the precursor of Vitamin D[25] and corticosteroid hormones, both critical for a healthy pregnancy.[26] In this study, we observed an increase of cholesterol in both groups that was higher in the third quarter of pregnancy. High cholesterol levels in pregnancy were believed to actually give rise to fetal programming for atherogenesis.[27]

Solomon *et al*.[28] found that pregnant women with high cholesterol levels and elevated insulin levels were more likely to develop pregnancy-induced hypertension or preeclampsia.

In our study, although cholesterol and triglycerides increased in both groups, the increase was more noticeable in triglycerides. As published previously, triglyceride levels increase up to three times as long as the pregnancy progresses through the third quarter.[5] Similar results were obtained in this study, suggesting changes in lipid metabolism, which may be accompanied by functional and morphological changes in adipocytes.

In our approach, we found no different methylation index in any case. In fact, all samples were found to be U3. Previous efforts have been performed to analyze the methylation changes in several genes, including PPARγ, with contrasting results.[29,30] Data from Jacoby *et al*.[31] suggest that inter-individual variability and co-regulation of DNA methylation differ among blood cell populations. It is noteworthy that each author might choose a different region of the same gene to be analyzed. The diet program during pregnancy should also be considered because strict diet supervision guaranteed adequate portions of methionine, folic acid, and Vitamin B12, all with a known role in preventing methylation disequilibrium.

The available information is overwhelming, in showing that the PPARγ2 promoter is particularly sensitive to nutritional changes.[32,33] Even more, animal models have shown that offspring of diet-induced obese dams have altered mRNA expression of PPARγ.[34,35] Thus, methylation status is one of the epigenetic changes that can explain maternal programming of metabolic syndrome-related phenotypes,[36] but further work is required to define the role of PPARγ.

It cannot be ruled out that the enzymatic activity in each tissue is of paramount importance because the profile of methylation observed in leukocytes might be different from fat tissue, which is directly involved in metabolic balance and obesity.

Finally, despite the great efforts invested in explaining some possible factors that predispose to obesity genetically and epigenetically, a single locus has not yet been identified as being entirely responsible for this pathology. Whether epigenetic reprogramming that operates during oocyte formation and in the initial stages of embryogenesis[37] is involved in the obesity transgenerational inheritance has not been clarified. The current trend, given the advances in molecular biology presented in the last few years, is to search for Genome-wide associations, which can provide a better understanding of the pathology of obesity and transgenerational health consequences.[38]

A limitation of this study is the evaluation of a sole promoter region, but the negative results in mothers and babies for a methylated status points out the relevance of evaluating other PPARγ promoter regions that could be useful in the maternal programming of metabolic diseases on the fetus. A significant edge of our work is the fact that while most of the studies related to the PPAR methylation have been performed in solid organ tissues,[39,40] the analysis in neonatal blood, as we did, is scarce.[30]

Conclusion

While further work is required to define in detail the epigenetic changes induced by obesity in pregnancy, our results show that the PPARγ promoter region (−359 to − 260) is unlikely to be easily methylated in peripheral leukocytes in this physiological weight gain condition.

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Conflicts of interest

There are no conflicts of interest.

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