

## RESULTS

The study was carried out from October 2016 to May 2017. During our study, we assessed 41 individuals for eligibility. Twenty-eight were excluded from our study: twenty did not meet inclusion criteria and eight declined to participate in our study. Thirty subjects were allocated to intervention for a period of eight weeks and were followed up for an additional eight weeks after withdrawal of treatment. Two out of the thirteen subjects were lost during follow up. 11 subjects' data were analyzed and none was excluded from analysis.

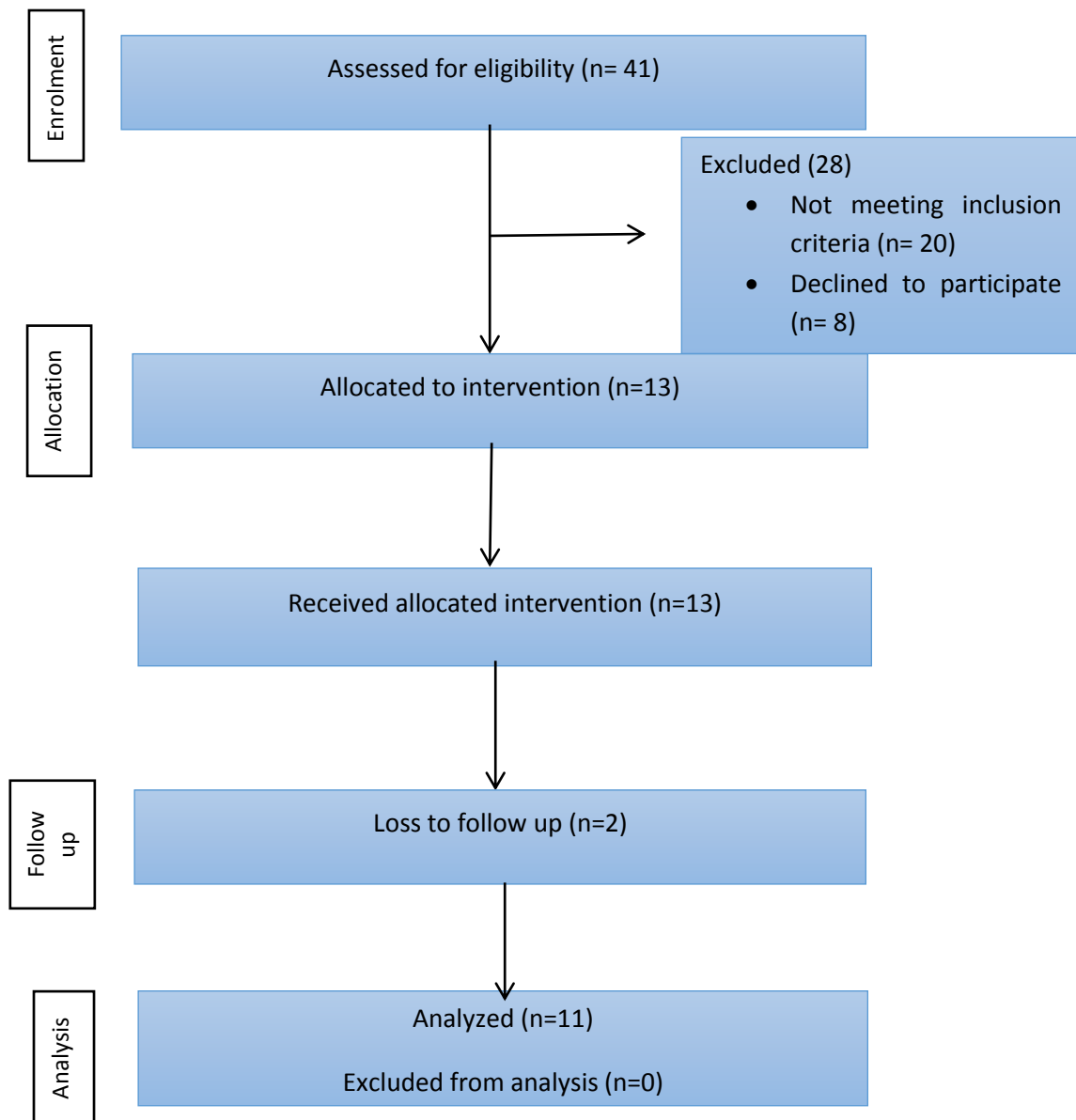


Figure 1: CONSORT flow diagram of the progress through the study

### 1.1. Sociodemographic characteristics of the population at baseline

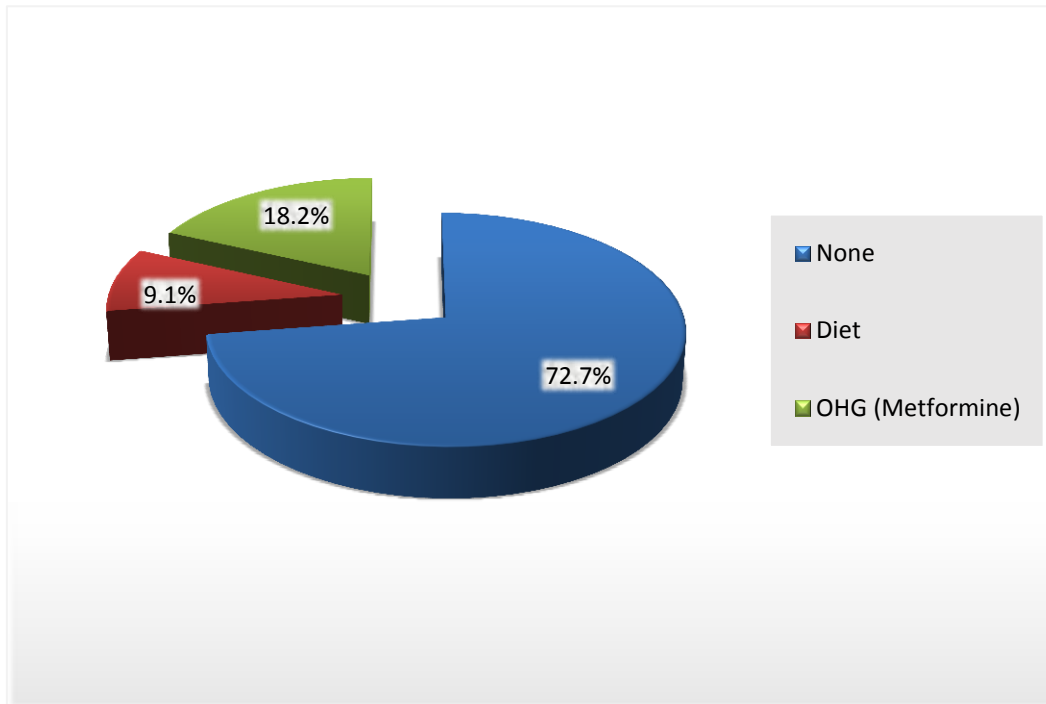
Of the eleven (11) volunteers retained to participate in this study, males constituted the majority of the study population comprising 8 subjects. The median age of the population was 53[38 -58] years. The *table I* below shows the socio-demographic characteristics of the study population.

**Table I:** Demographics of study population

<b>Variables</b>	<b>n(%)</b>
<b>Marital status</b>	
Married	9(81.8)
Widow	1(9.1%)
Cohabiting	1(9.1%)
<b>Region of origin</b>	
Center	2(18.2%)
Far North	1(9.1%)
Littoral	1(9.1%)
North West	2(18.2%)
West	4(36.4%)
South	2(9.1%)
<b>Occupation</b>	
Unemployed	2(18.2%)
Civil servant	2(18.2%)
Private sector	4(36.4%)
Retired	2(18.2%)
Informal sector	1(9.1%)
<b>Level of Education</b>	
Primary	2(18.2%)
Secondary	3(27.3%)
High school	1(9.1%)
University	5(45.5%)

## 1.2. History and diagnosis of diabetes

History taking revealed that majority 8(11) subjects had been diagnosed with diabetes less than six (06) months earlier meanwhile 3(11) had been diagnosed more than six months earlier. The median [IQR] fasting blood glucose at diagnosis was 12.7 [7.8-15.0] mmol/l. As concerns treatment, 8 (11) participants were naïve to all antidiabetic therapy, 2(11) were on oral hypoglycaemic (OHG) drugs: (all on Metformin only) and 1(11) on diet only.



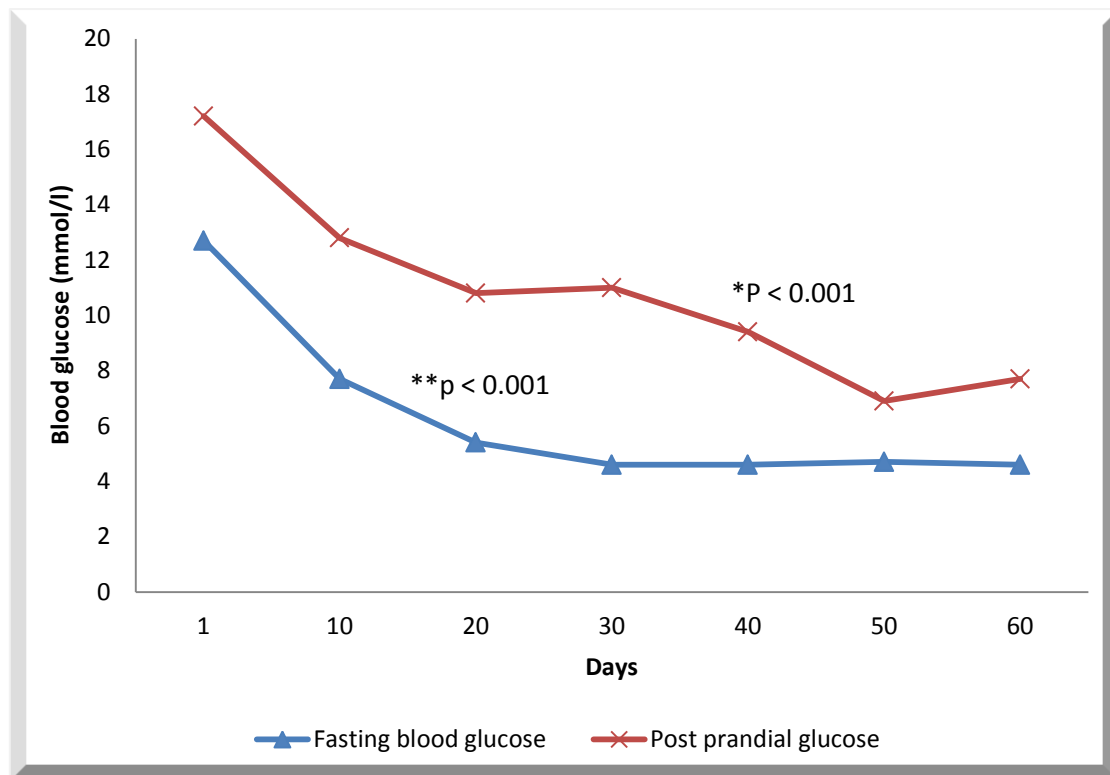
**Figure 2:** Diabetes treatment in our study population at baseline

## 1.3. Characteristics of study population before, during and after 8-week intervention

*Figure 3* below shows the gradual decrease in both fasting and post prandial blood glucose during the eight weeks of the intervention. Before BPIR, glycaemic control was poor with a median [IQR] fasting blood of 12.7[7.8 – 15.0] mmol/l and post prandial blood glucose of 17.2[13.7-19.8] mmol/l. This reduced significantly after treatment to 4.9[4.2-6.2] mmol/l,  $p=0.003$  and 7.7[6.4 – 10.0] mmol/l,  $p=0.004$  respectively. With BPIR, excellent blood glucose control was achieved within the first 8 [6-11] days with a maximal daily insulin dose of 0.42 [0.41-0.48] units/Kg.

\*: Compares median post prandial glycaemia obtained on various days during the intervention

\*\* : Compares median fasting blood glucose obtained on various days during the intervention



**Figure 3** Evolution of blood glucose during intervention

### 1.3.1. Clinical parameters of the study population

In our study population, there was no significant difference in the median [IQR] systolic blood pressure before and after intervention, 123[101-132] mmHg versus 127[109-135] mmHg,  $p=0.96$  and diastolic blood pressure from 83[63-96] mmHg to 84[67-93] mmHg,  $p=0.42$ . There was no significant change in weight (kg), from 79.6 [59.6-85.0] to 80.5 [60.3-84.2],  $p=0.33$ . There was no significance difference in both fat mass (%); 24.3 [18.1-31.1] versus 20.0 [17.0-29.6],  $p=0.29$  and BMI ( $\text{Kg}/\text{m}^2$ ) 28.7 [21.6-30.3] before versus 28.1 [21.9-30.7] after,  $p=0.33$ . See *Table II* below.

**Table II:** Clinical parameters before and after insulin therapy

Parameters	Basal-plus Insulin therapy		% Change	*p-value
	Before Median [IQR]	After Median[IQR]		
SBP (mmHg)	123.0[101.0-132.0]	127.0[109.0-135.0]	3.25	0.96
DBP (mmHg)	83.0 [63.0-96.0]	84.0 [67.0-93.0]	1.20	0.42
HR ( bpm)	83.0[75.0-93.0]	80.0[74.0-85.0]	3.61	0.38
Waist-Hip ratio	0.88 [0.84-0.96]	0.87 [0.86-0.97]	1.14	0.72
Weight (Kg)	79.6 [59.6-85.0]	80.5 [60.3-84.2]	1.13	0.33
Fat mass (%)	24.3 [18.1-31.1]	20.0 [17.0-29.6]	17.69	0.29
BMI (Kg/m <sup>2</sup> )	28.7 [21.6-30.3]	28.1 [21.9-30.7]	2.09	0.33

SBP: systolic blood pressure, DBP: diastolic blood pressure, BMI: Body mass index,  
\* Wilcoxon sum rank test  
Results were expressed in median [IQR].

### 1.3.2. Biological characteristics of our study population

Table III below shows that glycaemic control improved significantly after 8-week BPIR with a change in median [IQR] FBG and HbA1c from 12.7 [7.8-15.1] mmol/l and 101.0 [84.0-108.0] mmol/mol versus 4.6 [4.2-6.2] mmol/l,  $p = 0.003$  and 42.0 [36.0-50.0] mmol/mol,  $p = 0.003$  respectively.

We observed an improvement in lipid profile parameters. Total cholesterol, and LDL cholesterol decreased after the intervention,  $p < 0.05$ . There was no significant difference highly sensitive CRP before and after the intervention.

**Table I:** Biological profile of study population before and after intervention

Parameters	Basal-plus Insulin therapy		% Change	*p-value
	Before M [IQR]	After M [IQR]		
<b>FBG (mg/dl)</b>	228.0[140.0-270.0]	83.0[75.0-111.0]	63.78	<b>0.003</b>
<b>FBG (mmol/l)</b>	12.7 [7.8-15.0]	4.9 [4.2-6.2]	63.78	<b>0.003</b>
<b>HbA1c (%)</b>	11.4 [9.8-12.0]	6.0 [5.6-6.7]	47.37	<b>0.003</b>
<b>HbA1c (mmol/mol)</b>	101.0 [84.0-108.0]	42.0 [36.0-50.0]	47.37	<b>0.003</b>
<b>Serum creatinine (mg/L)</b>	11.7[8.7-13.6]	10.3[7.6-12.2]	11.97	0.51
<b>e-GFR (ml/min/1.73m<sup>2</sup>)</b>	67.0 [59.0-95.0]	82.0 [61.0-95.0]	22.4	0.42
<b>Total Cholesterol (mmol/l)</b>	5.40[5.17-5.87]	4.45[3.57-5.48]	17.70	<b>0.03</b>
<b>HDL-C (mmol/l)</b>	1.14 [1.03-1.40]	2.12 [1.86-2.69]	86.36	<b>0.008</b>
<b>LDL-C (mmol/l)</b>	3.83 [2.82-4.37]	1.06 [0.54-2.95]	72.30	<b>0.007</b>
<b>Triglycerides (mmol/l)</b>	1.51 [1.39-1.71]	1.18 [1.02-1.24]	23.39	0.32

TG: Triglycerides, HDL-C: HDL cholesterol, LDL-C: LDL cholesterol, FPG: Fasting Plasma glycaemia, CRP: C-reactive protein, e-GFR: Estimated glomerular filtration rate, HbA1c: Glycated haemoglobin, \*Wilcoxon sum rank tests.

### 1.3.3. Insulin sensitivity before and after intervention

The median [IQR] insulin-mediated glucose disposal rate expressed as the clamp-derived M-value increased significantly after the intervention from 6.50 [4.00-9.00] mg/kg/min to 9.00[8.00-11.50] mg/kg/min, p=0.004. When adjusted for lean mass it was still significantly higher after intervention; 7.94 [6.39-11.03]mg/kg/min versus 12.85[10.24-14.92] mg/kg/min. p=0.004. The result in *figure 4* is expressed in median [IQR].

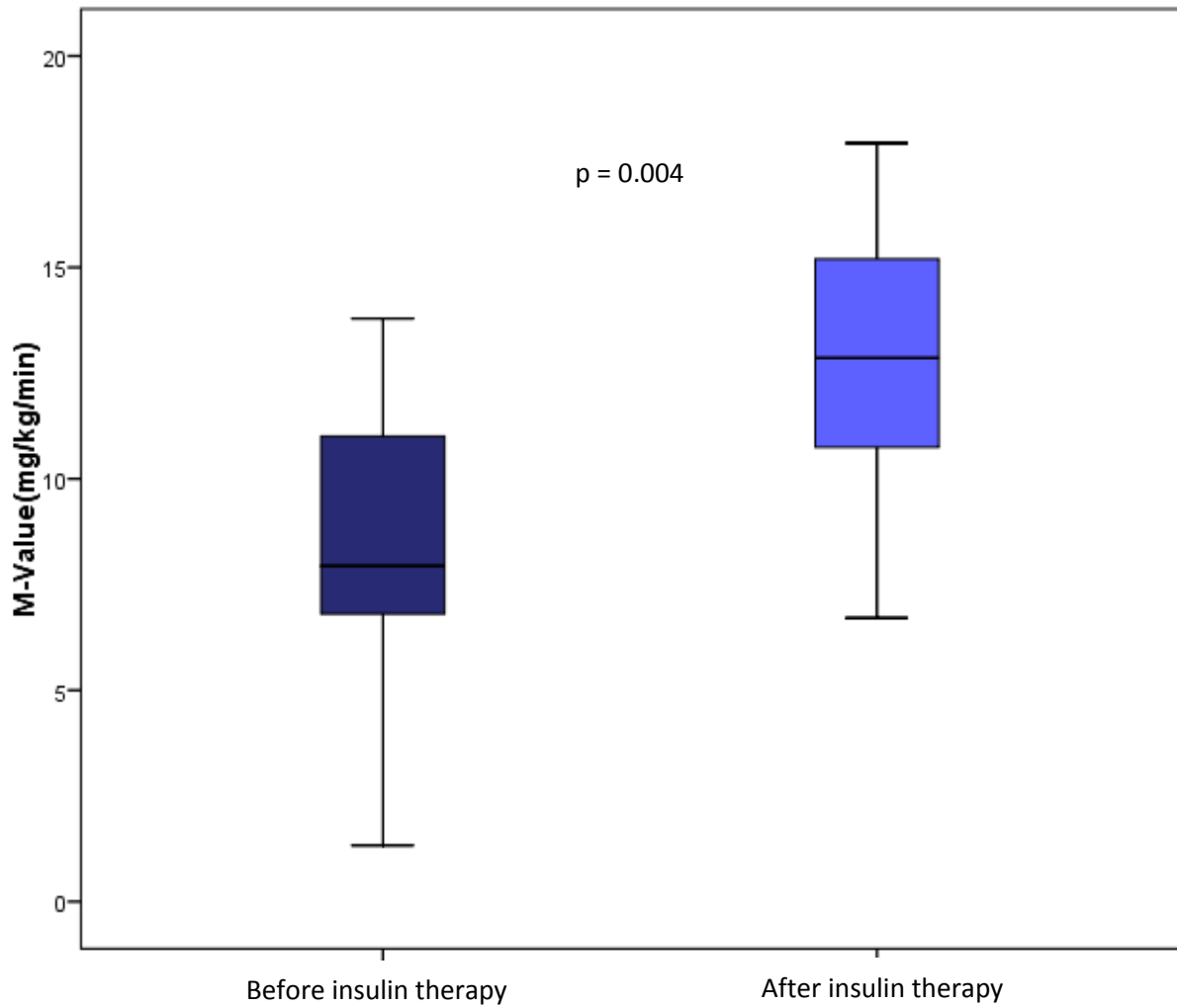


Figure 4: Comparison of M-values before and after basal-plus insulin therapy

#### 1.3.4. Plasma glucose before and after 8-week intervention

Plasma glucose assessment during the mixed meal tolerance test revealed a significant decrease in the area under the curve (AUC) of plasma glucose after intervention (*See table 4* below). There was a significant difference in plasma glucose level at all through the MMTT after the intervention.

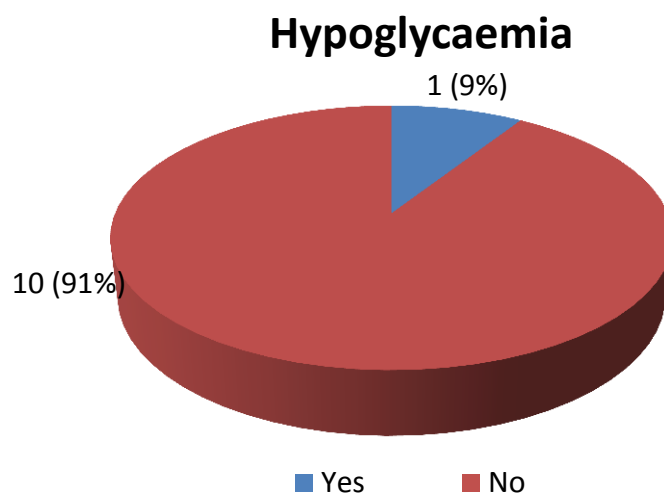
**Table IV:** Median plasma glucose during the mixed meal tolerance test before and after intervention

Parameters	Plasma glucose during MMTT		p-value
	Before M [IQR]	After M [IQR]	
AUC glucose (mmol/mol)	78.3 [31.5–144.3]	24.9 [5.1-60.0]	<b>0.01</b>
Plasma glucose T0 (mmol/l)	7.4 [6.6-9.1]	5.4 [4.7-5.7]	<b>0.004</b>
Plasma glucose T30 (mmol/l)	7.3 [6.2-7.7]	6.3 [5.0-6.8]	<b>0.02</b>
Plasma glucose T60 (mmol/l)	8.4 [7.3-9.6]	6.3 [5.0-6.8]	<b>0.02</b>
Plasma glucose T90 (mmol/l)	8.8 [7.3-10.1]	6.2 [4.8-7.3]	<b>0.009</b>
Plasma glucose T120 (mmol/l)	9.2 [7.9-9.8]	6.4 [5.0-7.0]	<b>0.003</b>

AUC: Area under the curve, MMTT: Mixed meal tolerance test, \*: Wilcoxon sum rank tests, T0: 0 minutes, T30: 30 minutes, T60: 60minutes, T90: 90minutes T120: 120minutes. AUC: Area under the curve.

**1.3.5. Adverse events**

One participant out of eleven experienced two episodes of symptomatic confirmed hypoglycaemia of less than 3.9 mmol/l (70mg/dl), but greater than 3.0 mmol/l (54mg/dl).



**Figure 5:** Proportion of participants who experienced hypoglycaemia

**Table V:** Comparison of clinical parameters before and after the follow-up phase

Parameters	Follow-up phase		*p-value
	Baseline – D0 Median [IQR]	Remission – D120 Median[IQR]	
<b>SBP (mmHg)</b>	123.0 [101.0-132.0]	123.0[113.0-138.0]	0.68
<b>DBP (mmHg)</b>	83.0 [63.0-96.0]	80.0 [72.0-94.0]	0.82
<b>Waist-Hip ratio</b>	0.88 [0.84-0.96]	0.89 [0.86-0.90]	1.00
<b>Weight (Kg)</b>	79.6 [59.6-85.0]	78.9 [62.7-82.2]	0.66
<b>Fat mass (%)</b>	24.3 [18.1-31.1]	25.4 [19.0-28.8]	0.93
<b>BMI (Kg/m<sup>2</sup>)</b>	28.7 [21.6-30.3]	27.8 [21.1-30.7]	0.66

D0: Day 0, D120: Day 120, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, IQR: Interquartile range. \*Wilcoxon sum rank tests.

#### 4.4.1. Glycaemic control during follow-up phase

During the follow-up phase, the early remission proportion (proportion of subjects maintaining near euglycaemia at 2 months) was 10 out of 11. One patient failed to maintain euglycaemia after one month of follow-up and was put on an OHG agent based on current clinical practice guidelines. We observed a non-significant change in HbA1c,  $p = 0.22$ , two months after withdrawal of insulin.

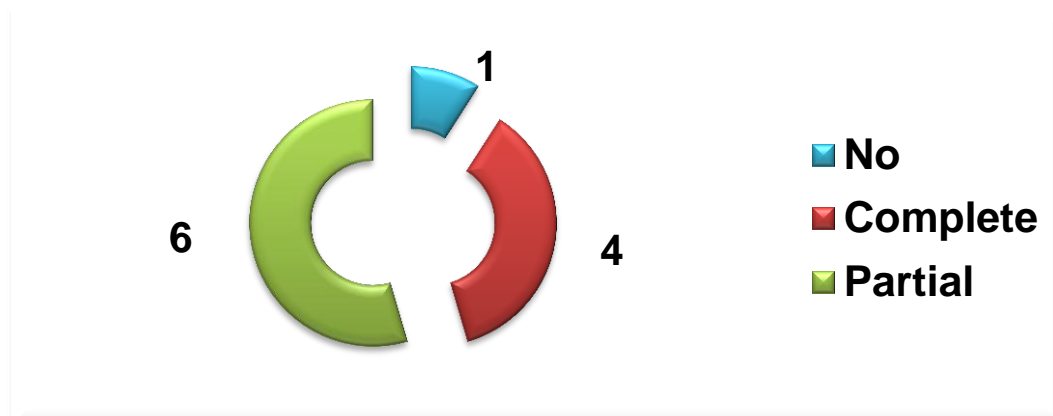


Figure 6: Proportion of participants in early remission

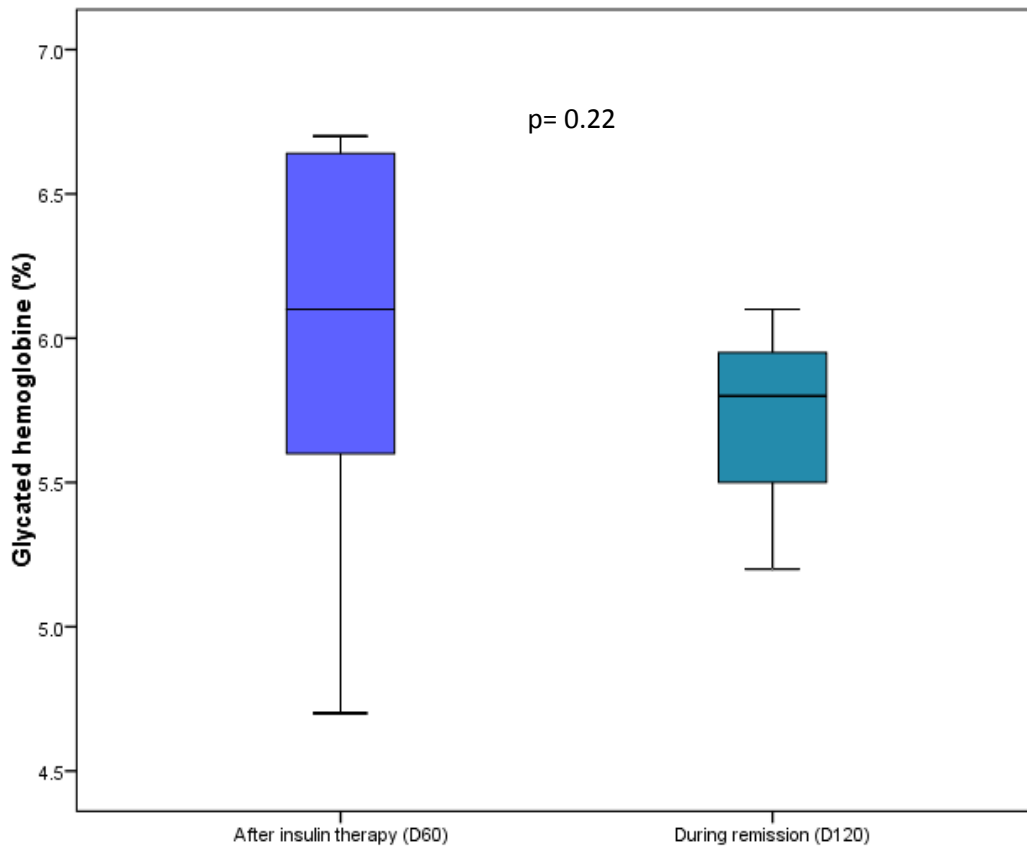


Figure 7: Comparison of HbA1c before and after the follow-up phase

There was no significant change in both postprandial glycaemia and fasting blood glucose at the beginning and end of the follow-up phase.

\*: Compares median post prandial glycaemia values obtained during follow-up phase

\*\* : Compares median fasting blood glucose obtained on various days during follow-up phase

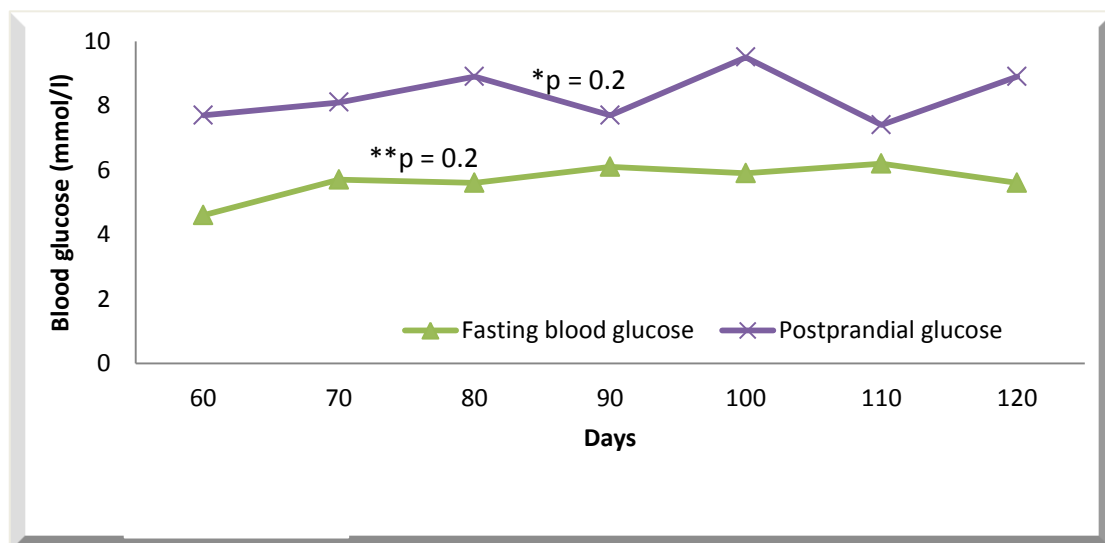


Figure 1: Daily variation in blood glucose during the follow-up phase