Optimizing estrogen level in women at reproductive age prior to start controlled stimulation (CO) for ART

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Introduction

Female reproductive health relies on the proper development of the follicle, the fundamental unit of the ovary.

As waves of follicles grow, they produce sex steroid hormones that regulate maturation in an autocrine/paracrine manner, supply endocrine feedback that sets the tempo of each reproductive cycle, prepare the reproductive tissues for pregnancy, and regulate bone, cardiovascular, and metabolic health.

steroid hormones form an integral part of normal development in mammalian organisms. Cholesterol is the parent compound from which all steroid hormones are synthesized. The product pregnenolone formed from cholesterol serves as precursor for mineralocorticoids, glucocorticoids, as well as dehydroepiandrosterone (DHEA) and its derived sexual hormones. DHEA assumes the prohormone status of a predominant endogenous precursor and a metabolic intermediate in ovarian follicular steroidogenesis. DHEA supplementation has been used to enhance ovarian reserve. Steroids like estradiol and testosterone have long been contemplated to play important roles in regulating meiotic maturation of oocytes in conjunction with estrogen is necessary to develop calcium (Ca2+) oscillations during maturation.

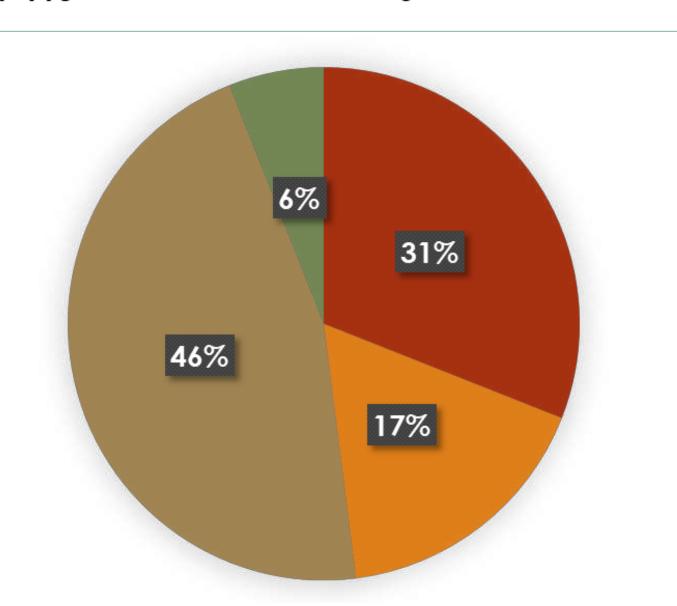
Accruing evidence from diverse studies suggests that DHEA and its sulfate (dehydroepiandrosterone sulfate, DHEA-S) play significantly vital role not only as intermediates in androgen and estrogen formation, but may also be the probable 'oocyte factor' and behave as endogenous agonists triggering calcium oscillations for oocyte activation. DHEA/DHEA-S have been reported to regulate calcium channels for the passage of Ca2+ through the oocyte cytoplasm and for maintaining required threshold of Ca2+ oscillations.

This role of DHEA/DHEA-S assumes critical significance in assisted reproductive technology and in-vitro fertilization treatment cycles where physical, chemical methods are employed for artificial oocyte activation to enhance fertilization rates.

The aim of this study is to evaluate the estrogen level and its relation to follicle size using ultrasound folliculometry in women seeking pregnancy to start pre-treatment in order to avoid ineffective induction. This was a prospective randomized controlled study, Conducted at the Reproductive unit /alhawari teaching hospital. 100 patients were enrolled in this study with an inclusion criteria of (primary infertility, menstrual cycle abnormality, abnormal day 2 and follicular phase test results, open tube and lastly normal semen analysis of the partner. Treatment was started to the patients in the form of multivitamins and DHEA (Ova Akt) for 3 months. All patients followed up the infertility clinic monthly.

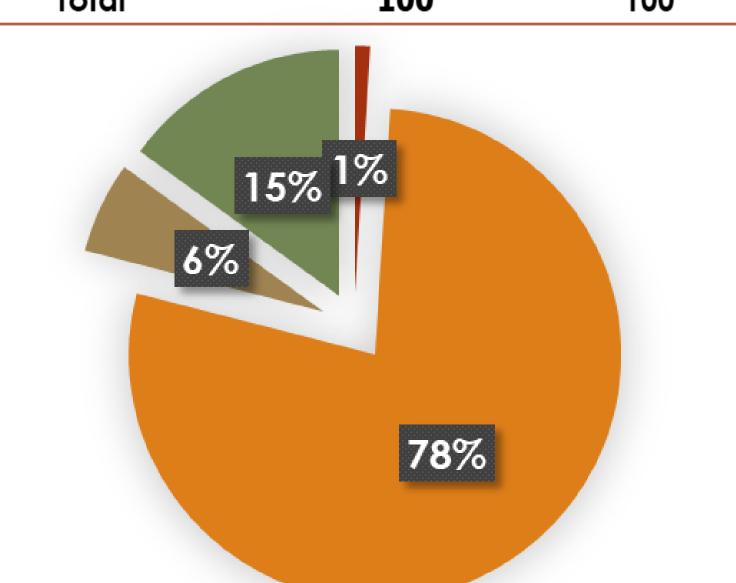
Distribution of patients according to level of estrogen in mid cycle.

Esrogen level	no	
30 -50	31	
51-70	17	
71-90	46	
91-110	6	



Distribution of patients according to level of E2 after treatment.

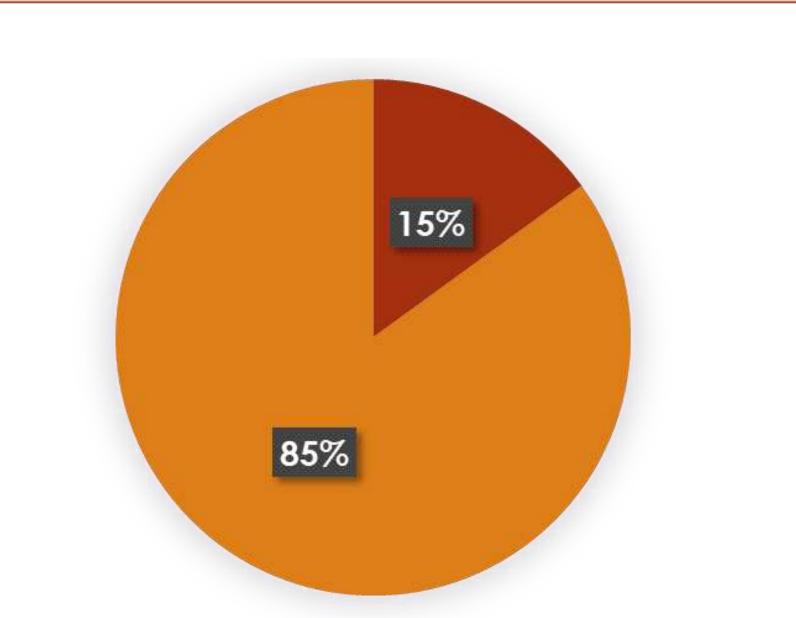
No.	%
1	1
78	78
6	6
15	15
100	100
	1 78 6 15



Results

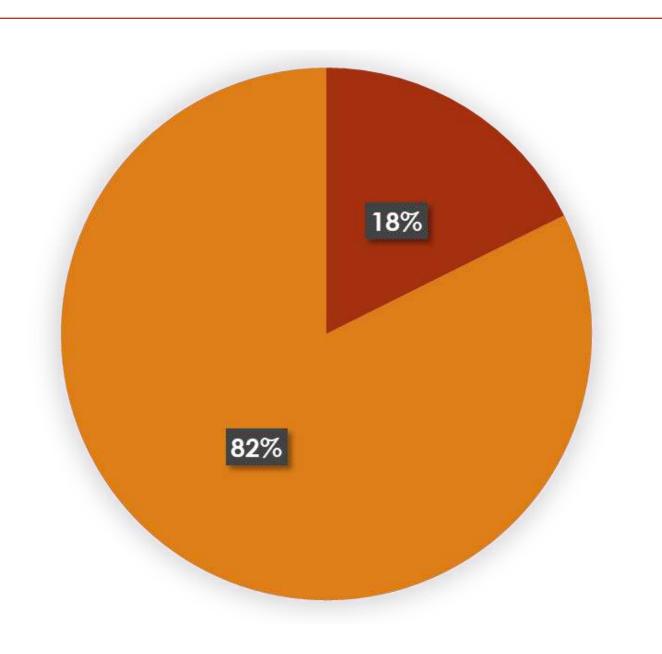
Distribution of patients according to out come of treatment 1

Outcome of treatment.	No.	%
Pregnant	15	15
Not pregnant	85	85
Total	100	100



Distribution of patients according to out come of treatment 2

Assisted tech	No.	%
IUI	15	17
Not done	70	83



Distribution of patients according to out come of treatment 3

no		
5		2207
3	40%	33%
1		
6	7%	20%
	531	5 3 1

Conclusion

In this study we demonstrated potential benefit of DHEA and multivitamin treatment in improving oocyte quality in women with low estrogen level at second day and at follicular phase. Our results demonstrate that pre-treatment with DHEA resulted in significant improvement of oocyte quality and decrease in the total amount of gonadotrophin needed to achieve ovarian response, higher peak E2 levels, shorter duration

The benefits of DHEA and multivitamin supplementation on controlled ovarian stimulation outcomes in patient with low estrogen on day2 and at follicular phase were significant, and the drug combination effects may be partially mediated by improving mitochondrial function and reducing apoptosis of cumulus cells. Our observations may provide a reasonable rationale for clinical uses of drug combination and supplementation in those patient undergoing IVF cycles to improve clinical outcomes.

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