Gut microbiota analysis in preeclampsia with fetal growth restriction

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Objective. Some forms of preeclampsia (PE) present a strong link with metabolic diseases; also, gut dysbiosis has been identified for causing metabolic diseases, but the role of gut microbiome in the pathogenesis of hypertensive disorder of pregnancy (HDP) and fetal growth restriction (FGR) remains unknown.

Materials and Methods. We performed a prospective case-control study. 16S and metabolomic analyses were performed by IRCCS Humanitas comparing faecal microbiome and metabolome of HDP or isolated FGR (iFGR) and normotensive pregnant women.

Results. We recruited six preeclamptic patients with fetal growth restriction (HDP-FGR), 12 HDP, 19 iFGR and 12 controls. Through the alfa and beta diversity analysis, we observed that the HDP-FGR group separated from the others ($p = 0.003$). At the analysis of the phylum, only the iFGR group showed a reduction in terms of *Firmicutes* bacteria both compared to HDP-AGA and to the healthy pregnant population ($p < 0.001$). Regarding the genus, in the HDP-FGR group, in particular *Ruminococcaceae* and *Sellimonas* were enriched, while *Clostridia*, and *Dorea* were markedly depleted. In the HDP-AGA group, *Escherichia* and *Streptococcus* were higher, while *Clostridium* were depleted. The iFGR showed a reduction in *Coprobacter* and enriched in *Ruminococcaceae*.

Finally, the metabolomic analysis confirmed the 16S clusterization and suggested metabolomic alterations linked to the carbohydrate metabolism in the HDP-FGR ($p = 0.002$).

Conclusions. This study suggests that the gut microbiome of patients with HDP-FGR is significantly different from a healthy pregnancy and contributes to disease pathogenesis, while this is not the case in the HDP-AGA or iFGR, that is in agreement with the multiple causes of HDP-AGA and iFGR.