurological features. Maternal testing was negative for the variant, and paternal testing was unavailable. The patient remained insulin-dependent, and given the severity of his neurological and systemic comorbidities, a trial of sulfonylurea therapy was not pursued. The patient later died of sepsis. This case highlights that neonatal-onset diabetes with profound insulin deficiency and neurological features should prompt urgent genetic testing, as *KCNJ11* mutations define a distinct clinical entity with important therapeutic and prognostic implications.

Case 6: familial neonatal diabetes due to an *INS* gene mutation

A male patient was diagnosed with diabetes at 15 months of age and required insulin therapy from presentation. There was a striking family history of early-onset diabetes. The patient's grandfather had been diagnosed with diabetes in his second decade; his father had been diagnosed with diabetes at 9 months of age and required lifelong insulin therapy, while the patient's younger brother was diagnosed with diabetes at 7 months of age and also required insulin. The pattern was consistent with autosomal dominant inheritance.

The proband presented in infancy with hyperglycaemia but had no history of diabetic ketoacidosis. Growth and development were otherwise unremarkable, and there were no clinical features of insulin resistance or syndromic abnormalities.

Across affected family members, islet autoantibodies were consistently negative. Affected relatives were initially diagnosed with type 1 diabetes and treated with insulin therapy. Given the familial clustering of neonatal and early-infantile diabetes, autosomal dominant inheritance, absence of islet autoantibodies, and lack of ketoacidosis, monogenic diabetes was suspected and genetic testing was undertaken.

Genetic testing in the proband identified a pathogenic intronic mutation in the insulin gene (*INS* c.188-31G > A), known to

cause neonatal diabetes by impairing insulin production, and consistent with the familial pattern of disease. Insulin therapy was required in the proband and other family members. The principal impact of the diagnosis was diagnostic clarification and provision of accurate genetic counselling for the family.

Case 7: *PPARG*-related partial lipodystrophy with severe insulin resistance

A 22-year-old woman was referred for specialist assessment after presenting with progressive dermatological, endocrine, and metabolic abnormalities. The patient's father was reported to have type 2 diabetes and ischaemic heart disease but was estranged from the family and unavailable for further clinical or genetic assessment. Her mother was clinically unaffected. The patient's brother, aged 24 years, was lean (BMI 22 kg/m²) and asymptomatic, although later biochemical testing demonstrated significant hyperinsulinaemia during an oral glucose tolerance test. The inheritance pattern was consistent with autosomal dominant transmission with variable penetrance.

The patient initially presented at the age of 20 years with hyperpigmented skin changes involving the neck, axillae, and groin and was diagnosed with severe acanthosis nigricans. She was subsequently referred for gynaecological assessment due to menstrual irregularity and mild hirsutism, with biochemical testing and pelvic ultrasonography consistent with a diagnosis of polycystic ovarian syndrome. At the age of 21 years she developed congestive cardiac failure, with cardiac investigations confirming a dilated cardiomyopathy. At the age of 22 years, she was hospitalised with severe acute pancreatitis secondary to marked hypertriglyceridaemia, at which time diabetes was diagnosed. On examination, she had extensive acanthosis nigricans, hirsutism, and features of partial lipodystrophy, with reduced subcutaneous fat over the limbs and buttocks and relative fat preservation centrally. There were clinical features of severe insulin resistance but no generalised lipodystrophy.

Biochemical investigations demonstrated severe insulin-resistant diabetes with labile glycaemic control, marked hypertriglyceridaemia, and elevated liver enzymes consistent with metabolic-associated steatotic liver disease. Hyperandrogenism was present. Insulin levels during oral glucose tolerance testing were markedly elevated, particularly in affected family members. These findings were consistent with a severe insulin resistance syndrome.

The patient was initially managed as having type 2 diabetes with severe insulin resistance. Progressive metabolic deterioration necessitated escalating insulin therapy, ultimately exceeding 300 units per day, with suboptimal glycaemic and lipid control, and standard lipid-lowering and heart failure therapies were instituted. Given the combination of severe insulin resistance disproportionate to body mass, early-onset diabetes, extreme hypertriglyceridaemia with pancreatitis, partial lipodystrophy, cardiomyopathy, and familial biochemical insulin resistance, a monogenic lipodystrophy syndrome was suspected. Targeted genetic testing was pursued after LMNA sequencing for laminopathies was negative.

Genetic sequencing identified a novel heterozygous missense variant in the *PPARG* gene (c.782C > A; p.Ala261Glu).²⁴ The variant was also identified in the patient's brother but was absent in her mother, supporting autosomal dominant inheritance, and was classified as pathogenic based on phenotype

concordance and functional implications. Following genetic confirmation, the patient was treated with the thiazolidinedione rosiglitazone on two separate occasions. On both occasions, she demonstrated marked improvement in glycaemic control and substantial reduction in triglyceride levels, confirming PPARG agonist responsiveness; however, treatment had to be discontinued due to fluid retention and worsening cardiac failure despite escalation of diuretic therapy. Her clinical course was complicated by persistent severe insulin resistance, recurrent metabolic decompensation, and progressive cardiac failure, and she died from refractory heart failure at the age of 26 years. This case illustrates a syndromic form of monogenic diabetes, and highlights that PPARG-related partial lipodystrophy can present with extreme insulin resistance, hypertriglyceridaemia, and cardiomyopathy, and that although PPARG agonists may produce dramatic metabolic improvement, their use may be limited by fluid retention in patients with coexisting cardiac failure (Table 1).

Discussion

Monogenic diabetes remains an under-recognised cause of atypical hyperglycaemia worldwide, despite accounting for approximately 1–2% of all diabetes.^{1–4} Even in well-resourced health systems, up to 80–95% of affected individuals are misclassified as having type 1 or type 2 diabetes, resulting in missed opportunities for targeted therapy, genetic counselling, and appropriate long-term surveillance.^{4–6} In low- and middle-income settings such as South Africa, diagnostic rates are likely to be even lower owing to limited access to molecular testing, the high background prevalence of young-onset type 2 diabetes, and the absence of structured screening pathways.^{6,7}

The seven cases presented in this series illustrate a wide range of monogenic diabetes phenotypes encountered in routine South African clinical practice. Collectively, they highlight three key considerations for clinicians: when to suspect monogenic diabetes, whom to prioritise for genetic testing, and how a confirmed molecular diagnosis alters clinical management.

When should clinicians suspect monogenic diabetes?

Several recurring diagnostic features emerged across the cases. Early-onset diabetes, particularly when diagnosed in childhood, adolescence, or early adulthood, should prompt consideration of monogenic aetiologies, especially in the absence of obesity or classical metabolic syndrome features.^{1–4} Sustained endogenous insulin secretion, evidenced by preserved C-peptide levels several years after diagnosis, strongly argues against type 1 diabetes and is characteristic of many MODY subtypes.^{4–6} This was evident in the HNF1A- and GCK-MODY cases described.

A strong multigenerational family history consistent with autosomal dominant inheritance was another prominent feature, particularly in HNF1A-, HNF4A-, HNF1B-, and GCK-related diabetes. In addition, specific syndromic features should prompt targeted genetic evaluation, including renal cystic disease and urogenital anomalies (HNF1B-MODY), sensorineural deafness or cardiomyopathy (mitochondrial diabetes), severe insulin resistance with lipodystrophy (PPARG-associated disease), and neonatal hyperglycaemia presenting before six months of age.

Unexpected treatment responses may provide further diagnostic clues. Marked sulfonylurea sensitivity in HNF1A- or HNF4A-

MODY, sometimes allowing complete withdrawal of insulin, contrasts sharply with the stable, mild hyperglycaemia of GCK-MODY, which does not respond to pharmacological therapy and generally requires no treatment.

Who should be tested in resource-constrained settings?

Given the limited availability of broad genetic panels in much of sub-Saharan Africa, a phenotype-driven testing strategy is necessary. A detailed family history, noting as many details as possible such as age at diagnosis, insulin use, episodes of DKA and glycaemic control achieved in all affected family members will often raise initial suspicion and remains an important component of the initial evaluation of patients with diabetes. Clinical tools such as the MODY probability calculator, which has been validated in several populations, may assist in identifying individuals at higher pre-test probability, although such tools should complement rather than replace clinical judgement.²³

Genetic testing should be prioritised in individuals with diabetes diagnosed before the age of 35 years who have a strong autosomal dominant family history, a non-obese phenotype with negative pancreatic autoantibodies and preserved C-peptide, syndromic features involving the kidneys, auditory system, nervous system, or adipose tissue distribution, or diabetes diagnosed before six months of age, where neonatal diabetes is overwhelmingly likely. Where comprehensive panels are unavailable, targeted single-gene sequencing – such as KCNJ11 in neonatal diabetes or HNF1B in renal cystic disease – may still yield high diagnostic value.

Although African data remain limited, available literature supports the presence of monogenic diabetes across diverse populations on the continent.^{9–13}

How does a genetic diagnosis change management?

This case series demonstrates the tangible clinical utility of molecular diagnosis serving as an example of precision medicine in diabetes care and hints at the future where genetic information may lead to tailored treatment.^{24–26} Individuals with GCK-MODY generally require no pharmacological treatment, and unnecessary therapy may expose them to avoidable hypoglycaemia.¹⁵ In contrast, patients with HNF1A-MODY often exhibit profound sulfonylurea sensitivity, allowing insulin withdrawal in selected cases.¹⁶

Diagnosis of HNF1B-MODY has implications beyond glycaemic management, prompting renal, hepatic, and endocrine surveillance and informing reproductive counselling.¹⁷ Recognition of mitochondrial diabetes is critical, as metformin may precipitate lactic acidosis, and proactive cardiac and neurological monitoring is required; maternal inheritance patterns also guide family risk assessment.¹⁸ In neonatal diabetes caused by KCNJ11 mutations, transition from insulin to sulfonylurea therapy can substantially improve glycaemic control and may enhance neurodevelopmental outcomes.^{18–20} Finally, identification of PPARG-associated familial partial lipodystrophy informs targeted therapeutic strategies and clarifies long-term metabolic and cardiovascular risk.²²

Implications for South Africa and sub-Saharan Africa

These cases illustrate that diverse forms of monogenic diabetes occur in African clinical settings and are encountered during routine practice. Clinicians frequently encounter phenotypes

Table 1: Clinical features, genetic diagnoses, and management implications in seven South African patients with monogenic diabetes

Case	Sex	Age at DM diagnosis	Gene (mutation)	Inheritance pattern	Key clinical clues prompting suspicion	C-peptide status	Initial classification	Change in management after genetic diagnosis	Key non-glycaemic implications
1	F	24 years	HNF1A (c.375_377dup)	Autosomal dominant	Lean phenotype; strong multigenerational family history; post-prandial hyperglycaemia; negative autoantibodies	Preserved (526 pmol/l, non-fasting)	Type 2 diabetes	Transition to low-dose sulfonylurea; insulin avoided	Cascade testing; counselling regarding autosomal dominant inheritance
2	F	26 years (pregnancy)	GCK (c.127C > T; p.Arg43Cys)	Autosomal dominant	Mild, stable fasting hyperglycaemia; strong family history; no progression; negative autoantibodies	Preserved (860 pmol/l, fasting)	Gestational diabetes	No pharmacological therapy required	Pregnancy counselling; avoidance of unnecessary lifelong treatment
3	M	14 years	HNF1B (whole-gene deletion)	De novo	Congenital renal cystic disease; urogenital anomalies; early-onset diabetes; negative autoantibodies	Reduced but present (200–330 pmol/l with stimulation)	Type 1 diabetes	Continued insulin therapy; targeted multisystem follow-up	Renal and electrolyte surveillance; reproductive counselling
4	M	32 years	mtDNA (m.3243A > G)	Maternal	Maternal inheritance; sensorineural deafness; cardiomyopathy; neurological features; elevated lactate	Preserved (530 pmol/l)	Type 2 diabetes	Avoidance of metformin; multidisciplinary management	Cardiac, neurological, and audiological surveillance; maternal family screening
5	M	Neonatal	KCNJ11 (c.878C > A; p.Thr293Asn)	Likely de novo	Neonatal-onset diabetes; profound insulin deficiency; neurological involvement; negative autoantibodies	Absent (< 20 pmol/l)	Neonatal diabetes	Insulin continued; sulfonylurea not trialled	Neurodevelopmental prognosis; genetic counselling
6	–	15 months	INS (c.188-31G > A)	Autosomal dominant	Familial neonatal diabetes; absence of ketoacidosis; persistent C-peptide	Detectable despite long duration	Neonatal diabetes	Insulin continued (non-sulfonylurea responsive)	Clarification of inheritance; family counselling
7	F	22 years	PPARG (c.782C > A; p.Ala261Glu)	Autosomal dominant	Severe insulin resistance; partial lipodystrophy; extreme hypertriglyceridaemia; cardiomyopathy	Markedly elevated insulin levels	Type 2 diabetes	Trial of thiazolidinedione with marked metabolic response (limited by cardiac failure)	Cardiovascular risk stratification; prognostic clarification

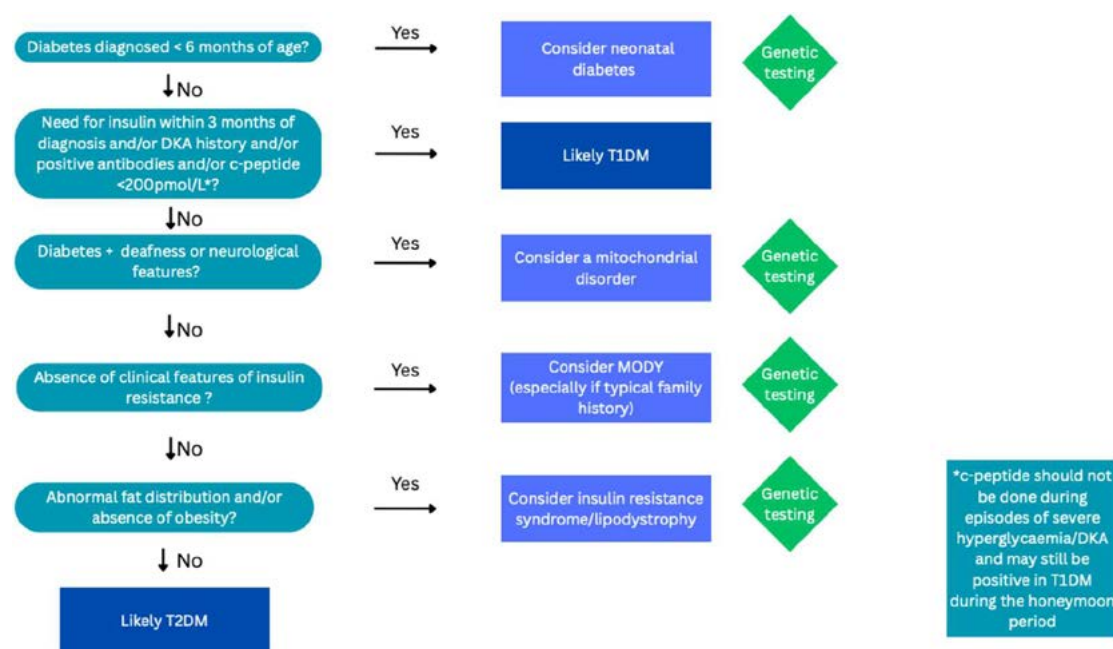


Figure 1: An illustrative clinical framework for considering monogenic diabetes.

Note: This figure is intended as an educational illustration of clinical features commonly associated with monogenic diabetes. It does not represent a validated diagnostic algorithm or comprehensive testing strategy, and clinical judgement and local resource availability remain central to decision-making.

suggestive of monogenic disease, yet genetic testing is seldom pursued. Improved clinician awareness, rational testing strategies, and expanded access to molecular diagnostics could substantially improve diagnostic accuracy, enable cascade testing, and optimise long-term outcomes.

Limitations

This study has several limitations. As a retrospective case series from tertiary referral centres, the cases are subject to selection bias and do not permit estimation of prevalence or diagnostic yield. Only individuals in whom genetic testing was pursued and completed are represented, and phenotypic or biochemical data were incomplete in some cases due to the retrospective design. Genetic testing strategies evolved over time and were influenced by availability and cost, limiting uniformity across cases. Nevertheless, the series reflects real-world clinical practice in a resource-constrained setting and highlights clinically relevant patterns that may prompt earlier recognition of monogenic diabetes. The educational framework presented is illustrative and not intended to substitute for formal guidelines or comprehensive diagnostic algorithms.

Conclusion

This South African case series demonstrates that monogenic diabetes presents with recognisable clinical patterns across a broad phenotypic spectrum and that timely genetic diagnosis can meaningfully alter clinical management. In routine practice, clinicians should maintain a high index of suspicion in individuals with early-onset, antibody-negative diabetes, preserved endogenous insulin secretion, strong family histories, syndromic features, or unexpected treatment responses.

In resource-constrained settings, careful clinical phenotyping remains central to identifying patients most likely to benefit from genetic testing. Wider adoption of structured clinical assessment, coupled with context-appropriate testing strategies and improved access to molecular diagnostics, has the potential to substantially improve diagnostic accuracy, enable

cascade testing, and optimise long-term outcomes for individuals and families affected by monogenic diabetes in South Africa and similar settings.

Disclosure statement – No potential conflict of interest was reported by the authors.

Ethics committee approval – Ethical approval for this case series was obtained from the University of Cape Town Human Research Ethics Committee (HREC Ref: 842/2025). The requirement for written informed consent was waived by the Committee. All data were anonymised, and no identifying patient information or images are included.

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Amyloid goitre in a patient with thyrotoxicosis: a diagnostic challenge

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Amyloid goitre is an uncommon cause of thyroid enlargement resulting from substantial amyloid deposition within the gland, sufficient to cause a clinically detectable goitre. Most affected patients are euthyroid. Amyloid deposition within the thyroid gland is typically detected incidentally or in association with thyroid malignancies, such as medullary thyroid carcinoma. The occurrence of a clinically detectable goitre secondary to amyloid deposition in a patient with concomitant thyrotoxicosis is exceptionally rare. We describe a case of an 81-year-old woman who presented with a multinodular goitre and biochemical thyrotoxicosis with suppressed TSH, elevated free T4, and negative thyroid antibodies (including TSH receptor antibodies). An ultrasound of the thyroid gland demonstrated a suspicious TI-RADS 3 nodule, and thyroid scintigraphy showed an enlarged right lobe with a large cold nodule in the inferior two-thirds of the right lobe with inhomogeneous uptake. Histopathology demonstrated extensive amyloid deposition within the nodule, confirming a diagnosis of amyloid goitre/amyloidoma. Systemic evaluation identified a monoclonal IgG kappa band on serum protein electrophoresis and bone marrow plasma cell infiltration of less than 10%, consistent with a monoclonal gammopathy of undetermined significance (MGUS). No clinical or investigative evidence of systemic amyloidosis was identified.

Keywords: amyloidoma, amyloid nodule, amyloidosis, thyroid nodule, thyrotoxicosis

Introduction

The thyroid gland plays a crucial role in regulating metabolic activity through the secretion of triiodothyronine (T3) and thyroxine (T4).¹ Thyrotoxicosis results from excess production of these hormones and can lead to various systemic symptoms such as weight loss, palpitations, and anxiety.¹ In clinical practice, the three most common causes of hyperthyroidism are Graves' disease, toxic multinodular goitre and toxic adenoma.¹

Thyroid nodules are often detected incidentally during routine imaging or clinical examination and may be either benign or malignant.² There are different ultrasonographic scoring systems, such as the American Thyroid Association scoring system and the Thyroid Imaging Reporting and Data System (TI-RADS), which assist in assessing nodules and determining which nodules require further evaluation. TI-RADS is a standardised radiological measure of whether a nodule is suspicious or not and is commonly used in South Africa.³ Depending on the score and size of the nodule, TI-RADS guides decision-making regarding a fine needle aspiration (FNA) versus serial ultrasound surveillance.³ In patients who are biochemically hyperthyroid with a thyroid nodule, a scintigraphy scan helps differentiate hyperfunctioning or "hot" (hyperactive compared with surrounding thyroid tissue) nodules from "cold" (hypoactive compared with surrounding thyroid tissue) nodules.² In a thyrotoxic patient, once biochemical euthyroidism is achieved, fine needle aspiration (FNA) may be safely performed.²

Amyloid refers to abnormal extracellular protein aggregates composed of misfolded precursor proteins that adopt a β -pleated sheet configuration.⁴ These deposits accumulate within tissues and organs, disrupting normal architecture and impairing physiological function, ultimately resulting in the clinical syndromes collectively termed amyloidosis.⁴

Primary amyloidosis, or AL amyloid, is usually systemic and arises from a clonal proliferation of abnormal plasma cells, which synthesise abnormal immunoglobulin light chains kappa (κ) or lambda (λ) that may aggregate and deposit in various tissues as amyloid.⁵ Secondary amyloidosis, or AA amyloid, occurs secondary to a chronic inflammatory condition in which interleukins 1 and 6 stimulate serum amyloid A (SAA) synthesis in liver cells.⁵ Sustained SAA levels are then prone to deposition in different organs. In contrast, familial amyloid is due to deposition of normal amounts of mutant transthyretin (TTR), which is a transporter of thyroxine.⁵ Wild-type TTR may also form amyloid fibrils within different tissues, such as cardiac tissue or peripheral nerves.⁶ When amyloid deposition is confined to a single organ site without evidence of systemic involvement, it is termed an amyloidoma; this may present as a nodular mass identified microscopically.⁵

Amyloid proteins can arise from several precursor proteins or fragments of precursor proteins, including monoclonal immunoglobulin light chains in AL amyloid, immunoglobulin light chains associated with multiple myeloma, serum amyloid A in chronic inflammatory states, β 2-microglobulin in renal failure and β -protein in Alzheimer's disease.⁴ These diverse precursors account for the heterogeneity of clinical presentations across amyloid subtypes.

Microscopically, amyloid appears as homogeneous, unstructured extracellular material that is eosinophilic on haematoxylin–eosin staining and stains red with crystal violet.⁴ Congo red staining highlights the deposits more specifically, demonstrating the pathognomonic "apple green birefringence" under polarised microscopy.⁴ These deposits cause tissue damage and organ dysfunction, giving rise to symptoms that are determined by the affected organ.⁴

Within the thyroid gland, amyloid deposits most commonly occur in association with medullary thyroid carcinoma, where the amyloid results from accumulation of calcitonin or other peptide precursors.⁷ Rarely, extensive amyloid deposition in the thyroid gland may lead to an amyloid goitre, where a clinically enlarged gland is palpable.⁸ Here we report a rare case of an elderly African female presenting with an amyloid goitre with background thyrotoxicosis.

Case report

An 81-year-old female patient with chronic previous biomass exposure and established chronic obstructive pulmonary disease (COPD) presented to the emergency department with an acute exacerbation of her underlying respiratory condition. Her past medical history included hypertension and dyslipidaemia with no previous documented end-organ damage. Incidentally, on clinical examination, she was found to have an enlarged thyroid gland with palpable nodules. There were no features of thyroid eye disease or thyroid dermopathy to suggest Graves' disease.

The results of the patient's investigations are summarised in Table 1. Thyroid function tests demonstrated a suppressed thyroid-stimulating hormone (TSH) level with an elevated T4 and normal TSH receptor antibody (TRAb) level. Thyroid scintigraphy using Technetium-99 m revealed an enlarged right lobe with a large cold nodule in the inferior two-thirds with overall inhomogeneous uptake of radiotracer. The left lobe was mildly enlarged with homogeneous uptake of radiotracer (Figure 1). An ultrasound identified a 4.7 × 2.3 cm TI-RADS 3 complex cystic lesion in the right lobe, while the left lobe and isthmus appeared normal on ultrasound.

The patient was initiated on carbimazole, and once biochemical euthyroidism was achieved, an ultrasound-guided biopsy of the cold nodule was done. Histological examination demonstrated features consistent with an amyloidoma, including fragments of fibrous connective tissue and extracellular homogeneous eosinophilic material within the background (Figure 2A–C).

Table 1: Summary of biochemical and immunological investigations

Item	Result	Reference
Renal		
Sodium (mmol/l)	145	136–145
Potassium (mmol/l)	4.4	3.5–5.1
Chloride (mmol/l)	101	98–107
Bicarbonate (mmol/l)	30	23–29
Urea (mmol/l)	10.1	2.1–7.1
Creatinine (μmol/l)	77	49–90
eGFR (mL/min/1.73 m ²)	62	–
Thyroid		
TSH (mIU/l)	0.09	0.3–5.5
T4 (pmol/l)	31	11.5–22.7
TRAb (U/l)	0.2	<1.8
Immunological		
Free kappa light chains (mg/l)	27	3.3–19.4
Free lambda light chains (mg/l)	24.5	5.7–26.3
Kappa:lambda ratio	1.1	0.26–1.65
Paraprotein 1 (g/l)	5	–
Paraprotein immunofixation	IgG kappa	–
Urine Bence Jones protein	Not detected	–



Figure 1: Thyroid scintigraphy demonstrating an enlarged right lobe with a cold nodule occupying most of the inferior two-thirds and inhomogeneous uptake of radiotracer. The mildly enlarged left lobe shows homogeneous radiotracer uptake.

Occasional vascular structures lined by benign endothelial cells were present within the fibrous connective tissue (Figure 2D). Hemosiderin-laden macrophages and areas of haemorrhage within the capillaries and the soft tissue were also noted. No plasma cells were observed, and there were no features suggestive of medullary thyroid carcinoma. Congo red stain showed strong salmon-pink positivity indicating extensive amyloid deposition; however, apple-green birefringence could not be demonstrated in the extracellular eosinophilic material because of technical limitations (Figure 3). Due to technical and economic constraints within the public sector, immunohistochemistry was not performed on the sample.

Further evaluation was undertaken to assess for systemic amyloidosis. A bone marrow aspirate and trephine biopsy (BMAT) demonstrated 5% plasma cells, consistent with a monoclonal gammopathy of undetermined significance (MGUS). Fluorescent in-situ hybridisation (FISH) was not performed on the sample. A cardiac echo showed no features suspicious of cardiac amyloid. A multidisciplinary team comprising haematology and medical oncology diagnosed amyloidosis in this patient with the available investigations. The patient was then referred to a quaternary centre for specialised oncological management and further evaluation.

Discussion

Amyloidosis encompasses a heterogeneous group of rare protein-misfolding disorders, with diverse clinical presentations making a diagnosis challenging. AL amyloidosis is multi-systemic and arises from an underlying plasma cell dyscrasia leading to progressive multi-organ dysfunction and failure.⁹ The estimated global incidence of AL amyloidosis is estimated at 10 cases per million population.⁹ In contrast, AA amyloidosis develops secondary to chronic inflammatory conditions, and its epidemiology has evolved with improvements in diagnosis and treatment.¹⁰ The prevalence of AA amyloidosis is therefore hard to determine because it varies depending on the diagnostic method, clinical stage (symptomatic or asymptomatic), and

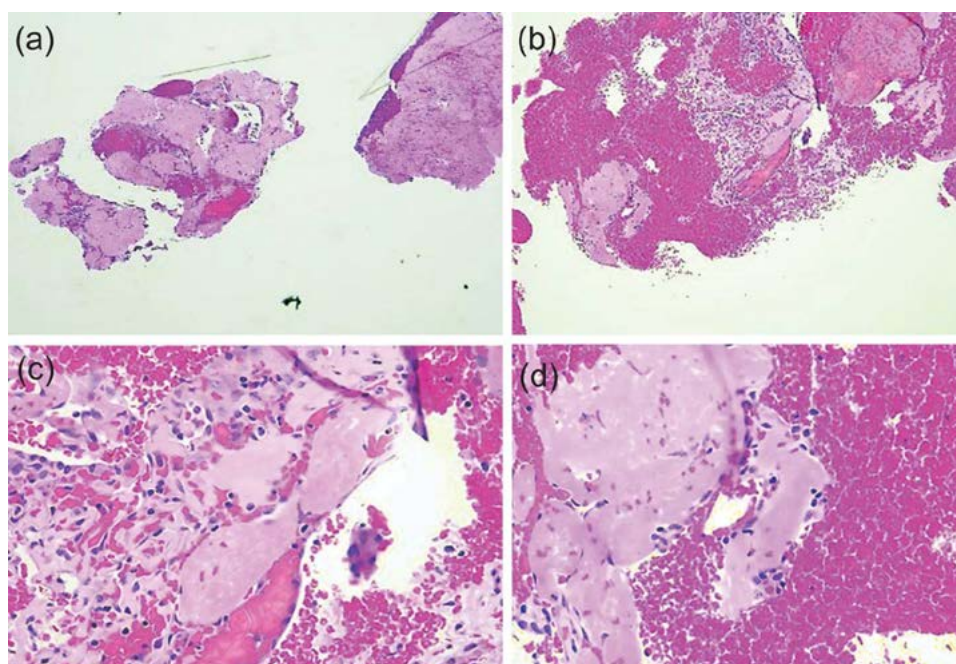


Figure 2: Histopathology of the thyroid nodule showing extensive extracellular eosinophilic amorphous material consistent with amyloid (haematoxylin and eosin [H&E] stain: A $\times 40$, B $\times 100$, C $\times 200$, D $\times 400$). Scattered benign vascular structures and hemosiderin-laden macrophages are present.

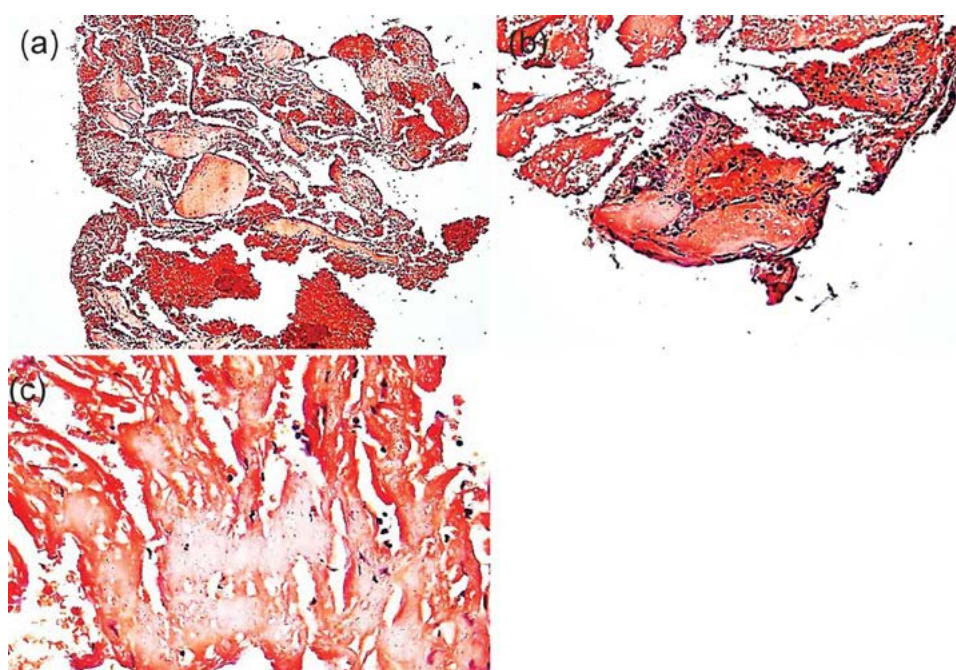


Figure 3: Congo red histochemical stain showing strong salmon-pink positivity within the extracellular eosinophilic material, confirming amyloid deposition (Congo red at (A) $\times 40$, (B) $\times 100$, and (C) $\times 400$ magnification).

study design.¹⁰ Hereditary TTR amyloidosis is an autosomal dominant condition with variable penetrance.⁶ This type of amyloidosis may manifest with cardiomyopathy, peripheral neuropathy, or mixed phenotypes.⁶ The prevalence of polyneuropathy and cardiomyopathy in patients with hereditary TTR amyloidosis is estimated at 10 000 and 50 000 worldwide, respectively.¹¹ These numbers are likely conservative given higher detection rates in autopsy studies.¹¹

The epidemiology of amyloidosis in African populations is poorly described owing to the lack of an established registry.

Earlier autopsy-based studies reported amyloid deposits in unspecified organs in 0.2–5.7% of patients in select African cohorts, often as incidental findings.¹² A single-centre study from Cape Town in 1984 estimated the prevalence of amyloidosis at 0.28% over a 5-year period based on autopsy findings.¹³ More recently, retrospective review of renal biopsies at a tertiary facility in South Africa found amyloidosis in 1.4% of biopsies over a 32-year period with AL amyloid accounting for 57% of cases and AA amyloid accounting for 43%.¹⁴ These findings highlight both the rarity of the disease and the likelihood of substantial underdiagnosis.

Table 2: Cases of amyloid goitre and concomitant hyperthyroidism

Goitre characteristics	T4 (pmol/l)	Presence of thyroid autoantibodies	Amyloid type	Scintigraphy	Reference
Diffuse	Not reported	Not assessed	AL	Not performed	¹⁷
Multinodular, size not stated	Not reported	Not assessed	AA	Not performed	²²
Nodular goitre, 2.5 cm isthmus nodule	90	Positive antithyroglobulin Ab	Not reported	Reduced uptake bilateral upper poles	²³
Diffuse	66.5	Negative thyroglobulin, thyroperoxidase, negative TSH receptor	AA	Not performed	²⁴
Nodular goitre, size not stated	61	Positive antimicrosomal antibodies, positive TRAb	AA	Not performed	²⁵
Multinodular intrathoracic goitre, size not mentioned	23	Negative thyroperoxidase and thyroid binding inhibitory immunoglobulins	AL	Increased heterogenous uptake	²⁶
Nodular goitre, 55 × 36 × 25 mm left lobe nodule	17	Negative antithyroglobulin, anti-thyroid peroxidase	AA	Hyperactive nodule compared with surrounding tissue	²⁷

The International Myeloma Working Group (IMWG) requires the presence of the following four criteria for the diagnosis of systemic AL amyloidosis.¹⁵ First, there must be clinical or biochemical evidence of amyloid-related organ involvement (e.g. renal, hepatic, cardiac, gastrointestinal tract, or peripheral nerve involvement). Second, Congo-red positive amyloid deposition must be demonstrated in tissue. Third, amyloid must be confirmed as light-chain derived using mass spectrometry-based proteomic analysis, or immunoelectron microscopy. Finally, a monoclonal plasma cell disorder must be identified through serum or urine monoclonal proteins, an abnormal free light-chain ratio, or the presence of clonal plasma cells in the bone marrow.¹⁵

Amyloid goitre refers to thyroid enlargement caused by substantial amyloid deposition within the gland.¹⁶ The term was introduced by von Eiselberg in 1904 following Beckmann's initial description in 1858.¹⁷ Microscopic amyloid deposits have been noted as incidental findings at autopsy or in thyroid glands that were resected for other reasons; however, a clinically detectable goitre due to amyloid is rare.¹⁸ Thyroid amyloid is more frequently associated with medullary thyroid carcinoma and less frequently with papillary thyroid carcinoma.¹⁶ The occurrence of amyloid goitre in the context of primary systemic amyloidosis is an even rarer entity, with existing literature largely comprising isolated case reports.¹⁹ An early case series looking at amyloid deposition within different organ tissue demonstrated that a clinical goitre with amyloid infiltration and a diagnosis of AL amyloidosis was present in only 4 out of 154 patients.²⁰

Amyloid goitre is typically diagnosed on histopathological assessment of resected thyroid tissue showing microscopic features characteristic of amyloid deposition.¹⁸ Fine needle aspiration (FNA) may be used as a diagnostic tool; however, its utility is limited by the heterogeneous distribution of amyloid within the thyroid gland, which may result in sampling uninvolved areas.²¹ Despite this limitation, FNA remains a safe, minimally invasive and reasonably sensitive diagnostic modality.⁸

The clinical presentations of systemic amyloidosis are often non-specific with fatigue and weight loss being the most frequently reported symptoms.⁴ Other symptoms arise from direct amyloid infiltration into specific organ systems.⁴ Where

amyloid goitres have been reported, most patients are euthyroid with some being hypothyroid.²² Hyperthyroidism in patients with an amyloid goitre is distinctly uncommon, with only a limited number of case reports documenting this phenomenon.^{17,22–27}

A summary of reported cases of thyrotoxic patients with an amyloid goitre is presented in Table 2. In the literature, only six cases describe hyperthyroidism in patients with an established amyloid goitre, including one case describing subclinical hyperthyroidism (TSH 0.20 mIU/L (0.3–5.5) FT4 17 pmol/L (11.5–22.7)).²⁷ No consistent relationship has been demonstrated between ultrasound characteristics of the goitre and the underlying amyloid subtype.^{17,22–27} Five cases described a nodular or multinodular goitre and one case described an intrathoracic multinodular goitre.^{22,23,25–27} Thyroid autoantibodies were present in two of the five cases.^{23,25} Although none of the cases described reported a TI-RADS classification, two cases had an underlying concern for thyroid malignancy based on rapid goitre growth with compressive symptoms and non-specific clinical findings; neither case reported malignancy.^{17,23}

Additional case reports describe an amyloid goitre with subacute thyroiditis-like symptoms (STLS) and another with concomitant Graves' disease.^{24,25} Scintigraphy was performed in three of the five nodular goitre cases with reduced uptake demonstrated in one case, increased heterogenous uptake with primary amyloidosis in another, and a hyperfunctioning nodule in a patient with negative thyroid autoantibodies and secondary amyloidosis.^{23,26,27}

At present, no consensus guidelines exist for the management of amyloid goitre.²⁸ Although total thyroidectomy has been described in several case reports, surgical intervention in these cases was typically done for coexisting indications such as compressive symptoms or for cosmetic improvement.^{28–30} As a result, the optimal management strategy remains individualised and guided by clinical presentation.

In our case the diagnosis of amyloidosis was made, but the subtype was not identified. The relationship between localised amyloid deposition and thyrotoxicosis remains unclear. The patient remains clinically and biochemically in a euthyroid

state on carbimazole and has been referred for further assessment.

Conclusion

Amyloid deposition may occur in virtually any organ system and may present either asymptotically or with significant clinical or biochemical dysfunction. Within the thyroid gland, amyloid may accumulate diffusely or within nodules. Although most reported cases are euthyroid, thyrotoxicosis associated with localised thyroid amyloidoma remains exceptionally rare.

This case highlights the diagnostic complexity that arises when thyroid imaging, functional status, and histopathology are discordant. It reinforces the importance of distinguishing localised thyroid amyloidoma from systemic amyloidosis, as the prognostic implications and management strategies differ substantially. Greater recognition and documentation of such presentations may help refine diagnostic pathways and improve clinical understanding of this uncommon entity.

Acknowledgments – The authors acknowledge Dr Van Der Merwe for the histology pictures.

Ethical considerations – The patient gave verbal and written consent for this case report. Ethics approval was granted by the Human Research Ethics Committee (Medical) from the University of the Witwatersrand and was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki.

Disclosure statement – No potential conflict of interest was reported by the authors.

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Received: 18-02-2026 Accepted: 26-03-2026

JEMDSA

Journal of Endocrinology, Metabolism and Diabetes of South Africa

JEMDSA 2026 Volume 31 Number 2

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1. Microalbuminuria is not a strong predictor of cardiovascular morbidity and mortality in people with diabetes.

- a. True
- b. False

2. What is the triad of thyrotoxic periodic paralysis?

- a. Low potassium, reversible paralysis, features of hyperthyroidism
- b. Low potassium, permanent paralysis, features of hyperthyroidism
- c. Low phosphate, reversible paralysis, features of hyperthyroidism
- d. Low magnesium, reversible paralysis, features of hyperthyroidism

3. What scoring system is used to risk stratify thyroid nodules?

- a. Bethesda
- b. NOSPECS
- c. Framingham
- d. TI-RADS

4. Patients with GCK-MODY need treatment with insulin because the hyperglycaemia is usually severe.

- a. True
- b. False

5. What is the prevalence of CKD in people living with HIV in Africa?

- a. 1–10%
- b. 20–29%
- c. 6–15%
- d. 30–39%

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References: 1. AndroGel[®] Package Insert; 2. Wang C et al. J Clin Endocrinol Metab 2000;85:2839-2853; 3. Wang C et al. J Clin Endocrinol Metab 2004;89:2085-2098; 4. Behre HM et al. Aging Male 2013;15:198-207

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FPG: fasting plasma glucose; PPG: post-prandial plasma glucose; HbA_{1c}: glycated haemoglobin.

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