STUDY OF *CTNNB1* SOMATIC MUTATIONS IN EARLY STAGE ENDOMETRIAL CANCER IN A COHORT OF EGYPTIAN PATIENTS

Nermine Hossam ELDin Zakaria, Eman Tayae Desouky, Samar Nabil El Achy*, Neamat Elsayed Elsayed Hegazy**, Asmaa Mostafa Mohamed Ali Salem
Department of Clinical and Chemical Pathology, Department of Pathology*, Department of Clinical Oncology and Nuclear medicine**, Faculty of Medicine, Alexandria University

Introduction

Endometrial cancer is the sixth most prevalent cancer among women and the thirteenth cause of mortality in women worldwide. It is the eighth most prevalent cancer in women in Egypt and the fifteenth cause of mortality in women in Egypt. Endometrioid endometrial carcinoma is the most common type (70%) of endometrial cancer. Most patients diagnosed at an early stage had good prognoses. However, some individuals with low-grade, low-stage cancers experience recurrence. Prediction of recurrence in those patients is crucial to improve prognosis. *CTNNB1* gene mutation is suggested to be associated with endometrial cancer recurrence. *CTNNB1* encodes beta-catenin protein. β-catenin is an important mediator in the Wnt/β-catenin signaling pathway. *CTNNB1* exon 3 mutations activate the canonical Wnt/β-catenin signaling pathway, leading to development of cancer.

Aim of the work

The aim of the present study was to study *CTNNB1* exon 3 somatic mutations in early stage endometrial cancer in a cohort of Egyptian patients.

Subjects and Methods

SUBJECTS: This study was conducted on 40 patients with early stage (stage I&II) endometrioid endometrial carcinoma presented to clinical oncology Department at Alexandria University Hospital. Patients were further divided into two groups; recurrent Group (20 patients with recurrent endometrial cancer who developed metastasis or insitu recurrence) and non recurrent group (20 patients with early stage endometrioid endometrial carcinoma with no recurrence after remission). Formalin fixed paraffin embedded (FFPE) samples were obtained from the Pathology departments at Alexandria University.

METHODS: *CTNNB1* exon 3 mutations were detected using Sanger sequencing (Applied Biosystems 3500 Genetic analyzer) (Thermo Fisher Scientific, USA).

Results

Patients with recurrent endometrial cancer showed a significant higher rate of *CTNNB1* exon 3 mutations than non recurrent group with *P* value = 0.011. Patients harbouring *CTNNB1* exon 3 mutations had 5 folds increased risk of recurrence than patient without mutation.

Table 1: Comparison between the two studied groups according to *CTNNB1* exon 3 mutations

	Recurrent group (n = 20)		Non recurrent group (n = 20)		X^2	p	OR (95%C.I)	p
	No.	%	No.	%				
Mutation								
No	6	30.0	14	70.0	6.400*	0.011*	5.444* (1.42 – 21.1)	0.014*
Yes	14	70.0	6	30.0				

There was no significant association between *CTNNB1* exon 3 mutations and clinicopathological characteristics of the patients.

Table 2: Association between *CTNNB1* exon 3 mutations and clinicopathological characteristics of the patients

	Wild group (n = 20)	Mutated group (n = 20)	p
Age (years)	59.40 ± 10.13	59.95 ± 5.89	0.835
Age of menarche (years)	12.60 ± 1.85	11.85 ± 1.66	0.185
Age of menopause (years)	52.0 ± 2.66	50.94 ± 2.33	0.266
Parity	17 (85%)	16 (80%)	1.000
Family history	3 (15%)	1 (5%)	0.605
History of oral contraceptives use	10 (50%)	10 (50%)	1.000
Obesity	15 (75%)	12 (60%)	0.311
Tumor size	4.05 ± 1.15	3.68 ± 1.62	0.301
FIGO staging I II	20 (100%) 0 (0 %)	18 (90%) 2 (18%)	0.487

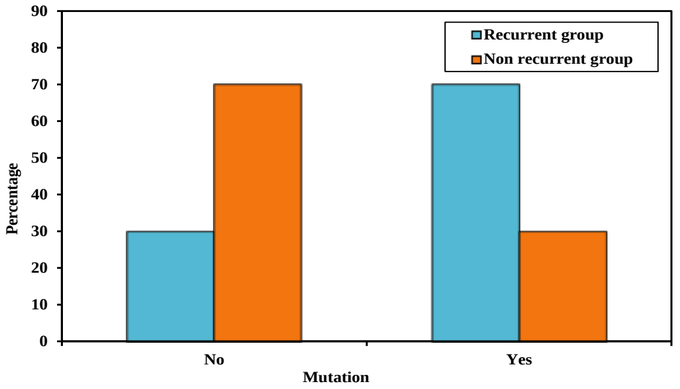

Figure 1 : Comparison between the two studied groups according to *CTNNB1* exon 3 mutations

Conclusion

- *CTNNB1* exon 3 mutations might be a risk factor for endometrial cancer recurrence.
- Sanger sequencing is an effective method for detection of genetic variants of *CTNNB1* gene