

Metformin treatment for obese children and adolescents with insulin resistance

Z. Todorova, E. Stefanova, K. Kazakova, D. Jordanova

Endocrinology Department, University Children's Hospital, Sofia, Bulgaria

Introduction

Obesity (Body Mass Index above 95-th percentile for sex and age) in children is already a global health problem. Obese children and adolescents with insulin resistance (IR) provide the pediatric healthcare professionals management challenge. Obesity with insulin resistance, dyslipidemia and elevated blood pressure constitute the metabolic syndrome and each of these is an independent risk factor for cardiovascular disease (CVD). Moreover childhood overweight/obesity are predictive of such in an adult. Metformin is well established oral hypoglycemic agent in the treatment of adult and young patients with type 2 diabetes, but it is not officially registered for obesity and IR

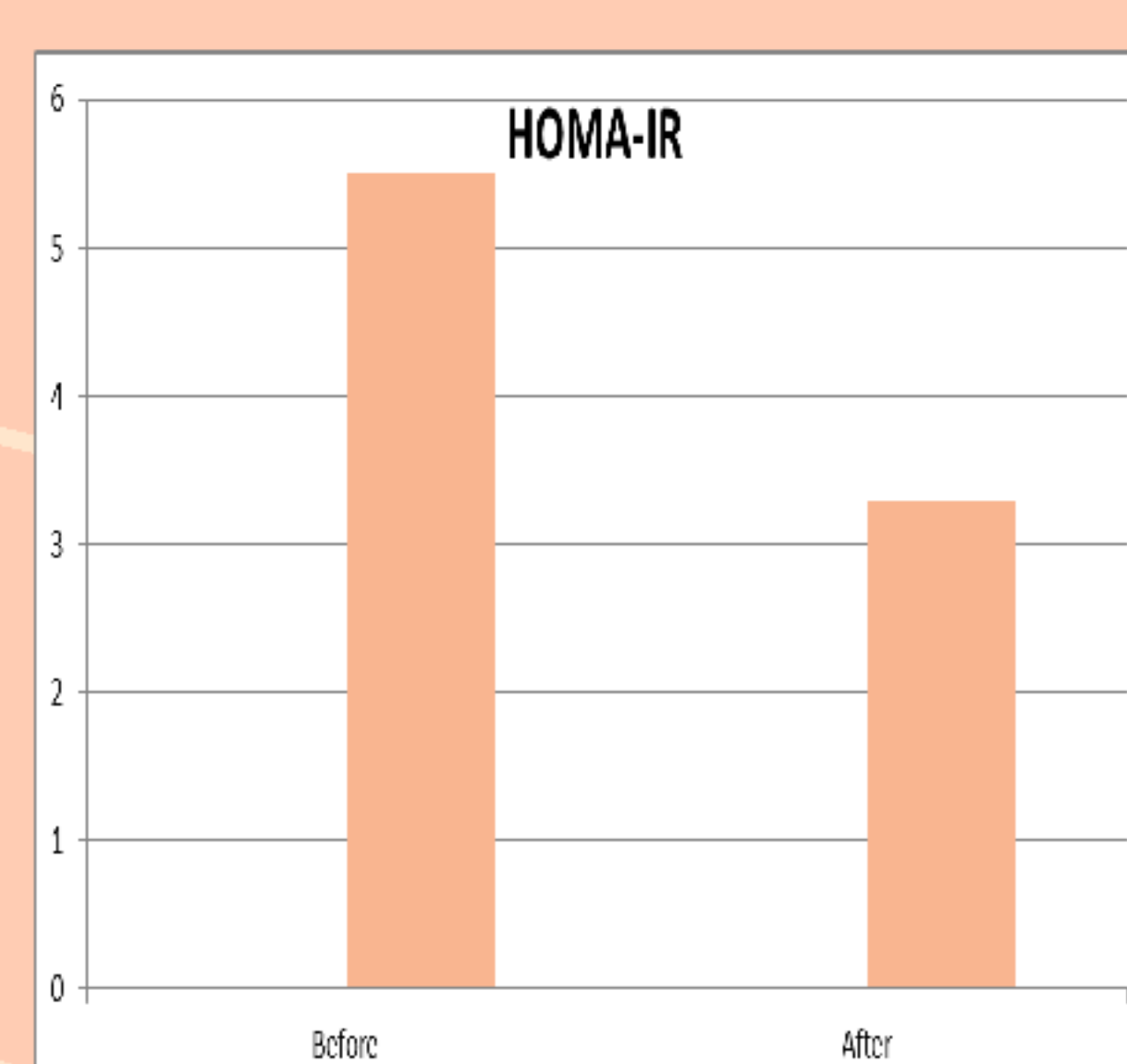
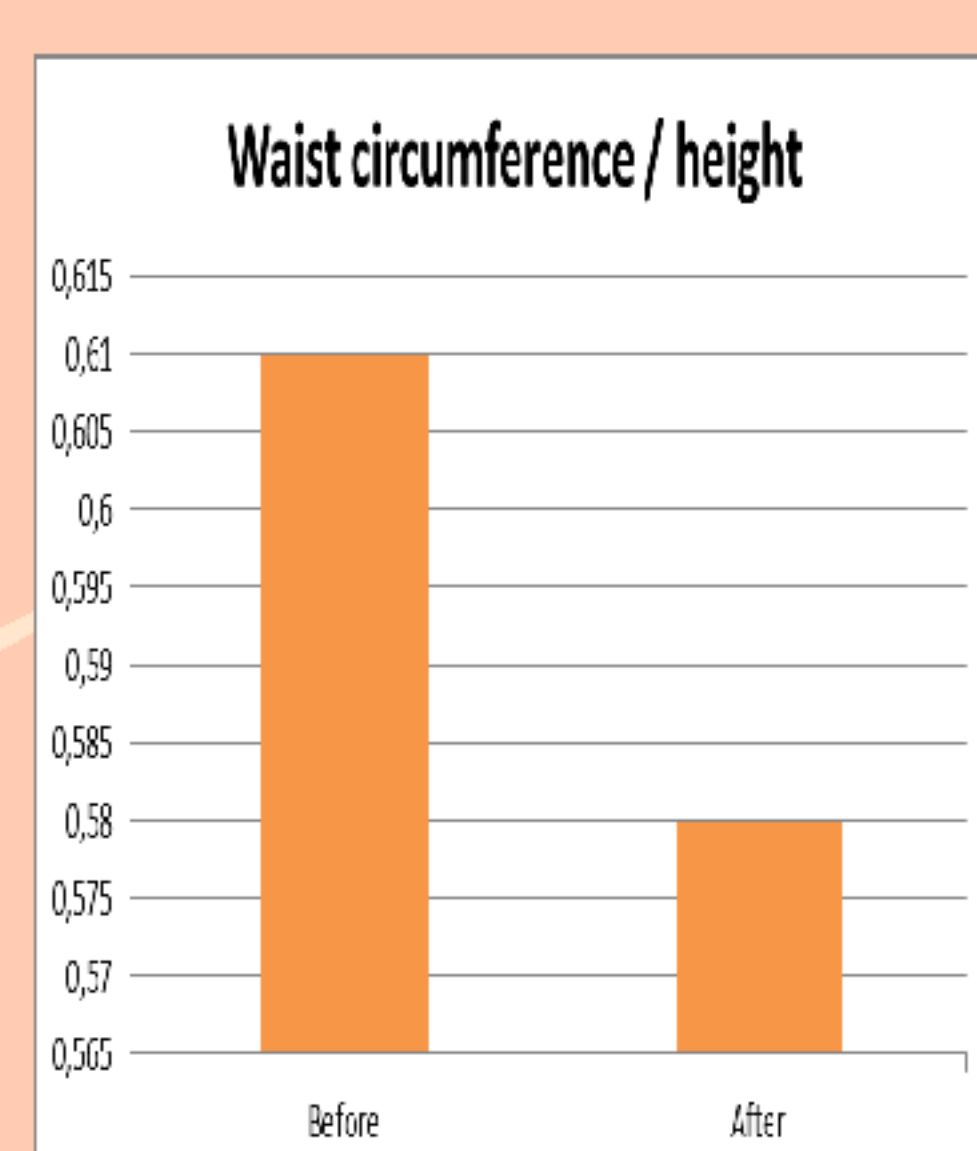
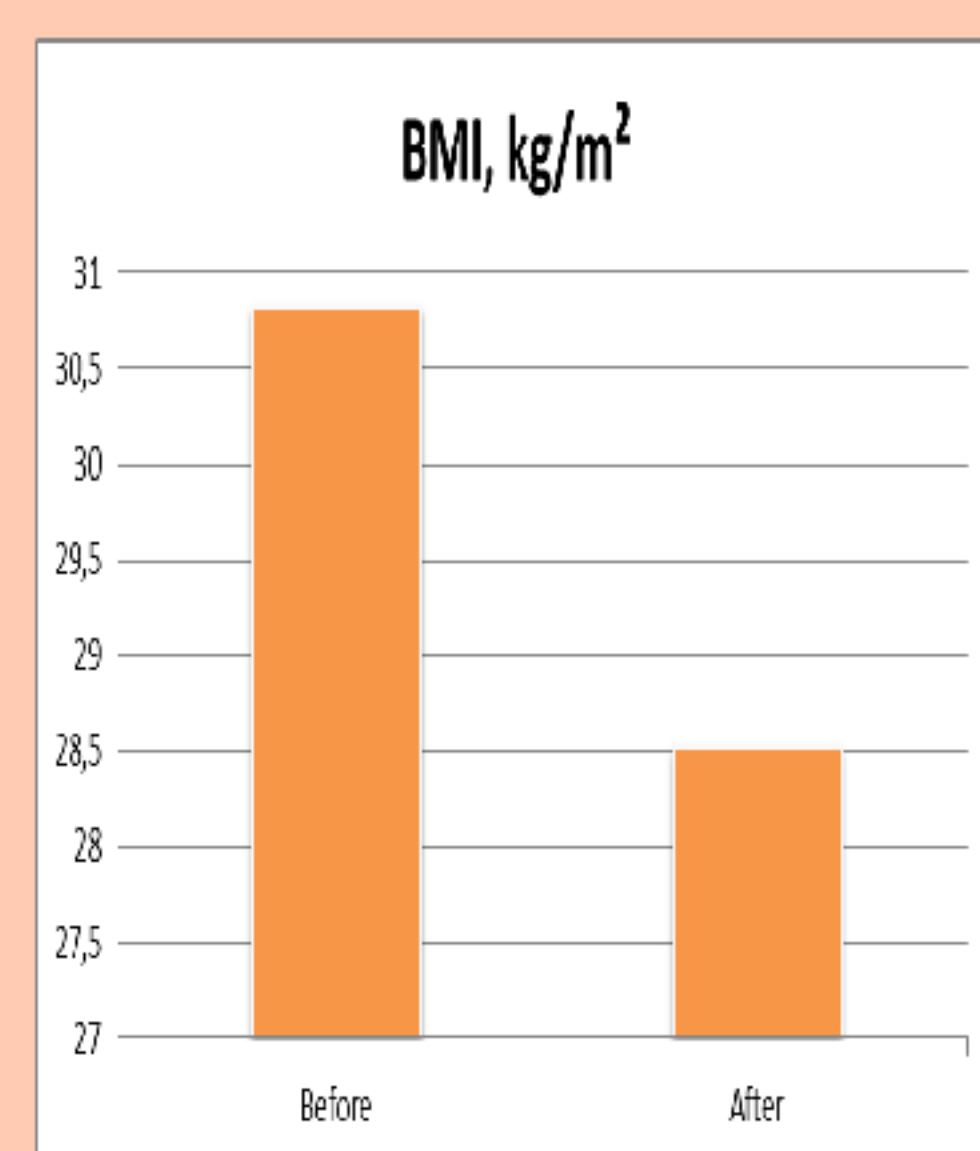
Objectives

To analyze the effect of metformin treatment of obese (non-diabetic) children and adolescents with insulin resistance, on the body mass index (BMI), fasting serum glucose and insulin (calculated as Insulin resistance index – HOMA IR) and the ratio waist circumference / height (as a sign of abdominal adiposity and risk factor for metabolic syndrome, CVD and type 2 DM). Additionally we analyzed the relation between acanthosis nigricans present in patients and stimulated hyperinsulinemia. All the patients received strong support for lifestyle modification (dietary, behavioral and physical activity)

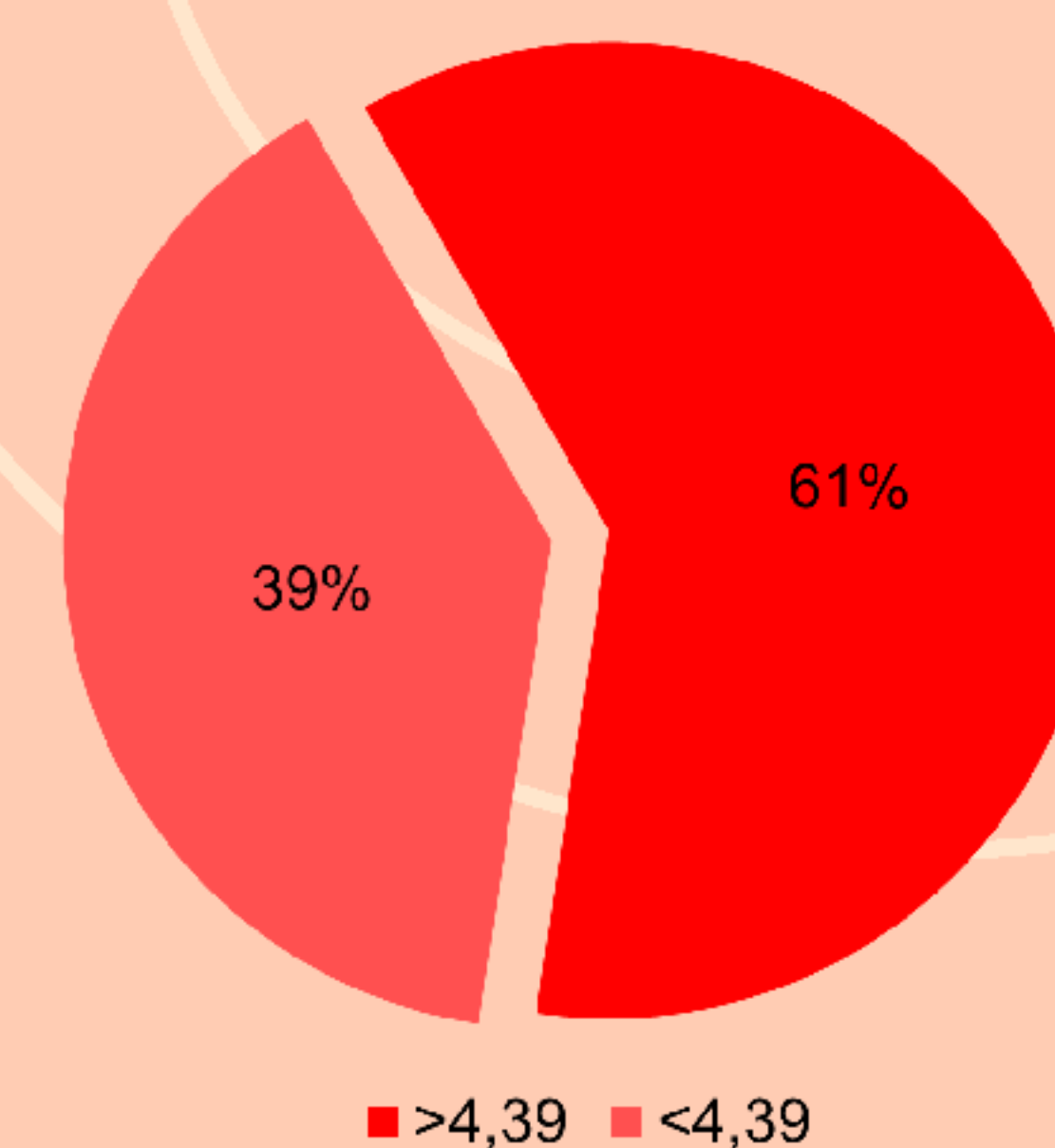
Methods

Investigation and follow up of 57 children and adolescents (16 boys), aged 7 years 6 months - 16 years 9 months. Patients received Metformin for an average period of 14,6 months (6-36 months) twice daily dosage of 1000 – 1700 mg which was reached in a stepwise manner. Anthropometry (height, weight, waist circumference), clinical examination with regard to presence of acanthosis nigricans and oral glucose tolerance test were performed at baseline, every six months and end of treatment period.

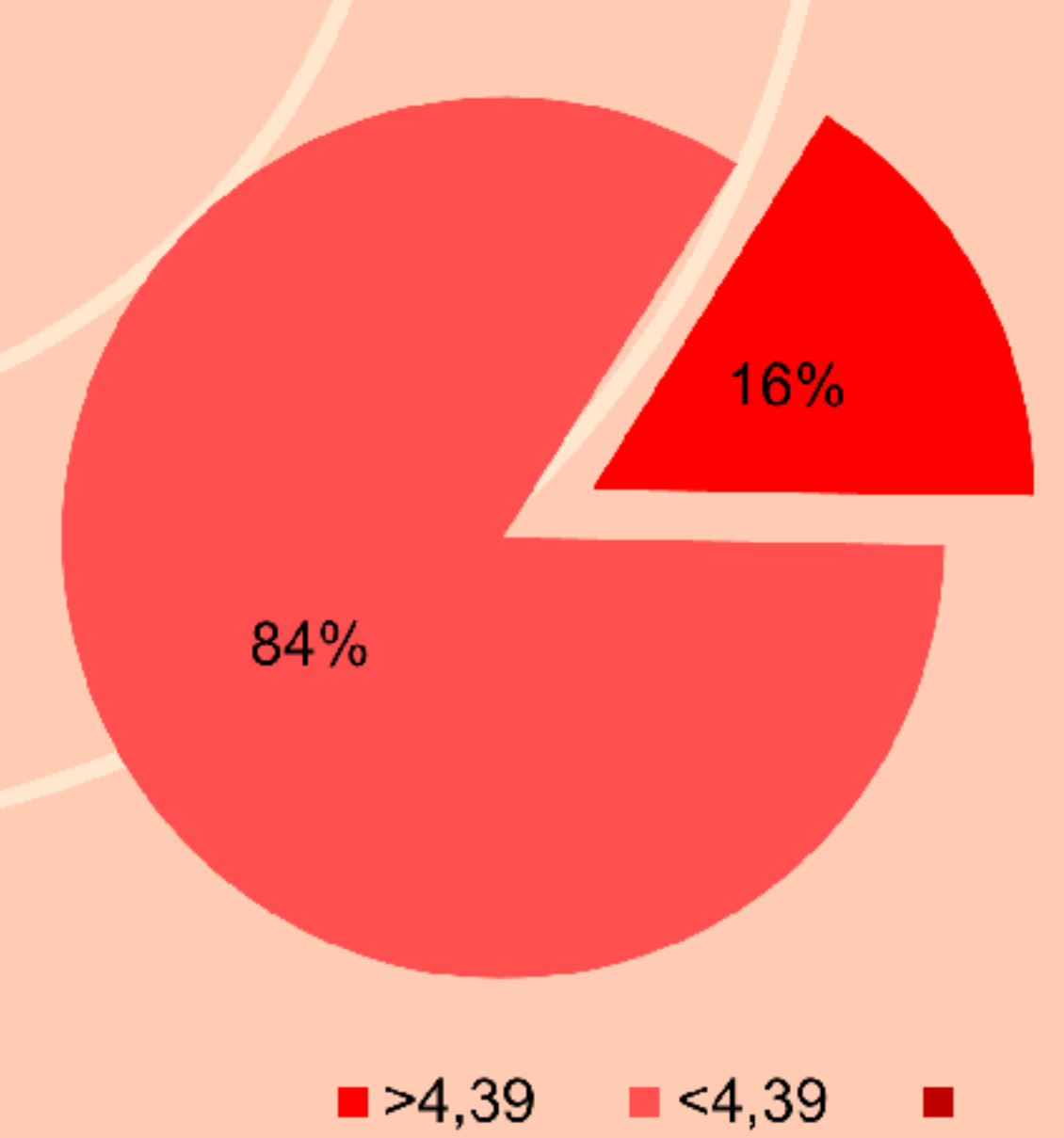
Results



HOMA-IR before treatment



After treatment



Mean age of subjects at baseline was 13 years 7 months with median BMI 30,95 kg/m² and waist circumference / height ratio 0,62. After the treatment period BMI was reduced to 28,51 kg/m² (t=2.33 p<0.05) and waist circumference / height ratio became 0,58 (t =2.14 p<0.05).

Insulin resistance, strictly related to excessive weight gain, is the first step in the pathogenesis of T2DM. Marker of IR is the HOMA-IR index, based on the measurement of fasting insulin and glucose with higher levels representing greater degrees of IR. Based on a study of 1,802 adolescents aged 12–19 yr from the 1999–2002 NHANES, a HOMA-IR 4.39 was recommended as evidence for IR. Pretreatment HOMA-IR was 5,52. Metformin therapy had beneficial effect on HOMA-IR which fall to 3,16 (t=4.4 p<0.001). Acanthosis nigricans was found in 51 % of the patients, but we could not prove a statistically significant relation between its presence and stimulated hyperinsulinemia.

Only several patients had mild gastrointestinal complaints, which were not reason for discontinuation of treatment and which resolved in a short period. No serious or life-threatening side effects were observed.

Conclusions

It appears that metformin use for the treatment of obese children and adolescents with insulin resistance lead to moderate improvement in BMI, fasting serum glucose and insulin as well as waist circumference / height ratio. In the era of alarming rise of childhood obesity and its consequences it is important to have an efficacious and safe treatment option.

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