Evaluation of Renal Artery Resistive Index and Morphological Parameters in Early Diabetic Nephropathy in the Zimbabwean Black/African population with Type 2 Diabetes Mellitus under "Good Glycaemic Control"

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Abstract

Diabetic nephropathy is a serious microvascular complication of diabetes mellitus and a leading cause of end-stage renal failure. Early detection is essential to enable timely intervention and slow disease progression. Conventional grey-scale ultrasound parameters such as renal length, cortical thickness, and echogenicity provide limited sensitivity in identifying early disease. Doppler ultrasound measurement of the intrarenal artery resistive index (RI) has been proposed as a complementary, non-invasive biomarker of renal perfusion. This study was conducted to investigate renal artery resistive index values together with renal morphological parameters and biochemical markers in patients with type 2 diabetes mellitus under good glycaemic control, with the aim of exploring their role in identifying early signs of diabetic nephropathy.

A prospective comparative study was conducted at Citimed Private Hospital, between October 2023 and April 2024. Fifty-one participants with type 2 diabetes mellitus under good glycaemic control were recruited using purposive sampling. Participants were divided into two groups based on biochemical evidence of nephropathy, defined as serum creatinine >131 µmol/L and/or urea >6.7 mmol/L according to hospital laboratory normal reference ranges. Group 1 included patients without biochemical nephropathy, while Group 2 included those with early biochemical nephropathy. Renal artery resistive index (RI) was measured using Doppler ultrasonography (Mindray DC-30 ultrasound machine, 3.5MHz curvilinear probe). RI was calculated as (peak systolic velocity – end diastolic velocity) / peak systolic velocity, averaged over three readings from intrarenal arteries in each kidney. All scans were performed by a trained ultra-sonographer under standardised conditions. Data were analysed using IBM SPSS Statistics 22™, with descriptive (means, standard deviations, frequencies, and percentages) and inferential statistics (independent t-tests, Pearson's correlation, ANOVA, and multiple regression) applied to examine group differences and identify predictors of RI.

Of the participants, 64.7% were female and the mean age was 45.9 ± 16.4 years. Group 2 (early nephropathy) patients were significantly older (53.9 ± 15.6 vs 41.6 ± 15.3 years, $p<0.05$), had longer diabetes duration (17.1 ± 8.3 vs 11.1 ± 7.2 years, $p<0.05$), and higher

mean RI (0.73 vs 0.61, p<0.05) compared to Group 1 (without nephropathy). RI correlated positively with age, disease duration, sodium, urea, and creatinine (p<0.05). Regression analysis showed these predictors explained 48.6% of the variance in RI (R^2=0.486, p<0.01). Age, duration of disease, urea levels, creatinine levels, and sodium levels were significant positive predictors of RI, while BMI and HbA1c showed no significant effect. Gray-scale parameters (renal length, cortical thickness) showed no significant differences between groups; however, increased parenchymal echogenicity was observed in 11.1% of patients in Group 2 (early nephropathy) to only 3% in Group 1 (without nephropathy).

This study found that elevated IRARI values (>0.70) were associated with biochemical evidence of early nephropathy in Zimbabwean patients with T2DM under good glycaemic control. While grey-scale ultrasound parameters showed limited utility, regression modelling highlighted age, disease duration, and renal biochemical markers as significant predictors of RI, underscoring its potential as a complementary biomarker for early detection. Larger, longitudinal studies with balanced gender representation and control groups are recommended to validate RI cut-offs and enhance diagnostic accuracy in diverse populations.

Keywords: Type 2 diabetes mellitus, intra-renal artery resistive index, diabetic nephropathy.

Introduction

The prevalence of type 2 diabetes mellitus (T2DM) is rapidly increasing and is considered a major contributor to mortality and disability (World Health Organisation, 2018). In Zimbabwe, diabetes mellitus is now one of the most common non-communicable diseases, affecting approximately 10 out of every 100 individuals over the past four decades (Zimbabwe Diabetes Association, 2013).

Diabetes mellitus (DM) is known as a group of metabolic conditions characterised by hyperglycaemia (World Health Organisation, 2018). There are two general types of diabetes mellitus. The first one is type 1 diabetes, also called non-insulin dependent diabetes mellitus (NIDDM), which is caused by lack of insulin secretion. The second one is known as type 2 diabetes mellitus, also called insulin dependent diabetes mellitus (IDDM), which is caused by decreased sensitivity of target tissue to metabolic effect of insulin (insulin resistance) (Guyton & Hall, 2006; Dabla, 2010). In both types of DM, metabolism of all food stuffs is altered while the basic effect of insulin lack or resistance on glucose metabolism is prevention of efficient uptake and utilisation of glucose by most body cells except for the brain (Guyton & Hall, 2006).

Blood glucose concentration increase due to uncontrolled and untreated diabetes leads to long-term damage, dysfunction and failure of organs, especially the retina (retinopathy), kidneys (diabetic nephropathy), nerves (neuropathy), heart (cardiomyopathy), arteries (atherosclerosis) and basement membranes of small vessels (micro-angiopathy) (Guyton & Hall, 2006; Caroll & Weerakkody, 2021; Pham et al., 2020; International Diabetes Federation, 2017).

Diabetic nephropathy is a serious microvascular complication which occurs in both diabetes mellitus type 1 (T1DM) and diabetes mellitus type 2 (T2DM) (Varghese & Jialal, 2022). It is characterised by persistent albuminuria and a progressive decline in renal function. In the early stages of diabetes, renal enlargement may be observed due to increased glomerular filtration caused by damage to the capillaries in the kidneys, resulting in an elevated glomerular filtration rate (Justinian et al., 2013; Omer et al., 2014). Conversely, in the later stages, the kidneys may decrease in size due to glomerulosclerosis, a condition characterised by the hardening of the glomeruli. Additionally, renal cortical hyper-echogenicity may indicate deteriorating renal function. As the disease progresses to end-stage, the kidneys may become smaller and more echogenic, with the medulla appearing as echogenic as the cortex. A renal ultrasound is typically performed to assess renal size and echogenicity (Fiorini & Barozzi, 2017; Omeret al., 2014).

Evaluating the segmental and interlobar renal vessels is an indirect method of interrogating the intra-renal vasculature (Hagen-Ansert, 2006). These are easily visualised with Duplex and colour Doppler imaging compared to the main renal artery, which demonstrates both normal and abnormal renal blood flow (Netter, 2007; Rumack & Levine, 2011). Renal Doppler ultrasound can measure the renal resistive index (RRI) which reflects alterations in blood flow profile of the intrarenal arcuate or interlobar arteries (Ponte et al., 2014). In an adult, normal values are reported between 0.47 and 0.70 with the difference between both kidneys being 5 to 8% (Darmon et al., 2010; Mehrnahad et al., 2019).

Several published studies have established that intra-renal arterial RI measured by Doppler ultrasound is a well-established technique for the investigation of renal morphology and renal hemodynamics, thus predicting the course of renal function in several causes and stages of nephropathy (Radwa & Ibrahim, 2019; Afsar & Elsurer, 2017; Masuli et al., 2009; Ozmen et al., 2015; Shirin et al., 2015). A study by Radwa and Ibrahim (2019) recommended that Doppler sonography could be a useful complementary test in the evaluation of diabetes nephropathy, even in the early stages. Renal Doppler assessment of RI is a reliable, non-

invasive evaluation of arterial function and is particularly useful for early diagnosis of vascular involvement (Radwa & Ibrahim, 2019).

Nowadays Doppler ultrasound is rapidly gaining ground as a screening tool in critically ill patients. Ultrasound is readily available, safe, non-invasive tool and lacks the risk of ionising radiation (Azevedo & Silveiro, 2005). Recent research has shown that clinical actions at the first stage, before proteinuria, can prevent nephropathy (Boddi, 2017). Colour Doppler ultrasonography has provided a hemodynamic evaluation of renal flow in a totally non-invasive manner (Patschan & Muller, 2016). Utility of renal artery Doppler will offer a relevant contribution to the prediction of early onset of renal damage in patients with type 2 diabetes mellitus (Tublin et al., 2003), and establishment of an ultrasound protocol for them specifically; rather than basing only on ultrasound appearances of renal size, parenchymal echogenicity and corticomedullary differentiation.

Methodology

Design

The study was designed as a prospective comparative study. Participants were scanned during the study period to allow real-time assessment of renal artery resistive index (RI) values and morphological parameters. Outcomes were compared between participants with normal RI values and those with abnormal RI values to establish differences in renal function parameters.

Research setting

The research study was conducted at Citimed Chitungwiza Private Hospital due to its convenient access to a resident urologist, a diabetic clinic, and an ultrasound department. These facilities and services played a crucial role in the recruitment process and data collection procedures for the study.

Study population, sampling population and technique

From the preliminary investigation conducted to determine the number of type 2 diabetic patients visiting at the clinic, approximately 100 participants formed the target population. Purposive sampling was employed to select patients with type 2 diabetes mellitus under good glycaemic control who presented at Citimed Hospital during recruitment within the limited timeframe. Based on a 95% confidence level and 5% margin of error, the minimum required sample size was calculated as 80 participants. However, during the study, 51 participants met the eligibility criteria and consented to participate. Although lower than the calculated

minimum, this sample size was considered sufficient given the finite population and strict inclusion criteria.

Participants recruitment

The study took place from October 2023 to April 2024, during which time the participants were recruited and their data was collected. Participants with well controlled DM 2, with age more than 10years, diabetes duration of more than 5years were selected into the study. Diabetic patients who were pregnant, with a known history of renal diseases, cardiovascular diseases, uncontrolled systemic hypertension, smokers and drug users were excluded from the study. These participants were excluded from the study because, according to Kmetec at al. (2002), this can lead to bias of the results since the renal RI in these pathologies affect the renal blood supply and could compromise the renal RI measurements.

Data collecting procedure

Written informed consent form was obtained from the participants. Once the patient consented to participating in the study, demographic and medical history taking was done before the patients were scanned. Two data collection sheets were used. The first one was the research questionnaire for patient's demographic data collection (age, gender, BMI) and clinical history. Normal blood pressure was categorised as below 129/80. The other one was the data collection form to record the findings from the ultrasound scan (grey scale appearance and renal artery restive indices from both kidneys).

After acquiring demographic information and medical history, an experienced sonographer from the ultrasound department scanned all the patients to avoid jeopardising the credibility of findings due to inexperience. The sonographer was however blinded from the renal functionality of each patient or any other clinical information to avoid bias. The same ultrasound machine was used on all the patients to prevent any bias.

Laboratory values

Serum creatinine, urea and electrolytes (sodium, potassium and chloride) values of the participants were obtained from the participant's laboratory data base. They were conducted on Mindray BS-220 Biochemistry Analyzer. Glycated Heamoglobin (HbA1c) was done using epithod 616 test kit. Normal reference ranges and cut-off values were obtained from the Citimed Hospital Laboratory Department database.

Table 1 Reference values adapted from Citimed Hospital Laboratory Department database

Parameter	Normal Reference range
Sodium – Na	133-146mmol/L
Potassium – K	3.5-5.2mmol/L
Chloride – Cl	96-109mmol/L
Urea	2-6.7mmol/L
Creatinine	48-131umol/L
HbA1c	4-6%

Ultrasound scanning protocol

Participants were scanned using the same technique and protocol. Duplex sonography was performed using a Mindray DC30 ultrasound machine together with a 3,5MHz curvilinear probe. The participants were examined in a supine position using a transabdominal technique. During the scan, renal length was measured as the maximum bipolar dimension in longitudinal plane. Renal length more than 13cm was considered enlarged. Cortical thickness was taken over a medullary pyramid, perpendicular to the capsule as the shortest distance from the base of the medullary pyramid to the renal capsule. Normal cortical thickness was considered equals or more than 6mm. At least three measurements were taken to determine renal bipolar lengths and cortical thickness. The average values were then calculated to obtain mean measurements. Parenchymal echogenicity was described as normal, increased or decreased.

Renal artery Doppler

The indirect method was employed. Colour Doppler ultrasound was used to demonstrate the intra-renal blood vessels and, in this study, segmental and interlobar arteries were assessed. Spectral Doppler was used to demonstrate the arterial spectral waveform which was insonated using a 3-mm Doppler gate. Patient was asked to suspend respiration or perform quiet breathing for a few seconds to capture the intra-renal artery Doppler waveform pattern. Three Doppler measurements of the intra-renal arteries of the kidney(s) were taken at three different points in the kidney(s) to reduce the margin of error and were averaged to get the mean renal RI values. The RI value was determined by pre-set formula incorporated in the machine. To ensure accuracy and generalisability, all patients were scanned by the same technique and protocol using the same type of transducer. An IRARI value higher than 0.70 was considered abnormal.

Figure 1 and 2 shows the indirect method of examining the intra-renal arteries to indirectly infer the status of the main extra-renal artery(s).

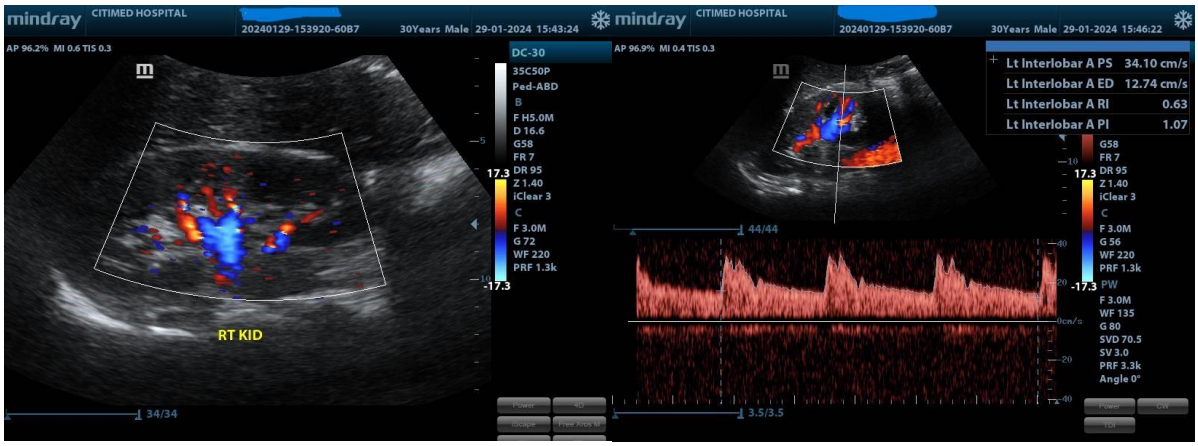

Figure 1a Figure 1b

(Images adapted from ultrasound scans performed on study participants using the Mindray DC-30 system).

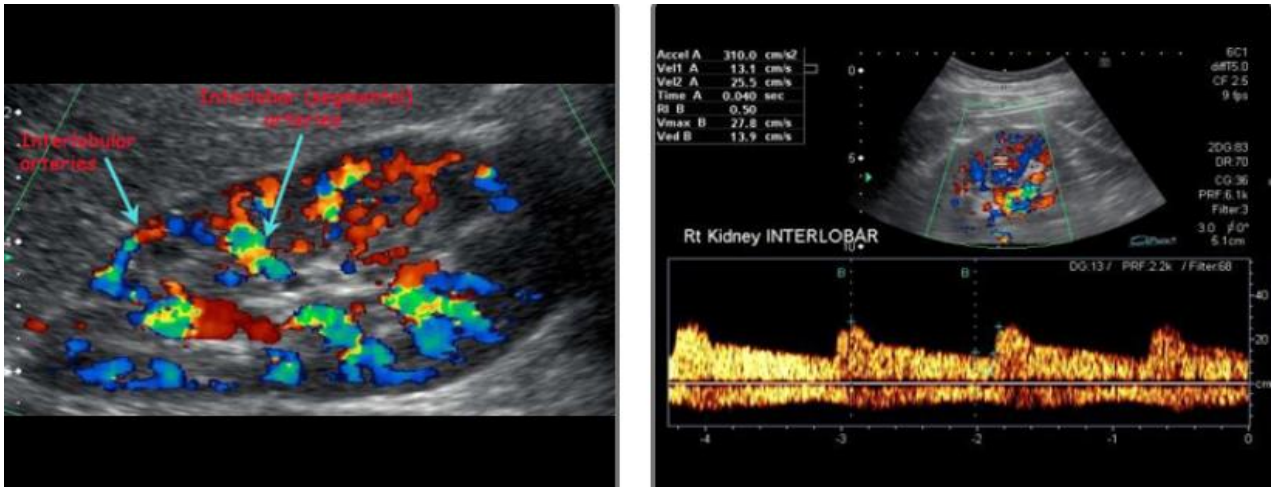

Figure 2a Figure 2b

(Ultrasoundpedia, n.d.)

Statistical analysis

During data curation, all variables were assessed for consistencies and missingness of responses. However, if found missing, the researcher assumed data was missing at random and performed complete case analysis. Data was analysed using IBM SPSS Statistics 22™. Descriptive and inferential statistical analysis were carried out. In descriptive statistics, data were expressed as mean and standard deviation (SD) for continuous variables, and as frequency and percentages for categorical variables. In inferential statistics, independent t-test was the statistical test of significance for the two groups. Shapiro-Wilk's test and a visual inspection of their histograms showed that the exam scores for all the variables were normally distributed as indicated by significance levels greater than 0.05. Pearson's correlation analysis was used to determine the relationship of the dependent variables with the independent variable of the

study. Multiple regression analysis was used to ascertain which dependent variable is the best determiner of early onset of diabetic nephropathy. Level of significance was set at 0.05 and $p<0.05$ was considered as significant (Shirin et al., 2015).

Results

Participants' basic characteristics

Table 1 presents the distribution of the respondents' basic characteristics collected from the data collecting tools. Among diabetic patients, 33 (64.7%) were females, and 18 (35.3%) were males.

Table 2: Basic characteristics of study participants (n=51)

Characteristic	Value
Gender: Female	33 (64.7%)
Male	18 (35.3%)
Age (years)	45.9±16.4
Body Mass Index (kg/m^2)	24.5±3.6
Duration of diabetes (years)	13.2±8.1
Medication being taken: Injection	8 (15.7%)
Oral	43 (84.3%)
Mean cortical thickness (cm)	1.05 ± 0.21
Mean renal length (cm)	9.59 ± 0.90
Parenchymal echogenicity: Right	Normal (n=48; 94.1%); Increased (n=3; 5.9%)
Left	Normal (n=48; 94.1%); Increased (n=3; 5.9%)
Mean Resistive Index	0.65 ± 0.07
Sodium levels (mmol/L)	141.0 ± 6.28
Potassium levels (mmol/L)	4.34 ± 0.66
Chloride levels (mmol/L)	100.3 ± 14.7
Urea levels (mmol/L)	6.35 ± 3.67
Creatinine levels (µmol/L)	100.9 ± 33.1
HbA1c (%)	5.08 ± 0.299

Note: Values in Table 1 are given in number, percentage, mean ± SD.

Presence of early signs of nephropathy vs without

Participants were divided into two groups (Table 3) based on biochemical evidence of early nephropathy, defined as serum creatinine >131 µmol/L and/or urea >6.7 mmol/L, according to the hospital laboratory reference ranges.

- Group 1 (No nephropathy): 20 females (60.6%) and 13 males (39.4%) with type 2 diabetes showing no biochemical evidence of nephropathy. These patients provided baseline data on intrarenal artery resistive index (IRARI) in diabetic individuals without kidney complications.
- Group 2 (early nephropathy): 13 females (72.2%) and 5 males (27.8%) with type 2 diabetes showing biochemical evidence of early nephropathy. These participants were analysed to examine the association between IRARI values and early nephropathy.

Table 3: Gender of respondent * GROUP

		GROUPS		Total
		Without signs of Nephropathy (1)	With early signs of Nephropathy (2)	
Gender of Respondent	Female	20 (60.6%)	13 (72.2%)	33
	Male	13 (39.4%)	5(27.8%)	18
Total		33 (100%)	18(100%)	51

Descriptive statistics on parenchymal echogenicity

In Table 4, 97% of all participants in group 1 (without nephropathy) had normal parenchymal echogenicity in both kidneys whereas only 1 participant constituting 3.0% had hyper-echogenicity changes in the renal parenchyma of both kidneys. In group 2, out of 18 diabetic patients, 16 (88.9%) of them had normal parenchymal echogenicity and 2 (11.1%) showed increased parenchymal echogenicity.

Table 4: Distribution of parenchymal echogenicity between groups

SUBGROUP	Renal side	Parenchymal echogenicity		Total
		Normal	Increased	
Without Nephropathy (n=33)	Right	n = 32 (97%)	n = 1 (3%)	100
	Left	n = 32 (97%)	n = 1 (3%)	100
With signs of early onset Nephropathy (n=18)	Right	n = 16 (88.9%)	n = 2 (11.1%)	100
	Left	n = 16 (88.9%)	n = 2 (11.1%)	100

Comparison of means between two groups

There was a statistically significant increase in age, duration of diabetes, sodium levels, urea levels, creatinine levels and mean RI in group 2 patients when compared with group 1; $p < 0.05$ (Table 4). No statistically significant difference was seen in the BMI, HbA1c, potassium levels,

chloride levels mean cortical thickness and mean renal length between the two groups; $p > 0.05$. The difference was observed having a small margin in both groups.

Table 5: Comparison between groups

	Group 1 (Without signs) n=33	Group 2 (With signs) n=18	*P*
Age (years)	41.6 ±15.3	53.9±15.6	.008*
BMI in kg/m2	24.7 ±4.15	24.2±2.24	.665
Duration of Diabetes (years)	11.1±7.23	17.1±8.3	.009*
Sodium Levels (mmol/L)	139.18±4.25	144.6±8.06	.015
Urea Levels (mmol/L)	5.05±2.02	8.93±5.44	.002*
Creatinine Levels (umol/L)	91.9±30.2	119.0±33.3	.005*
HbA1c level (%)	5.07±0.25	5.10±0.38	.707
Potassium Levels (mmol/L)	4.29±0.57	4.40±0.86	.632
Chloride Levels (mmol/L)	98.0±17.2	105.8±7.39	.096
Mean Cortical Thickness (cm)	1.05±0.20	1.05±0.22	.895
Mean Renal Length (cm)	9.50±0.833	9.76±1.00	.327
Resistive Index	0.609±0.458	0.729±0.38	.000*

P<0.05* significant, *P*>0.05 non-significant.

HbA1c: Glycated haemoglobin **BMI**: Body Mass Index.

Renal Doppler descriptive statistics

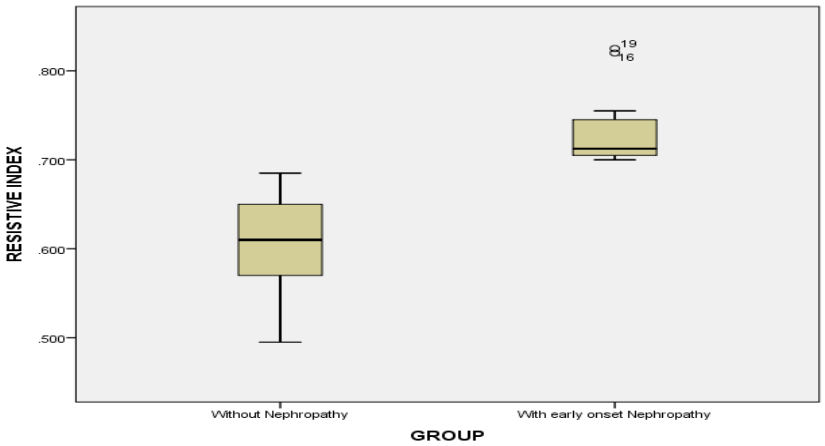

Figure 3: Distribution of intrarenal artery resistive index between two groups

The box plots in Figure 3 above shows that the intra-renal artery RI in the group without signs ranges from 0.59 to 0.63, with mean RI of 0.609. In the other group with participants showing signs, the intra-renal artery RI ranged from 0.71 to 0.75, with mean RI of 0.73.

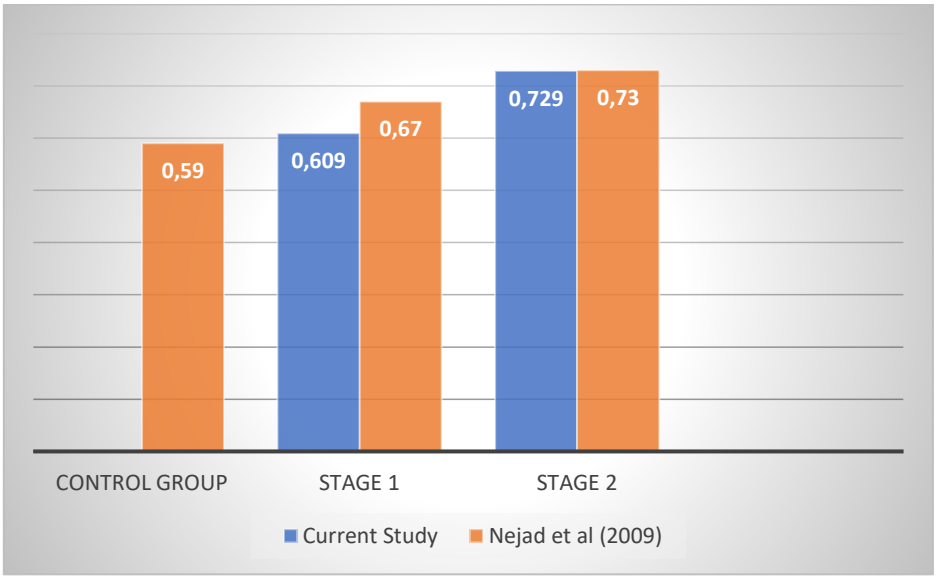

Figure 4: Comparison of the current study and a previous study by Nejad et al., (2009).

According to Nejad et al. (2009), an RI value higher than 0.7 was considered abnormal. Stage 1 comprised of diabetic patients with intrarenal artery RI <0.7 and normal laboratory parameters (urine content and serum creatinine). Stage 2 comprised diabetic patients with intrarenal artery RI >0.7 and abnormal urine content and serum creatinine. There was no significant difference between the mean intrarenal RI of the current study and that obtained in the study by Nejad et al. (2009), but significant difference in the standard deviation in stage 1.

Pearson's correlation between different parameters and mean intra-renal artery RI

Based on Table 6, age, duration of disease, sodium, urea and serum creatinine levels showed a moderate and positive relationship with intra-renal artery RI which is statistically significant ($p < 0.05$

A weak and positive association was observed between mean renal length, mean cortical thickness, potassium levels and mean intrarenal artery RI value. These associations were not statistically significant ($p > 0.05$). There is a negative and very weak relationship between BMI and glycated Hb whilst chloride levels showed a positive but very weak relationship with intrarenal artery RI value. The relations were not statistically significant ($p > 0.05$).

Table 7: Pearson's correlation

	R	*P*
Age in years	0.374	0.007*
Duration of disease in years	0.391	0.005*
BMI (kg/m^2)	-0.087	0.542•
Mean renal length (cm)	0.101	0.479•
Mean cortical thickness (cm)	0.198	0.165•
Sodium levels(mmol/L)	0.368	0.008*
Potassium levels (mmol/L)	0.136	0.340•
Chloride levels(mmol/L)	0.088	0.539•
Urea levels (mmol/L)	0.439	0.001*
Serum Creatinine levels (umol/L)	0.387	0.001*
HBA1c (%)	-0.001	0.992•

*P<0.05 significant, •P>0.05 non-significant **HBA1c:** Glycosylated Haemoglobin

Multiple regression analysis

The multiple regression analysis was carried out to estimate the influence of demographic characteristics. Results are presented in Tables 8-10.

Table 8 presents a summary of the model. **R** represents the multiple correlation coefficient, which in this case R is 0.697, suggesting a moderately strong positive relationship. **R Square** is 0.486, meaning that the model explains 48.6% of the variation in MEAN RI. Adjusted R square adjusts for the number of predictors in the model. In this case, the adjusted R square is 0.358, which is lower than R square, implying that some predictors might not be adding much explanatory power. The standard error of the estimate is the standard deviation of the residuals (the differences between predicted and actual values). A smaller standard error indicates better model fit. Here, the standard error is 0.057868.

Table 8: Model summary

Model	R	R Square	Adjusted R Square	Std. Error of Estimate
1	**.697[a]**	**.486**	**.358**	**.057868**

a. Predictors: (Constant), HBA1C, Mean RL, Mean CT, K^+, Na^+, BMI, diabetes duration, creatinine, urea, age
b. Dependent variable: MEAN RI

ANOVA results

Table 9 presents the analysis of variance (ANOVA) results. It is also known as model fit results. Of interest in this table are the F-statistics and its associated significance value. The results show that the F-statistics is 3.175% ($p < 0.01$), which is highly significant, rejecting the null hypothesis and suggesting that the model is a good fit. The model is statistically significant,

meaning it can explain a significant amount of variance in MEAN RI. The model explains 48.6% of the variability in MEAN RI.

Table 9: ANOVA[a]

Model		Sum of Squares	Df	Mean Square	F	Sig.
1	Regression	.123	11	.011	3.175	.004[b]
	Residual	.138	39	.004		
	Total	.261	50			

a. Dependent Variable: Resistive Index

b. Predictors: (Constant), MEAN Cortical Thickness, Chloride Levels in mmol/L, HBA1C level in %, Sodium Levels in mmol/L, Potassium Levels in mmol/L, MEAN Renal Length, Duration of Diabetes (years), Creatinine Levels in umol/L, BMI in kg/m2, Urea Levels in mmol/L, Age (years)

Regression model results

Table 10 presents the estimated coefficients for each predictor variable in the regression model. MEAN RI is the dependent variable. This is the outcome variable, the primary focus of the analysis. The study sought to understand how the other variables impact MEAN RI. Holding other factors constant, the coefficients results show that age, duration of disease, urea, creatinine and sodium levels positively predict an increase in intrarenal artery resistive index ($p < 0.05$). BMI and HBA1c are negative predictors of an increase in intrarenal artery resistive index ($p > 0.05$) indicating they do not have a statistically significant effect.

Table 10: Regression model coefficients

Coefficients[a]

Model		Unstandardised Coefficients		Standardised Coefficients	T	Sig.	Collinearity Statistics	
		B	Std. Error	Beta			Tolerance	VIF
1	(Constant)	.331	.288		1.152	.256		
	Age (years)	.001	.001	.276	1.550	.011*	.404	2.477
	BMI (kg/m^2)	-.005	.003	-.248	-1.897	.065	.749	1.335
	Duration of Diabetes (years)	.040	.002	.257	.039	.043*	.430	2.325
	Sodium Levels (mmol/L)	.003	.001	.282	2.341	.024*	.885	1.130
	Urea Levels (mmol/L)	.010	.003	.486	3.098	.004*	.522	1.916
	Creatinine Levels (µmol/L)	.060	.020	.318	-.758	.003*	.526	1.900
	HBA1C level (%)	-.050	.030	-.206	-1.662	.104	.835	1.197
	Potassium Levels (mmol/L)	.019	.013	.169	1.406	.167	.891	1.122
	Chloride Levels (mmol/L)	.000	.000	.047	.340	.736	.709	1.411
	MEAN Renal Length (cm)	.000	.010	.005	.044	.965	.827	1.210
	MEAN Cortical Thickness (cm)	.059	.044	.168	1.324	.193	.802	1.247

a. Dependent Variable: RESISTIVE INDEX

*P<0.05 significant

Collinearity statistics

Multicollinearity statistics show tolerance figures ranging from 0.404 to 0.891 while variance inflation factors (VIFs) ranged from 1.210 to 2.477. These figures suggest that multicollinearity is not suspected amongst the independent variables. Field (2005) suggests that multicollinearity would be suspected if tolerance figures are below 0.10 or reciprocally if VIF statistics are 10.0 or higher.

Discussion

Demographic data of participants

Gender

The present study revealed that females comprised a significant proportion of the participants, making up 64.7% of the sample, with a female-to-male ratio of 1.8:1. This finding is consistent with a similar study by Ishimura et al. (2011), which also reported a majority of female participants (75%).

Age

The analysis revealed that the majority of patients were in their 40s (mean age of 45.9 ± 16.4 years). However, a notable difference was observed in the age distribution between patients with (53.9 ± 15.6 years) and without signs of nephropathy (41.6 ± 15.3 years) having a significant statistical difference between the two groups. Age was found to be a positive predictor of diabetic nephropathy, with a significant increase in intrarenal artery resistive index value by 27.6% as age progressed. In contrast, Nejad et al.'s (2009) reported a mean age of 55.9 ± 12.8 years for patients with diabetes in their study. In another related study, Wang et al. (2018) found that age ≥50 years was correlated with early development of diabetic nephropathy, which is consistent with our findings. However, the results of our study and these two studies suggest that, as age increases, the risk of developing diabetic nephropathy also increases.

Disease duration

In current study, there was a statistically significant increase in duration of diabetes in group 2 patients (RI ≥ 0.7; 17.1 ± 8.3years) when compared with group 1(RI ≤ 0.7; 11.1 ± 7.23years); $p< 0.05$. From the correlation analysis, duration of disease showed a moderate and positive relationship with intrarenal artery RI which was statistically significant ($p <0.05$). Additionally, from regression analysis, duration of disease positively predicted an increase in intrarenal artery resistive index ($p<0.05$). Genov et al. (2018), Nejad et al. (2009), and Shaw et al. (2025) found no significant differences among groups at various stages of nephropathy regarding the duration of diabetes. This study differ from these 3 studies as the margin between stage 1 and stage 2 was large with a significant difference possibly because genetic predispositions,

environmental factors, disease management, methodological differences, disease management, epidemiological factors and socioeconomic factors. The clinical significance of duration of diabetes in type 2 diabetes mellitus (T2DM) patients is substantial, as it can help identify patients at high risk of developing diabetic nephropathy and kidney disease.

Body mass index (BMI)

In a study conducted by Genov et al. (2018) in Bulgaria, patients with renal artery resistive index values ≤ 0.7 and those with values ≥ 0.7 did not differ significantly in their BMI. Mean BMI in group 1 (RI ≤ 0.7) was 29.9 ± 6.4 kg/m^2 and 30.34 ± 3.7 kg/m^2 in group 2 (RI ≥ 0.7) indicating that the participants were overweight. In contrast, our study found that the mean BMI in group 1 (24.7 ± 4.15 kg/m2) and group 2 (24.2 ± 2.24 kg/m2) did not differ significantly, but the participants had normal weight. This difference may be attributed to variations in body composition, nutritional status, lifestyle, ethnicity, and genetic factors.

Medication being taken

In our study, the majority of participants (84.3%) were taking oral medications, with metformin being the most common medication. In contrast, 15.7% of participants were using insulin analogues. This is in line with a national study conducted by the American Diabetes Association (ADA) in 2018, which found that 65.4% of adults with type 2 diabetes in the United States were taking metformin, while the remaining participants were on injectable medications.

Ultrasound findings

Gray scale parameters

Sonographic features of chronic renal disease typically include small renal size, increased parenchymal echogenicity, and reduced cortical thickness nevertheless, non-specific**.** In current study, the mean renal length and cortical thickness in the study population were 9.59cm ± 0.90cm and 1.05cm ± 1.21cm, respectively. Other previous studies (Lee et al., 2020; Zhang et al., 2020) reported a similar mean renal length with the current study, but a significantly lower mean cortical thickness. The difference in findings may be attributed to difference in population being studied. No statistically significant difference was seen in the mean cortical thickness and mean renal length between the two groups; $p > 0.05$. In addition, a weak and positive association was observed between mean renal length and mean cortical thickness with mean intrarenal artery RI value. However, in regression analysis, both variables had no statistically significant effect on MEAN RI. Both kidneys had normal parenchymal echogenicity in 48 participants (94.1%) and increased echogenicity in 3 participants (5.9%).

From these grey scale appearances found in current study, it shows that these parameters may not be useful for distinguishing between early stages of diabetic nephropathy.

Previous studies such as Shaw et al. (2015), Nejad et al. (2009), Shah et al. (2015), Mishra et al. (2018), Jain et al. (2019), Singh et al. (2017) and Kumar et al. (2016) have consistently shown that early stages of diabetic kidney disease are characterised by normal or minimal changes in renal morphology and function. Findings in current study support this idea, suggesting the need for more sensitive biomarkers to detect early changes in diabetic kidney disease. This is consistent with these previous studies that have also highlighted the need for more sensitive biomarkers to detect early stages of diabetic kidney disease such as renal artery resistive index and biochemical parameters.

Intrarenal artery Doppler

In our study, the mean resistive index ± SD in the study population was 0.65 ± 0.07years. Notably, mean RI was significantly higher in diabetic patients suspected of developing nephropathy (0.609 ± 0.458 vs 0.729 ± 0.38). Moreover, the mean RI correlated well with level of sodium, potassium, urea and serum creatinine in urine. This is in accordance with the findings of Nejad et al. (2009), Shaw et al. (2015), Wang et al. (2017), Zhang et al. (2019), Genov et al. (2018), Choi et al. (2015), and Elshweey et al. (2021). However, our results differ from those of Ferehiwot et al. (2021) who found no significant relationship between mean RI and 24hour urine protein. Additionally, Shankar et al. (2019) reported no significant correlations between mean RI and of fasting blood sugar, total cholesterol and triglycerides, although a positive correlation existed with blood, urea nitrogen and serum creatinine. Furthermore, Youssef and Fawzy (2012) found no significant differences in serum creatinine or albumin excretion rate between diabetic patients and the control group.

In light of the above findings, the following are clinical implications drawn from the results:

i) In pre-clinical stage (asymptomatic stage), the mean RI value of 0.609 ± 0.458SD was in the normal range (<0.7) and suggests inability of intrarenal RI to detect changes without laboratory parameters.

ii) The RI values greater than 0.7 were pathological in our current study. Therefore, renal Doppler played a significant role implying that it can be a useful biomarker for detecting early changes in diabetic kidney disease.

iii) Intrarenal or renal RI (RARI) can also be used as complimentary to various biochemical parameters in detecting early stage (preclinical) diabetic nephropathy. This could potentially lead to earlier intervention and treatment, which could slow down the progression of kidney disease.

iv) The correlation between RARI and biochemical markers of kidney disease also suggests that RARI may be a surrogate marker for monitoring disease progression over time. Changes in RARI could reflect changes in kidney function, allowing clinicians to adjust treatment strategies accordingly (Zhang et al., 2015).

v) RARI may be a useful biomarker for identifying high-risk patients who are more likely to develop diabetic nephropathy. This could potentially lead to targeted intervention and prevention strategies.

vi) Combination of RARI and biochemical markers may improve diagnostic accuracy leading to more accurate diagnoses and better treatment outcomes.

vii) RARI could be used as a biomarker to evaluate the effectiveness of treatment strategies aimed at preventing or slowing down diabetic nephropathy. Changes in RARI could reflect changes in kidney function, allowing clinicians to assess the effectiveness of treatment (Lee et al., 2020).

Strengths of the study

The study focuses on a specific population (T2DM under good glycaemic control), which allows for a more precise and relevant analysis of the research question. The study could also have isolated the specific effects of diabetic nephropathy on RI values without confounding factors related to hyperglycaemia.

The use of resistive index values provides an objective measure of renal perfusion, which can help reduce the variability associated with subjective clinical evaluations.

The study adopted a prospective comparative design, which allowed comparing participants' characteristics to identify differences. Prospective designs tend to have higher internal validity due to ability to control confounding variables.

All participants recruited provided complete information. There was no missing data contributing to higher internal validity.

The intra-renal artery resistive index values obtained in the study were comparable to the values reported in previously published studies. This suggests the study design is robust and findings can be generalised to other populations.

Limitations

i) The sample size was relatively small as participants with incomplete or missing data were not included as well as those who did not meet the inclusion criteria.

ii) The predominance of female vs male might be due to confounding effect of gender.

iii) The absence of a true control group without nephropathy limits the ability to establish RI >0.7 as a definitive diagnostic threshold.

Validity and reliability

Validity refers to the degree to which the measurement is a true reflection of the concept or trait being measured (Hartling et al., 2012). Face validity test was done to ensure the measurements appear to be measuring what is intended to measure; for instance, ensuring that renal length, cortical thickness and measurement of intra-renal artery resistive index (IRARI) are accurate and reliable by using a standardised protocol, by ensuring the measurement of IRARI is not influenced by extraneous factors such as observer bias.

Reliability refers to the degree to which repeated measurements yield similar results (Hartling et al., 2012). In this study, test-retest reliability was assessed by using multiple measurements of IRARI. Intra-observer reliability was also assessed by using multiple measurements taken by the same observer. All the Doppler examinations were performed by the same examiner to avoid inter-observer variability.

Conclusions and recommendations

The study findings are summarised according to the objectives of the study as follows:

i) The study established that grey-scale ultrasound findings in patients with type 2 diabetes mellitus under good glycaemic control present with varying patterns. However, no statistically significant differences were observed in renal length and cortical thickness between groups with different resistive index values. Renal echogenicity was noted to be increased only in advanced nephropathy. This suggests that while grey-scale ultrasound may provide some insights, its utility in differentiating

between early-stage diabetic nephropathy and normal renal appearances might be limited in this population.

ii) The study effectively determined the renal artery resistive index in participants, revealing a mean RI that indicates early changes consistent with diabetic nephropathy. A significant finding was that individuals in group 2 (mean RI >0.7) exhibited notable differences in age, duration of diabetes, sodium levels, urea levels, and creatinine levels compared to group 1 (mean RI<0.7). This suggests that elevated RI values may correlate with the presence of renal impairment, underlining the diagnostic utility of RI in early detection.

iii) The analysis of the relationship between RI and grey-scale renal appearances indicated weak positive associations, which were not statistically significant. However, the positive correlations between RI and factors such as age, duration of diabetes, and biochemical markers (sodium, urea, and creatinine) emphasize the importance of these clinical parameters in monitoring renal health in this population.

In conclusion, this research contributed to a better understanding of early-stage diabetic nephropathy in type 2 diabetes mellitus patients by highlighting the diagnostic significance of the renal artery resistive index and its relationship to specific biochemical parameters. The findings underscore the importance of routine RI measurements and laboratory evaluations in patients with diabetes to facilitate early identification of renal complications, thereby promoting timely interventions to prevent progression to end-stage renal failure.

Areas for further research

Future research may benefit from larger sample sizes and long-term follow-up to confirm the predictive value of RI and its correlation with clinical outcomes in diverse populations.

The researcher recommends implementing renal artery Doppler ultrasound into routine abdominal practices in Zimbabwe, particularly for patients with underlying conditions such as diabetes mellitus and hypertension, as it may provide early detection and management of renal disease.

Importantly, future studies should include a true control group of patients without nephropathy to allow clearer comparison of RI values and to establish more reliable diagnostic thresholds.

A control for gender is also needed to account for differences between men and women by recruiting equal number of both sexes.

Finally, combining RI with other biomarkers, such as urinary biomarkers or circulating biomarkers, may provide a more comprehensive picture of diabetic kidney disease and improve diagnostic accuracy.

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