Contribution of the exome sequencing in the context of prenatal diagnosis in our environment
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Objective
Nowadays prenatal genetic tests open up a range of diagnostic possibilities which can guide pregnancy management. Genetic diagnosis has advanced rapidly and chromosomal microarray has become widely used, in addition to conventional karyotype. Exome sequencing may provide an even higher detection rate of genetic anomalies. The objective is to review the exome sequencing performed recently in our hospital.

Methods
We performed a descriptive analysis, collecting results of patients from the Hospital Universitario de San Juan in Alicante (Spain), who underwent an exome sequencing between 2019 and 2021. This exome was requested due to findings in obstetric ultrasound (major malformations and early-onset intrauterine restrictive growth) with previous normal results of karyotype and chromosomal microarray.

Results
We collected data from twelve patients. Five of them had shortened fetal long bones, three major cardiac abnormalities, two early-onset intrauterine growth restriction, two cases of renal malformation and a case with multiple abnormal ultrasound findings. Among these five patients with shortened fetal long bones, abnormal results in the exome sequencing were observed in three of them. In one of them, the foetus presented a heterozygous mutation of the THRA gene related to autosomic dominant skeletal anomalies. In the second patient a pathogenic variant in the EIF2AK3 gene was found, related to Wolcott-Rallison syndrome. In the third patient with pathogenic results, a set of anomalies in the ultrasound were observed (shortened fetal long bones, cerebral ventriculomegaly, lissencephaly and right ventricular hypertrophy). The exome sequencing showed a pathogenic variant in the RBM10 gene related to TARP syndrome. In one of the two cases of renal malformation, renal dysplasia was observed which turned out to have a pathogenic variant on the HNF1B gene related to renal disfunction. The other one had findings compatible with polycystic kidney syndrome and/or genitourinary malformation, which finally had normal results in the exome sequencing. No pathogenic variant was observed in the exome sequencing from the patients with cardiac abnormalities and these with isolated early-onset intrauterine growth restriction.

Conclusion
In conclusion, our experience shows how the exome sequencing in prenatal diagnosis of different malformations and early-onset growth restriction can provide more information and diagnose rare genetic diseases that would not have been detected in routinely requested genetic studies.