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**Single Nucleotide Polymorphism 45T/G of Adiponectin Gene
in Egyptian Patients with Leukemias**

**A Thesis submitted in partial fulfillment of the requirements for the
degree of Master of Science**

In

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SUMMARY AND CONCLUSION

Leukemia is a group of cancers that usually begin in the bone marrow and result in high numbers of abnormal white blood cells. These white blood cells are not fully developed and are called blasts or leukemia cells. Symptoms may include bleeding and bruising problems, feeling tired, fever, and an increased risk of infections.

Leukemia can be divided into multiple subtypes. The first separates leukemias into acute and chronic forms, the second is based on which kind of blood cell is affected, leading to lymphoblastic and myeloid leukemias. The above two divisions lead to a total of four major subtypes: ALL (acute lymphoblastic leukemia), CLL (chronic lymphoblastic leukemia), AML (acute myeloid leukemia), and CML (chronic myeloid leukemia).

Adipokines have been shown to regulate the survival, proliferation, differentiation and function of normal hematopoietic and leukemic cells. Two adipokines, leptin and adiponectin in particular, have come to be recognized for their influence on tumor biology.

In leukemia it was shown that adiponectin levels were significantly lower in both AML and ALL patients as compared to healthy controls. The Adiponectin protein is found in a high concentration in the blood, accounting for approximately 0.01-0.05% of total serum protein. Four domains including a total of 247 amino acids make up adiponectin including an amino-terminal signal sequence, a variable region, a collagenous domain, and a carboxyterminal globular domain (called "globular adiponectin"). Adiponectin is present in serum and plasma in several of these higher order forms including as a trimer, a hexamer (which consists of two trimers bonded in a head-to-head manner via disulphide bond) and as higher-order structures called high molecular weight (HMW) adiponectin.

The human adiponectin gene, known as ADIPOQ, has been identified and is located on chromosome 3q27. ADIPOQ is approximately 17,000 base pairs in length and consists of three exons and two introns.

Two adiponectin receptors have been identified to date, AdipoR1 and AdipoR2. These receptors are found in the cell membrane and are located throughout the body in liver, muscle, and adipose tissue although AdipoR1 is found predominantly in muscle cells while AdipoR2 is primarily found in the liver.

SNPs are changeable sites within a genome, occurring once every 1000-2000 nucleotides, where the rarer nucleotide is present at a frequency of greater than one percent in a population. These genetic variations alter protein structure and function when the nucleotide base substitution occurs in a gene's coding region.

There are three primary regions of the ADIPOQ gene that contain genetic variants associated with plasma adiponectin levels and other diseases. Those regions are located in the 5' sequence, the exon 2 and intron 2 region, and exon 3. Among the many SNPs identified in the ADIPOQ gene, the focus of many studies has been on four SNPs, rs17300539 (-11391G > A) and rs266729 (-11377C > G) located in the 5' promoter of the gene, rs2241766 (+45T > G) located in exon 2, and rs1501299 (+276G > T) located in intron 2 of ADIPOQ.

Aim of our study:

So, the aim of the present work was studying Single Nucleotide Polymorphism 45T/G of Adiponectin Gene in Egyptian Patients with Leukemias.

This study included: Group1: Involved 20 healthy volunteers clinically free from any disease (controls group), their mean age was 33.25 years and were chosen randomly.

Group2: Involved 80 newly diagnosed as leukemia patients.

Controls in group I were of matched age as the patients group recruited from Hematology department, MRI, Alexandria University and hematology unit, Faculty of Medicine, Alexandria University. An informed consent was taken from all contributors in this study.

Results of the study revealed that:

- There was statistically significant difference between patients and controls regarding weight and BMI ($P = 0.031, 0.001$) respectively
- Statistical significant difference was found between patients and controls regarding to hemoglobin, platelets and white blood cells, ($P = 0.002, 0.0001, 0.0001$) respectively.
- A statistical significant difference between patients and controls regarding Fasting blood sugar level ($P = 0.001$).
- A statistical significant difference between patients and controls regarding Uric. acid ($P = 0.000$).
- A statistically significant difference was found between the two studied groups regarding albumin ($P = 0.000$).
- There was a statistical significant difference was found between the two studied groups regarding TG, HDL-C, TC/HDL ratio and LDL/HDL ratio ($P = 0.024, 0.000, 0.000, 0.002$) respectively
- The frequency (prevalence) of T allele is more frequent in healthy person compared to leukemic patients, while G allele is more frequent in Leukemia patients than in healthy persons ($P < 0.005$). Our result is consistent with major studies which documented that T allele is more frequent in healthy person while G allele is more frequent in metabolic disorders and diseases compared to healthy person.
- T-allele frequency was significantly lower (77.5%) in patients compared to 92.5% in controls individuals. On the other hand, G -allele frequency was significantly higher (22.5%) in patients compared to 7.5% in controls.
- The G allele frequency at the 45TG polymorphism was associated with a higher risk of leukemia [Odds ratio (OR) = 4.02 and Risk Ratio (RR) = 3.68 at 95% confidence interval (CI), $P = 0.032^*$].

- Statistical analysis also showed a significant difference ($p=0.005$) between the patients and controls groups regarding adiponectin gene polymorphism frequencies.
- A statistically significant difference was observed in FBS level and adiponectin polymorphism frequency ($P= 0.013$).
- On the other hand a significant differences was observed between adiponectin polymorphism in relation to lipid profile regarding HDL-C.

Conclusions:

- The present data revealed an association between adiponectin 45T/G polymorphism and risk of developing leukemia in Egyptian population.
- Regarding leukemia subtypes the mutant genotypes (TG+GG) was most frequent in CML patients.