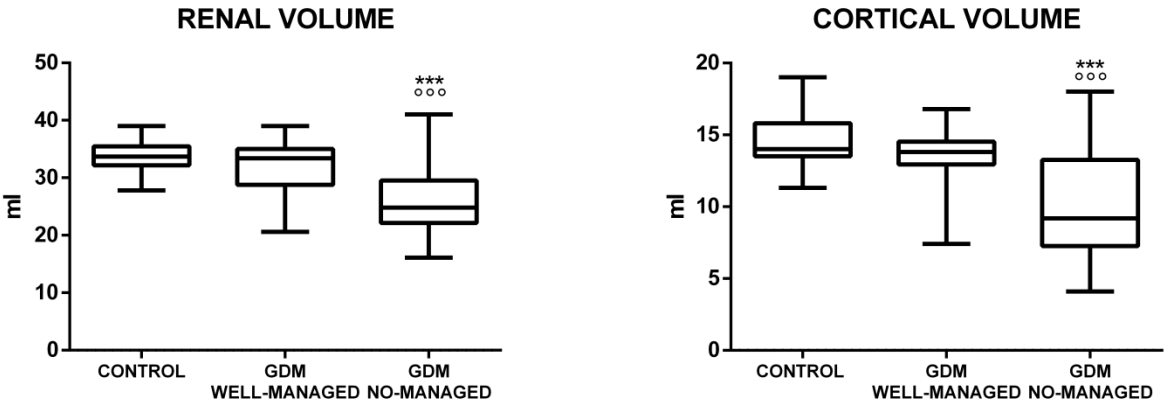
Can adverse effects on kidney in GDM newborn be prevented?

M.C. Aisa[1], B. Cappuccini[2,3], A. Barbati[1], C. Grasselli[1], S. Troiani[2], E. Torlone[4,3], G.C. Di Renzo[1,3]

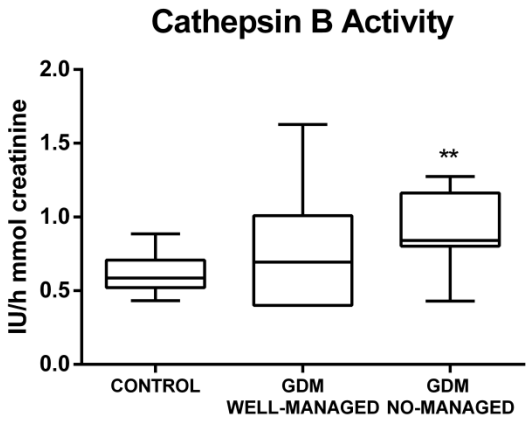
[1] Department of Surgical and Biomedical Sciences, Section of Obstetrics and Gynecology, University of Perugia, Perugia, Italy
[2] Department of Neonatology, Hospital S.M. della Misericordia, Perugia, Italy
[3] GEBISA, Research Foundation, Perugia, Italy
[4] MISEM, University of Perugia, Italy

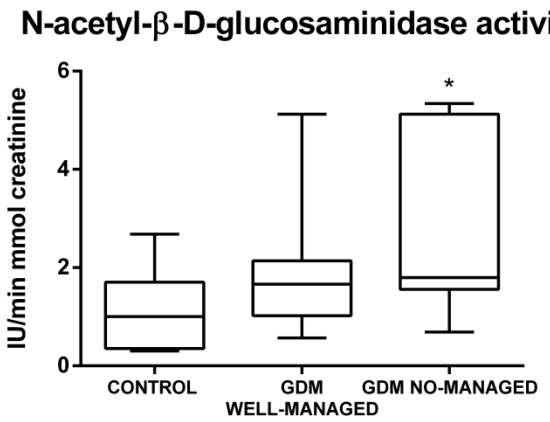
Abstract

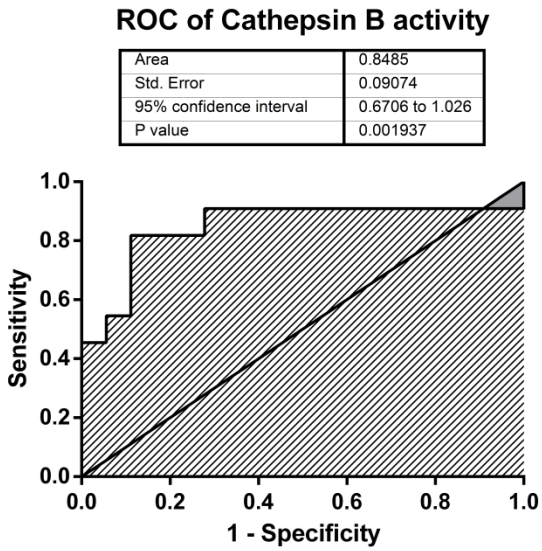
Background: Gestational Diabetes (GDM) has reached epidemic proportions worldwide and dysregulation of glucose metabolism is found in up to 15% of pregnancies, according to the International Association of Diabetes in Pregnancy Study Group and the World Health Organization. Investigations with animal models have demonstrated that exposure to maternal hyperglycemia during *in utero* development can detrimentally affect nephrogenesis which, in turn, would represent a risk factor for the onset of chronic renal disease and hypertension in adulthood. Studies on renal physiology in GDM neonates at the early stage of postnatal age are scarse and no reports concerning the correlation between nephron number-data and renal function in this group have been performed yet. We here examined the effect of GDM on kidney development and physiology at the postnatal age of 30-40 days in 170 newborns (sub-classified in no- and well-managed GDM) versus 65 matched healthys. **Methods**: Biochemical parameters of glomerular and tubular function or impairment/injury (i.e albumin, β-2 microglobulin and the activity of N-acetyl-β-D-glucosaminidase, cathepsin B, glucuronidase and legumain) were evaluated in the urine of the two GDM groups and compared to results from the healthy control neonate population. Data were then associated with predominant susceptibility factors of renal damage related to low nephron number, such as birth weight, total renal volume and renal cortex volume. Renal volumes were estimated using 3D-ultrasounds (VOCAL II, GE Ultrasounds, USA). **Results:** Compared to control, the well-managed GDM group did not show significant differences in all biochemical and anatomical parameters tested whereas the no-managed GDM neonates exhibited significant higher levels of cathepsin B and N-acetyl-β-D-glucosaminidase activity as well as significantly reduced values of total renal volume and cortical volume. **Conclusions:** Our data indicate that, at the early stage of postnatal age, GDM correlates with impairment of both kidney's development and function. Conversely, an appropriate management of this disease may counteract these effects. Data also indicate that, at this postnatal age, GDM affects renal tubule and cathepsin B and N-acetyl-β-glucosaminidase may be suggested as early indicators of such condition. Our findings support the efficacy of global actions about GDM.

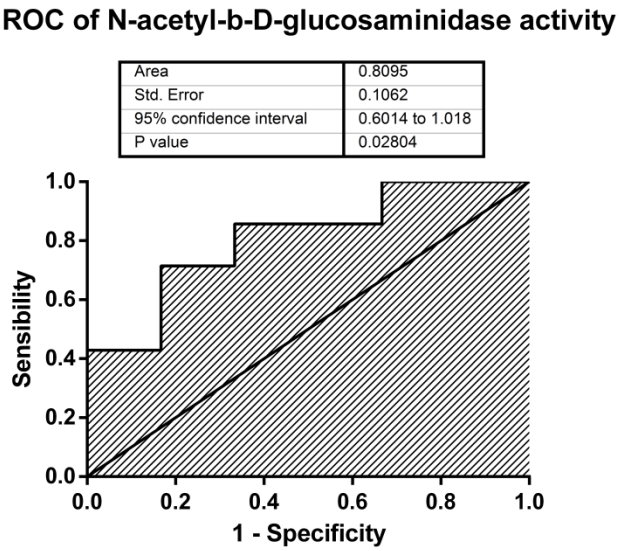


***, statistically different from CONTROL, p<0.001
°°°, statistically different from GDM WELL-MANAGED, p<0.001


Cathepsin B Activity
IU/h mmol creatinine
2.0
1.5
1.0
0.5
0.0
**
CONTROL
GDM WELL-MANAGED
GDM NO-MANAGED


N-acetyl-β-D-glucosaminidase activity
IU/min mmol creatinine
6
4
2
0
*
CONTROL
GDM WELL-MANAGED
GDM NO-MANAGED


ROC of Cathepsin B activity
Area 0.8485
Std. Error 0.09074
95% confidence interval 0.6706 to 1.026
P value 0.001937
Sensitivity
1.0
0.8
0.6
0.4
0.2
0.0
0.0 0.2 0.4 0.6 0.8 1.0
1 - Specificity


ROC of N-acetyl-b-D-glucosaminidase activity
Area 0.8095
Std. Error 0.1062
95% confidence interval 0.6014 to 1.018
P value 0.02804
Sensibility
1.0
0.8
0.6
0.4
0.2
0.0
0.0 0.2 0.4 0.6 0.8 1.0
1 - Specificity