

ASSESSMENT OF LAG3 AND GALNT11 GENE EXPRESSION IN PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA AND THEIR IMPACT ON DISEASE PROGRESSION

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ABSTRACT : Chronic lymphocytic leukemia (CLL) is the most common type of leukemia among adults in Western countries. Interestingly, LAG3 expression was recently suggested as a prognostic marker in patients with CLL, as gene expression profiling of CLL cells detected increased LAG3 expression levels that were in correlation with *UM-IGHV* and with reduced treatment-free survival. The enzymes encoded by the *GALNT* gene family catalyze the first step of O-glycosylation. Little is known about the link between expression of the genes encoding GALNAC-T enzymes and tumor progression, including CLL that can be classified as either low or high risk. The aim of the study is to determination of level genes LAG3 and GALNT11 expression in CLL patients and relationship with progression of disease. This is cohort prospective study was carried out between December 2018 and December 2019 at medical city complex in Baghdad, Iraq. This is conducted on 70 patients with CLL and 40 healthy person as controls group. Patients groups was divided into 2 group: first group included 38 patients before receiving treatment, second group included 32 patients post treatment. Diagnosis was based on lymphocyte count of $> 5 \times 10^9/L$ and Immunophenotyping. Measurement of level of gene expression the LAG3 and GALNT11 genes by RT-PCR. Quantitative RT-PCR assay analyzed the mRNA expression of *LAG3* and compared its expression between apparently control group, pretreatment group and post treatment group. There were 53 male and 17 female, the mean age was 59.12 ± 14.23 . The gene expression was significantly higher in pretreatment group than control group, 6.58 times. Fold number in post treatment group was 2.31 times then the control group, Fold number in pretreatment group was 2.84 times then the post treatment group. The fold of gene expression in pretreatment group was higher than control group in 49.35 times. Fold number in post treatment group was 2.83 times a control group. This gene have effect on progression of CLL disease and as marker for response to treatment. In conclusion, the expression of LAG3 and GALNT11 genes were associated with progressive disease and poor response to therapy.

Key words : LAG3, GALNT11, CLL.

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INTRODUCTION

Chronic Lymphocytic Leukemia (CLL) is the most common type of leukemia among adults in Western countries (Kawa, 2018). The clinical course of CLL is highly variable, ranging from no symptoms to the rapid development of features of high-risk disease. Lymph node swelling is the most common presenting feature of CLL, although fever, night sweats and weight loss are sometimes seen. The most common physical findings are lymphadenopathy, splenomegaly and, less frequently, hepatomegaly (Abbott, 2006). Both the modified Rai and Binet clinical staging systems are widely used to classify CLL patients into different prognostic groups according

to the extent of lymph node involvement, enlargement of the liver and/or spleen and blood findings (*i.e.* anemia and thrombocytopenia) (Ali *et al*, 2020). Interestingly, LAG3 expression was recently suggested as a prognostic marker in patients with CLL, as gene expression profiling of CLL cells detected increased LAG3 expression levels that were in correlation with *UM-IGHV* and with reduced treatment-free survival (Kotaskova *et al*, 2012). The enzymes encoded by the *GALNT* [UDP-*N*-acetyl—D-galactosamine: polypeptide *N*-acetylgalactosaminyltransferase (GALNAC-T)] gene family catalyze the first step of O-glycosylation. Little is known about the link between expression of the genes