

ABSTRACT

Objective: To investigate the prevalence of empty follicle syndrome (EFS), a condition in which no oocytes were retrieved after ovarian stimulation, categorized into genuine EFS (g-EFS) and false EFS (f-EFS), at the King Chulalongkorn Memorial Hospital (KCMH), Thailand.

Materials and Methods: A retrospective study was conducted at the infertility clinic of the KCMH. Medical records of the reproductive technology (ART) patients from January 2001 to October 2019 (5,523 patients) were reviewed. Exclusion criteria were the cases where ovulation occurred before oocyte retrieval or the cases with < 4 follicles larger than 14 mm diameter (to minimize the absence of oocyte from the poor response) on the day of triggering ovulation. The patients with EFS, genuine EFS (g-EFS), EFS with detectable urinary human chorionic gonadotropin (hCG), and false EFS (f-EFS), EFS with undetectable urinary hCG, were identified. Prevalence of EFS was calculated.

Results: There were 3 cases with EFS in this study, g-EFS was identified in 1 case and f-EFS in 2 cases. The prevalence of EFS was 0.054 %, g-EFS was 0.018% and f-EFS was 0.036 %.

Conclusion: Empty follicle syndrome is a rare condition, particularly the g-EFS. Although EFS is rare, it causes tremendous stress and anxiety to both the patients and physicians. Further study in the etiopathogenesis of EFS is required.

MATERIALS AND METHODS

A retrospective study was conducted at the infertility clinic of the KCMH. Medical records of the reproductive technology (ART) patients from January 2001 to October 2019 (5,523 patients) were reviewed. Exclusion criteria were the cases where ovulation occurred before oocyte retrieval or the cases with < 4 follicles larger than 14 mm diameter (to minimize the absence of oocyte from the poor response) on the day of triggering ovulation. The patients with EFS, genuine EFS (g-EFS), EFS with detectable urinary human chorionic gonadotropin (hCG), and false EFS (f-EFS), EFS with undetectable urinary hCG, were identified. Prevalence of EFS was calculated.

RESULTS

There were 3 patients included in the analysis. All three patients underwent the GnRH antagonist ovarian stimulation protocol (Fig. 1). Urine β -hCG on the day of oocyte retrieval was not detected in 2 patients. These 2 cases were diagnosed with f-EFS. Only one patient had detectable urine β -hCG and was diagnosed with g-EFS.

The overall prevalence of empty follicle syndrome in the KCMH was 0.054 %. The prevalence of f-EFS was 0.036 % and g-EFS was 0.018%. Baseline characteristics of the patients with empty follicle syndrome are described in Table1.

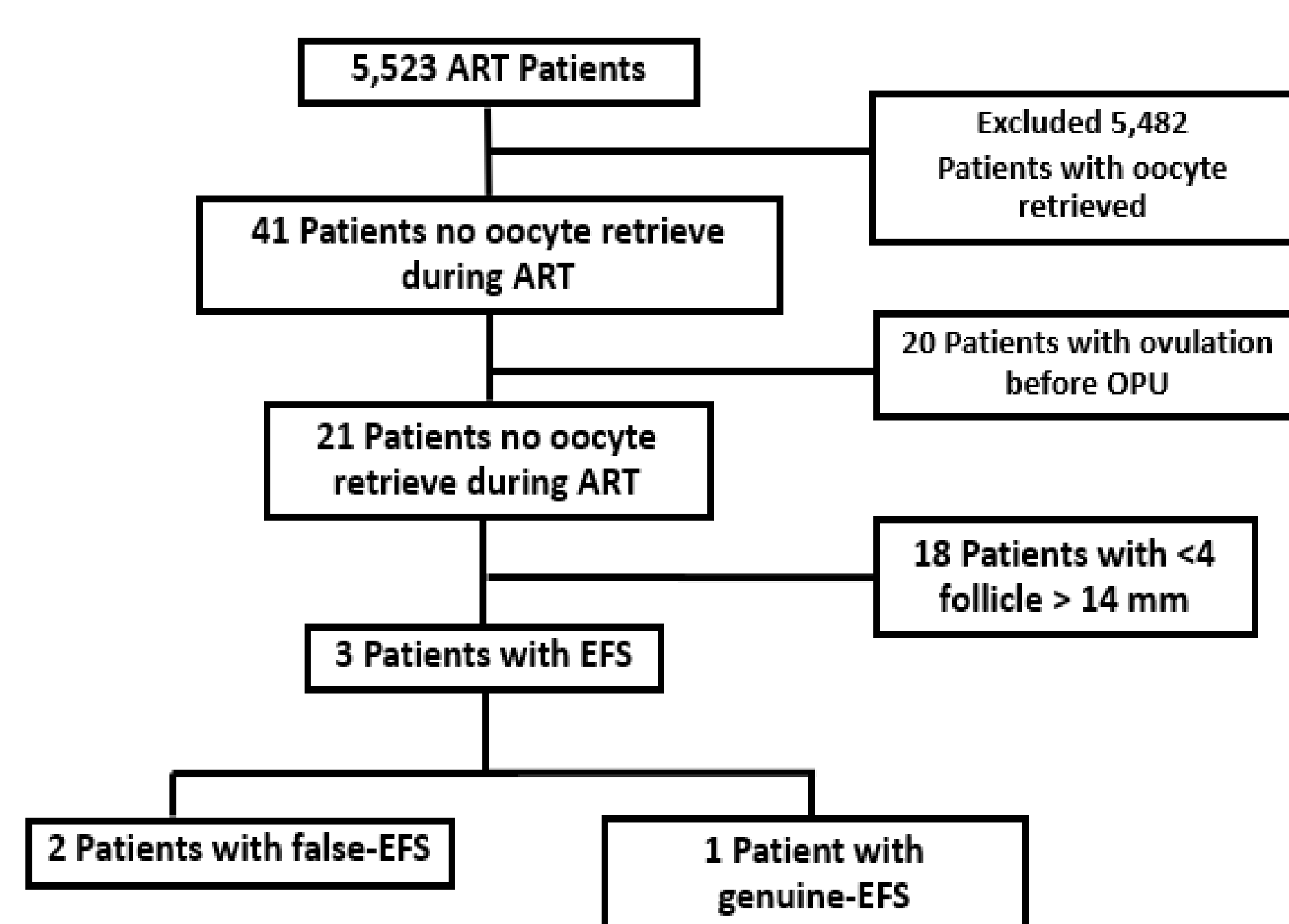


Fig. 1 Diagram of the study
EFS; Empty follicle syndrome, ART; Assisted reproductive technology

Table 1. Baseline characteristic of patients with Empty follicle syndrome (EFS)

	False-EFS		Genuine-EFS
	Case1	Case2	
Age (years)	44	45	45
BMI (kg/m ²)	24.2	21.2	19.8
Infertility Etiology	Advanced age	Tubal factor	Advanced age
Total days of stimulation	8	8	9
Total dose gonadotropin (IU)	2000	2400	2950
No. of follicles on hCG triggering 4 day		9	4
Size of follicles (mm)	19,17,15,15	20,19,18,16,16, 15,15,15,15	20,18,16,15
Peak Estradiol level (pg/mL)	816	1462	1416
LH level on hCG triggering day (IU/L)	9.9	4.2	9.0
Day 2 FSH level (IU/L)	5.5	6.2	5.0

EFS, Empty follicle syndrome; BMI, Body mass index; FSH, Follicle stimulating hormone; LH, Luteinizing hormone; hCG, Human chorionic gonadotropin

CONCLUSIONS

In conclusion, EFS is a rare condition, particularly the g-EFS. Only one patient with g-EFS in the review of 5,523 patients was identified, supporting the conclusion that empty follicle syndrome is a rare phenomenon.. Although EFS is rare, it causes tremendous stress and anxiety to both the patients and physicians. Further study in the etiopathogenesis of EFS is required.

REFERENCES

1. Revelli A, Carosso A, Grassi G, Gennarelli G, Canosa S, Benedetto C. Empty follicle syndrome revisited: definition, incidence, aetiology, early diagnosis and treatment. *Reprod Biomed Online* 2017;35:132-8.
2. Coulam CB, Bustillo M, Schulman JD. Empty follicle syndrome. *Fertil Steril* 1986;46:1153-5.
3. Ben-Shlomo I, Schiff E, Levran D, Ben-Rafael Z, Mashiah S, Dor J. Failure of oocyte retrieval during in vitro fertilization: a sporadic event rather than a syndrome. *Fertil Steril* 1991;55:324-7.
4. Aktas M, Beckers NG, van Inzen WG, Verhoeff A, de Jong D. Oocytes in the empty follicle: a controversial syndrome. *Fertil Steril* 2005;84:1643-8.
5. Stevenson TL, Lashen H. Empty follicle syndrome: the reality of a controversial syndrome, a systematic review. *Fertil Steril* 2008;90:691-8.
6. Mesen TB, Yu B, Richter KS, Widra E, DeCherney AH, Segars JH. The prevalence of genuine empty follicle syndrome. *Fertil Steril* 2011;96:1375-7.

ACKNOWLEDGEMENT

We would like to sincerely thank the staff of the Infertility Unit, Division of Reproductive Medicine, Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University, for supporting the present study. We also wish to thank Ms. Pranee Numchaisrika and Ms. Panitta Luangteang for their helps in data collection.

CONTACT

Chanakarn Suebthawinkul, MD: Chanakarn.su@chula.ac.th