

OBJECTIVE

The antidiabetic drug metformin has been associated in a number of patients with lactic acidosis. In spite of the fact that diabetes mellitus is the commonest cause of end-stage renal disease (ESRD) and that peritoneal dialysis (PD) is an expanding modality of treatment, little is known about the optimal treatment strategies in this large group of patients. The use of metformin has been limited in patients with ESRD because of the perceived risk of lactic acidosis and/or severe hypoglycemia. However it is likely that the use of this drug would be beneficial and that PD itself may be a safeguard against the alleged complications.

METHODS

The study involved 35 insulin-dependent type-2 diabetes patients (median age 54 (IQR 47-59) years on automated PD (APD) therapy. Patients with additional risk factors for lactic acidosis were excluded. Metformin was introduced with the daily dose ranging between 0.5-1.0 gm. All patients were monitored for glycemic control by blood sugar levels and Hgb-A1C. Plasma lactic acid levels were measured on weekly basis for 4 weeks then monthly till the end of the study. Plasma and peritoneal fluid metformin and plasma lactate levels were measured simultaneously.

RESULTS

The median diabetes duration was 18 (IQR 14-21) years, the median time on PD was 31 (IQR 27-36) months and the median Hgb-A1C was 6.8% (IQR 5.9-6.9). The median anion gap was 11 (IQR 9-16) mmol/L and 12 (IQR 9-16) mmol/L ($p > 0.05$) and the median pH was 7.33 (IQR 7.32-7.36) and 7.34 (IQR 7.32-7.36) ($p > 0.05$) at metformin introduction and at the end of the study period respectively. The overall mean \pm SD plasma and peritoneal fluid metformin concentrations were 2.57 ± 1.49 mg/L and 2.83 ± 1.7 mg/L respectively. The mean lactate level across all patients was 1.39 ± 0.61 mmol/L, and hyperlactemia (level > 2.5 mmol/L) was found in 4/525 (0.76%) plasma samples whereas the patients presented no symptoms. None of the patients had plasma lactate level above 5 mmol/L. There was no correlation between plasma metformin and plasma lactate levels ($r = 0.27$).

CONCLUSION

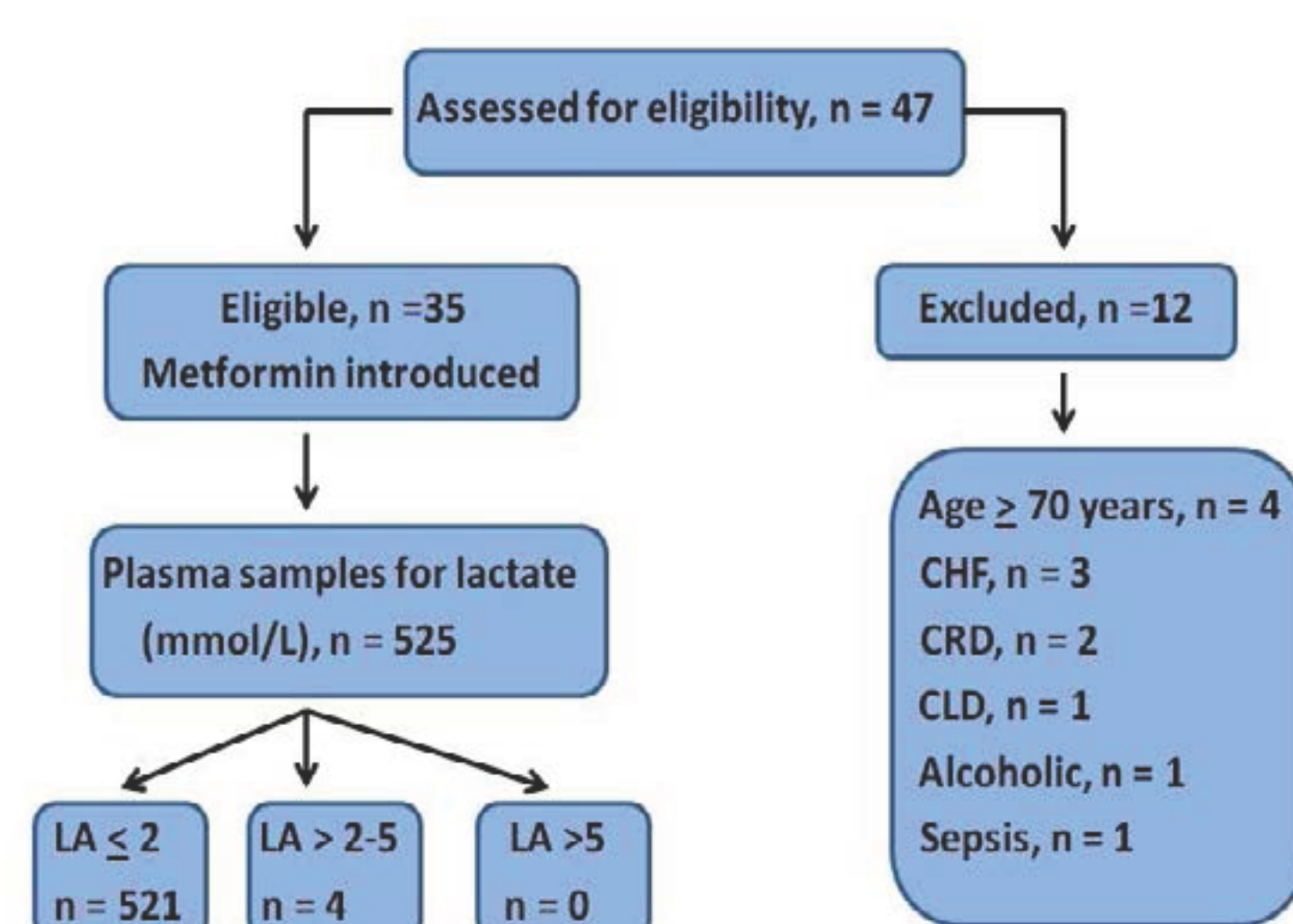
Metformin may be used with caution in insulin-dependent type 2 diabetes mellitus patients on APD therapy. Although this study has demonstrated feasibility of metformin use in APD, it has not been large enough to demonstrate safety and a large scale study is needed.

KEYWORDS

Metformin, lactic acid, BMI, ESRD, PD, acidosis, hypoglycemia.

FIGURE

Figure 1: Consort diagram demonstrating study design and patients' progress



CHF = chronic heart failure, CRD = chronic respiratory disease, CLD = chronic liver disease, LA = serum lactic acid

Figure 2 A and B: Median pH and anion gap in relation to the study duration

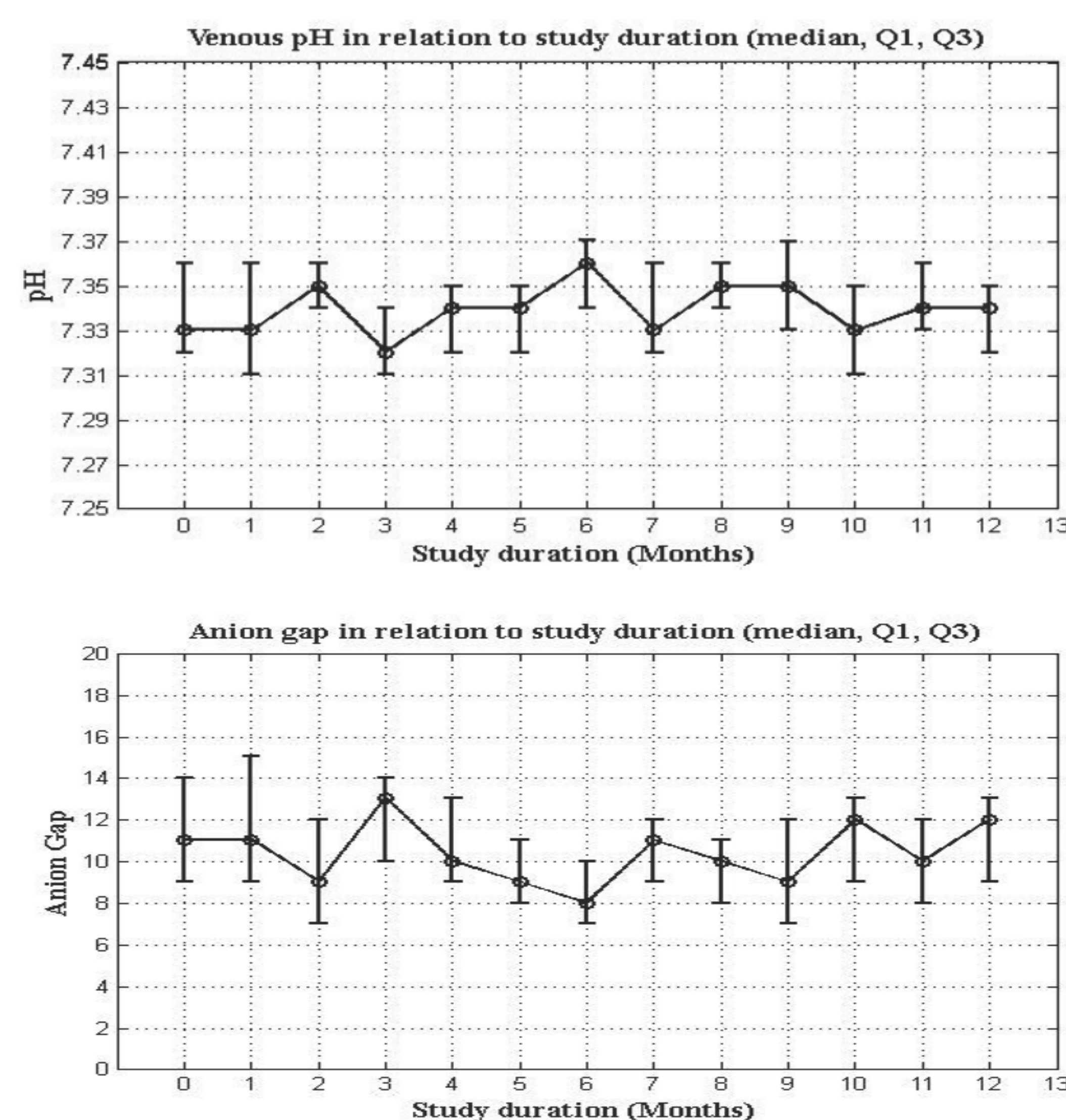
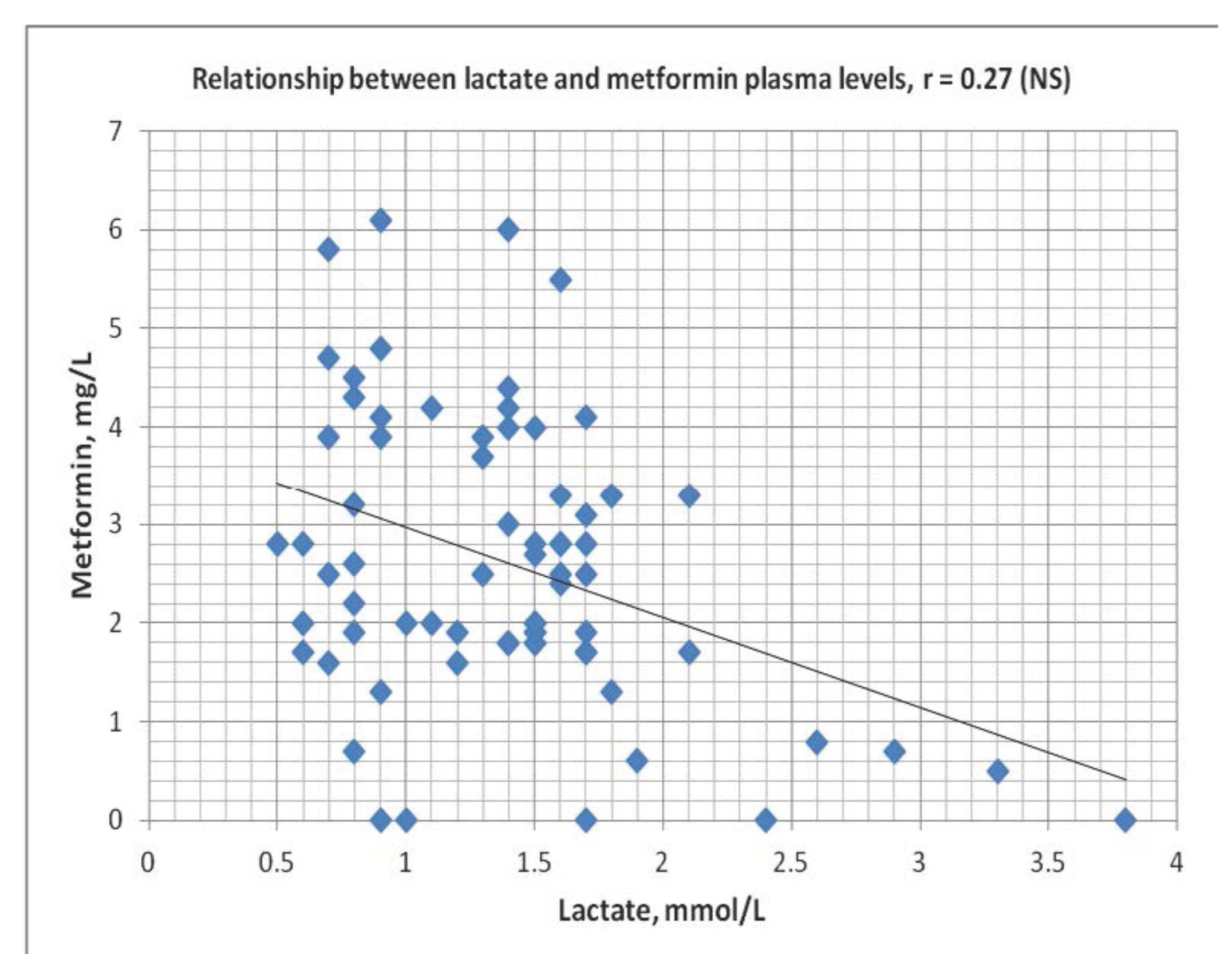


Figure 3: Relationship between plasma lactate and plasma metformin levels in the study population, $r = 0.27$ (NS)



NS = not significant