Abstract title:
Cumulative live birth rates in women with poor ovarian response (POR) meeting the Bologna criteria: the importance of the phenotype

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Study question:
Does reproductive outcome differ among the various types of women with poor ovarian response (POR) meeting the Bologna criteria?

Summary answer:
Live birth rates (LBR) and cumulative LBR differ significantly among Bologna POR patients

What is known already:
In 2011, the European Society of Human Reproduction and Embryology (ESHRE) elaborated on the definition of women with inadequate response to ovarian stimulation. This consensus definition—known as the Bologna criteria—was initially introduced with the primary objective of standardising the definition of POR. However, the Bologna criteria may have merged various patient categories with potentially different prognosis. Evidence regarding the reproductive outcome of different categories of patients is sparse.

Study design, size, duration:
This was a retrospective cohort analysis carried out at a university based tertiary centre aiming to evaluate cumulative LBR in different categories of Bologna POR. All Bologna POR patients who underwent ovarian stimulation for ART using a GnRH-antagonist protocol from 1st January 2011 until 31st December 2017 were included in the study.

Participants/materials, setting, methods:
Women were divided in four categories according to their Bologna criteria pattern: group A women ≥ 40 years with an abnormal ovarian reserve test; group B women ≥ 40 years with an abnormal ovarian reserve markers and one previous cycle with poor response; women in group C were ≥ 40 years and had one previous cycle with poor response; group D patients with an abnormal ovarian reserve test and one previous cycle with poor response.

Main results and the role of chance:
In total 846 cycles in 706 Bologna POR patients were included in the analysis: 310 cycles in group A, 169 in group B, 52 in group C and 315 in group D. There were significant differences in female age, antral follicle count, antimüllerian hormone, cycle cancellation rates and number of retrieved oocytes between
the four groups. LBR and cumulative LBR differed significantly between groups and were highest in Group D (LBR: 7.4% (A) vs. 4.1% (B) vs. 5.8% (C) vs. 13.4% (D), p = 0.001 and CLBR: 8.3% (A) vs. 4.1% (B) vs. 9.6% (C) vs. 16.8% (D) p < 0.001). In particular, the p values for the unadjusted cumulative LBR between groups were as followed: Group B vs A (p = 0.15), Group C vs A (p = 0.9), Group D vs A (p < 0.001), Group C vs B (p = 0.2), Group D vs B (< 0.001), Group D vs C (p = 0.08). A multivariate regression model accounting for relevant confounders demonstrated that the Bologna criteria pattern was an independent predictor of cumulative LBR (coefficients Group (A): reference group, Group (B): -0.6, Group (C): 0.05, Group (D): 0.8, p value < 0.001). The number of oocytes retrieved was also significantly associated with cumulative LBR.

Limitations, reasons for caution:
The retrospective study design should be taken into consideration when interpreting these results.

Wider implications of the findings:
POR represent a heterogeneous population with distinct clinical prognosis. This is the first study evaluating cumulative LBR in the different Bologna criteria patterns.

Trial registration number:
Not applicable

Keywords:
poor responder
Bologna criteria
GnRH-antagonist protocol