

BACKGROUND

Gonadotropin is commonly administered during IVF cycles. The number of oocytes were positively correlated with FSH dose, but the correlation between FSH dose and live birth rate were not clear and conflicted result in some study.

OBJECTIVE

This study to investigated the correlation between total dose of FSH and cumulative live birth rate (cumulative LBR) of patient who underwent IVF/ICSI with GnRH antagonist and expected normal response.

PATIENTS AND METHODS

A retrospective study conducted at IVFMD, My Duc Hospital, Ho Chi Minh City, Viet Nam from January 2016 to September 2018. Live birth was defined as one complete expulsion from a woman of a product of fertilization, after 22 completed weeks of gestational age with any evidence of life. All patients had ovarian stimulation using GnRH antagonist protocol. Egg-donor, surrogacy, poor responder following Bologna criteria, PCOS and uterus congenital anomalies were excluded from the study. Cumulative LBR was calculated by including all fresh and frozen transfer of embryos derived from one stimulated IVF/ICSI cycles.

ENDPOINTS

Main outcome was cumulative live birth rate after one complete cycle, defined as the chance of having ongoing pregnancy after all fresh and frozen transfers of embryos derived from one stimulated cycle.

RESULTS

Overall, seven-thousand one-hundred and thirty patients were enrolled in the study.

Table 1. Patient's characteristics.

Characteristics	N = 7130
Age (year)	32.74 ± 4.63
BMI (kg/m ²)	21.01 ± 2.31
AMH (ng/mL)	3.89 ± 2.85
AFC (n)	15.95 ± 22.32
Infertility duration (year)	4.72 ± 3.43
Infertility causes (%)	
– Primary	4082 (57.3%)
– Secondary	3048 (42.7%)
Number of underwent IVF cycles (%)	
– First cycle	5188 (72.8%)
– Second cycle	1329 (18.6%)
– Third cycle and more	613 (8.6%)
IVF indication (%)	
– Male factor	2658 (37.3%)
– Diminished ovarian reserve	1625 (22.8)
– Tubal damages	1446 (20.3%)
– Unexplained reasons	1230 (17.3%)
– Recurrent Miscarriage	55 (0.8%)
– Others	116 (1.6%)

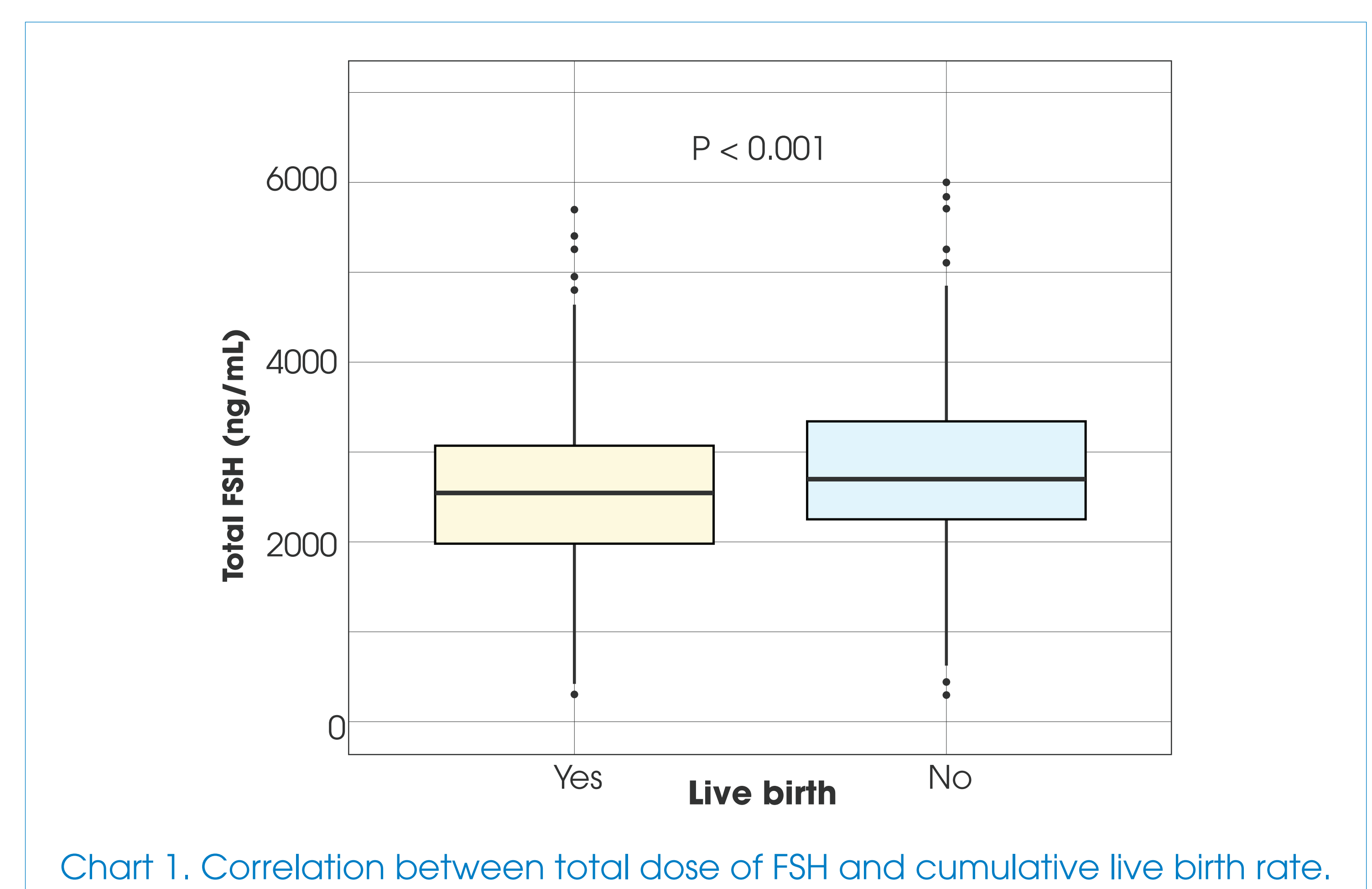
Table 2. Treatment cycle's characteristics.

Characteristics	N = 7130
Duration of stimulation (n)	8.84 ± 1.56
Total FSH dosage (IU)	2659.55 ± 863.07
Number of oocyte retrieval (n)	13.08 ± 7.03
Number of matured oocytes (n)	10.41 ± 6.02
FSH/matured oocyte rate (IU)	392.40 ± 382.90
Number of fertilized (n)	8.81 ± 5.30
Fertilization rate (%)	85.00 ± 14.77
Number of embryos (n)	5.99 ± 3.70
Number of good embryos (n)	3.72 ± 2.90
Number of frozen embryos (n)	3.58 ± 2.58
Number of transferred embryos (n)	2.00 ± 0.45
Day of transferred embryos (%)	
– Day- 3	5200 (72.9%)
– Day- 5	1930 (27.1%)

Table 3. Clinical outcomes.

Outcome	N = 7130
Pregnancy rate (%)	4290 (60.2%)
Clinical pregnancy rate (%)	3568 (50.0%)
Ongoing pregnancy rate (%)	3065 (43.0%)
Live birth rate (%)	3032 (42.5%)
Miscarriage rate (%)	623 (8.7%)
Ectopic pregnancy rate	153 (2.1%)
Multiple pregnancy rate	1159 (16.3%)

There was negative correlation between Cumulative LBR and total of FSH and FSH/oocyte ($r = -0.06$ (95%CI -0.11, -0.02); $p = 0.004$ and $r = -0.17$ (95%CI -0.19, -0.14); $p < 0.001$).



DISCUSSION

Total dose of FSH from our study (2659.55 ± 863.07 IU) were the same as study from Hamamah et al (2658 ± 1064 IU) and higher than study from Munch et al (2350 IU). Our study, there was negative correlation between Cumulative LBR and total of FSH ($r = -0.13$ (-0.15, -0.10); $p < 0.001$). This result was the same from work published by Hamamah et al. Baker et al reported that a negative correlation between total dose of FSH and live birth rate in fresh cycle. In study from Much et al, fresh LBR was negatively impacted by a high dose of total FSH used. However, frozen transfer LBR seemed unaffected by the total FSH dose used in the fresh cycle. The main limitation of this study is its study design.

CONCLUSION

Cumulative live birth rate decreased with increasing total FSH dose. Our analysis suggests that physicians may wish to avoid prescribing a high dose of FSH, particularly for women predicted to have a normal response.

REFERENCES

- BungZhao, Z., Shi, H., Li, J., Zhang, Y., Chen, C., & Guo, Y. (2020). Cumulative live birth rates according to the number of oocytes retrieved following the "freeze-all" strategy. *Reproductive Biology and Endocrinology*, 18(1), 1-8.
- Vuong, L. N., Dang, V. Q., Ho, T. M., Huynh, B. G., Ha, D. T., Pham, T. D., ... & Mol, B. W. (2018). IVF transfer of fresh or frozen embryos in women without polycystic ovaries. *New England Journal of Medicine*, 378(2), 137-147.
- Chen, Z. J., Shi, Y., Sun, Y., Zhang, B., Liang, X., Cao, Y., ... & Tian, L. (2016). Fresh versus frozen embryos for infertility in the polycystic ovary syndrome. *New England Journal of Medicine*, 375(6), 523-533.
- Pal, L., Jindal, S., Wilt, B. R., & Santoro, N. (2008). Less is more: increased gonadotropin use for ovarian stimulation adversely influences clinical pregnancy and live birth after in vitro fertilization. *Fertility and sterility*, 89(6), 1694-1701.
- Sterrenburg, M. D., Veltman-Verhulst, S. M., Eijkemans, M. J. C., Hughes, E. G., Macklon, N. S., Broekmans, F. J., & Fauser, B. C. J. M. (2010). Clinical outcomes in relation to the daily dose of recombinant follicle-stimulating hormone for ovarian stimulation in in vitro fertilization in presumed normal responders younger than 39 years: a meta-analysis. *Human reproduction update*, 17(2), 184-196.
- Xu, H., Deng, K., Luo, Q., Chen, J., Zhang, X., Wang, X., ... & Zhang, C. (2016). High serum FSH is associated with brown oocyte formation and a lower pregnancy rate in human IVF practice. *Cellular Physiology and Biochemistry*, 39(2), 677-684.
- Baker, V. L., Brown, M. B., Luke, B., Smith, G. W., & Ireland, J. J. (2015). Gonadotropin dose is negatively correlated with live birth rate: analysis of more than 650,000 assisted reproductive technology cycles. *Fertility and sterility*, 104(5), 1145-1152.
- Munch, E. M., Sparks, A. E., Zimmerman, M. B., Van Voorhis, B. J., & Duran, E. H. (2017). High FSH dosing is associated with reduced live birth rate in fresh but not subsequent frozen embryo transfers. *Human Reproduction*, 32(7), 1402-1409.
- Hamamah, S., Avril, C., & POULY, J. (2017). r-FSH total dose is negatively associated to live birth rate: a retrospective analysis. *Fertility and Sterility*, 108(3), e22.

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