

# The role for autocrine regulation of IGF-1 in pregnancy related obesity, a potential biomarker for weight loss

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## OBJECTIVES

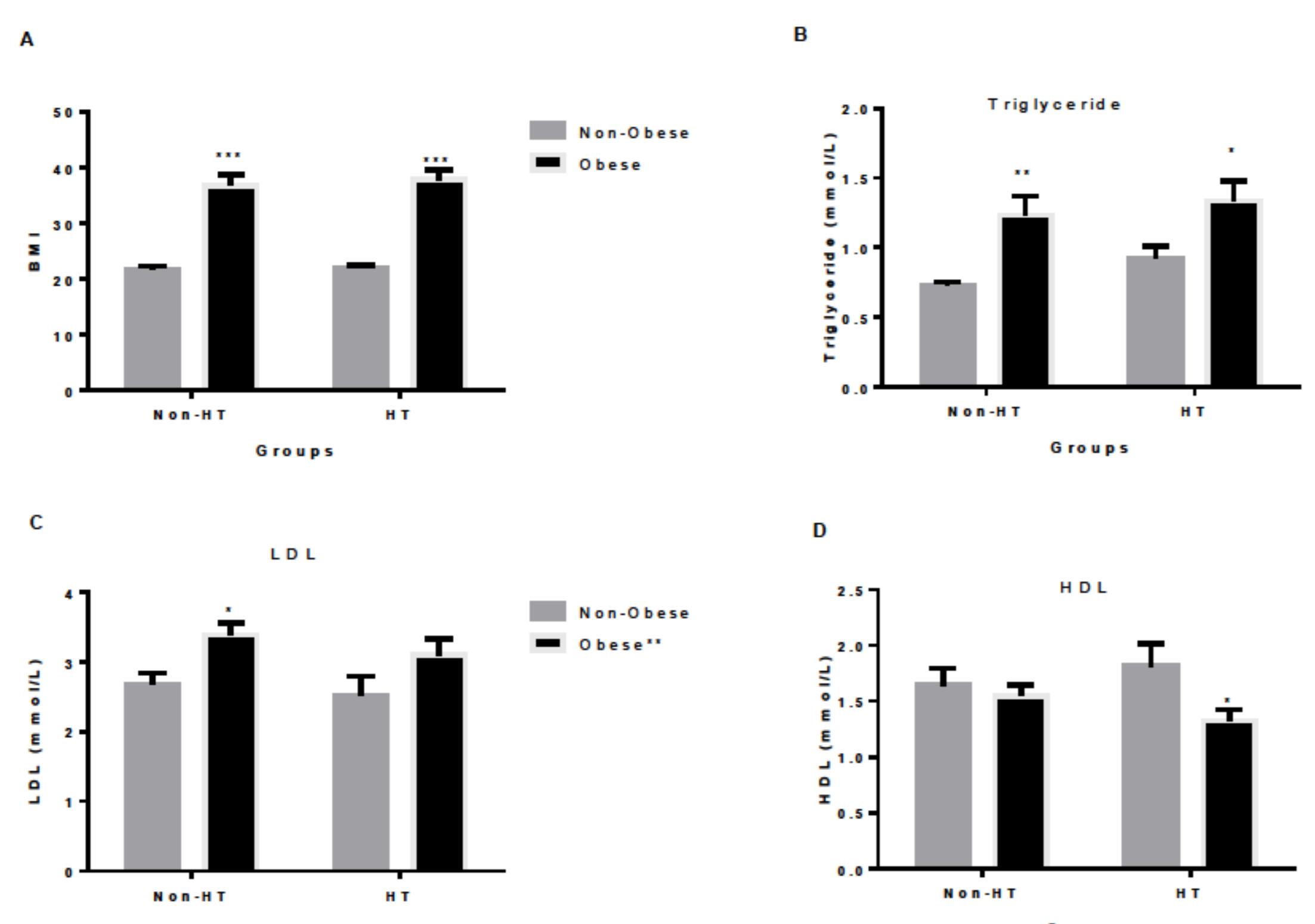
Impaired insulin-like growth factor-1(IGF-1) function associates with obesity and hypertension with weak correlation to circulating IGF-1. As a metabolite of IGF-1, the ratio of cyclic Glycine-Proline (cGP)/IGF-1 regulates IGF-1 bioavailability. We evaluated its association with obesity and/or hypertension and the changes of obesity status between early pregnancy and post-partum.

## METHODS

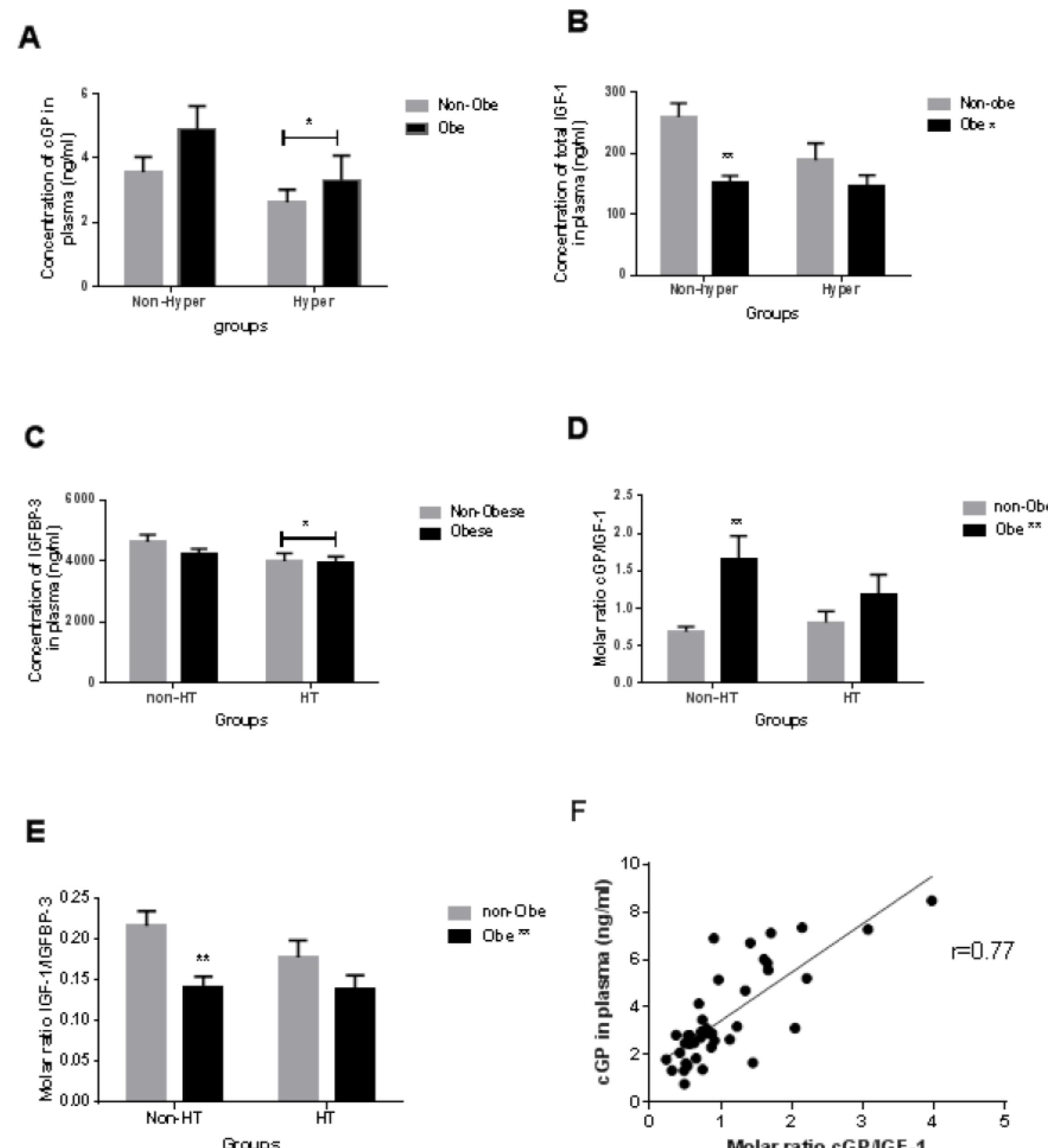
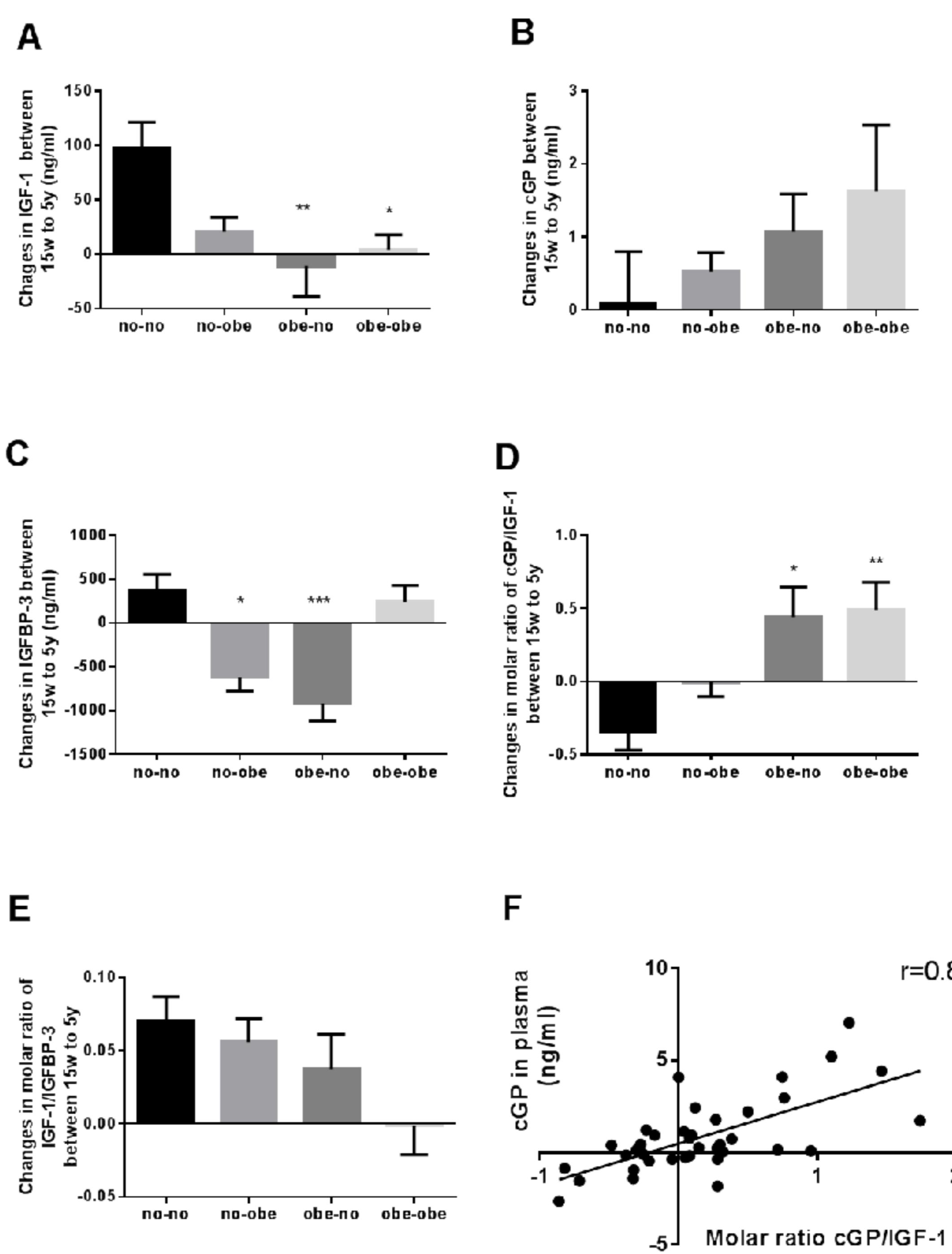
We compared plasma concentration of IGF-1, cGP and IGF binding-protein (IGFBP)-3 in the women with obesity and/or hypertension to normal controls. We then compared the differences of these parameters between 15weeks gestation and 6years post-partum in women who were either remained to be normal, or become obese or recovered from obese or remained to be obese at 6years post-partum. cGP was measured using HPLC-ms and IGF-1 and IGFBP-3 were measured using ILESA.

## RESULTS

### Changes in Obesity and hypertension



### Changes between 15 week of pregnancy and 6 year of post partum



## CONCLUSIONS

cGP/IGF-1 ratio may be associated with obesity. The autocrine regulation with collective responses of reduced IGFBP-3 and increased cGP/IGF-1 ratio may play a role in weight loss.

In general we found an increase of cGP/IGF-1 ratio in pregnancy related obesity, but not hypertension, possible a specific autocrine response to low circulating IGF-1 in obesity. As a compensatory response to low circulating IGF-1 both reduction of IGFBP-3 and increase of cGP/IGF-1 ratio were essential for the weight loss after pregnancy, possibly mediated through autocrine regulation to improve bioavailability of IGF-1. Thus integrative interpretation of cGP/IGF-1 ratio and IGFBP-3 would be more relevant biomarker for predicting IGF-1 bioavailability.

## References

1. Guan J, Gluckman P, Yang P, Krissansen G, Sun X, Zhou Y, et al. Cyclic glycine-proline regulates IGF-1 homeostasis by altering the binding of IGFBP-3 to IGF-1. *Sci Rep* 2014; 4.
2. Savastano S, Di Somma C, Pizza G, De Rosa A, Nedi V, Rossi A, et al. Liver-spleen axis, insulin-like growth factor-(IGF)-axis and fat mass in overweight/obese females. *Journal of translational medicine* 2011; 9: 136.
3. Schutte AE, Volpe M, Tocci G, Conti E. Revisiting the relationship between blood pressure and insulin-like growth factor-1. *Hypertension* 2014; 63: 1070-1077.