شبكة المعلومات الجامعية

التوثيق الإلكتروني والميكروفيلم

# بسم الله الرحمن الرحيم


HANAA ALY

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# جامعة عين شمس

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# قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات

# يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار

HANAA ALY

# The Relation between Genetic Variance of Some Selected Genes and Therapeutic Effect of Asparaginase in Childhood Acute Lymphoblastic Leukemia

**For the Partial Fulfillment of the Master Degree of Science in Zoology**


**Submitted By**

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*I declare that this thesis has been composed by myself and the work herein has not been submitted for a degree at this or any other university.*

*Yomna Hesham Youssef*

*To my beloved parents, my inspiration source and who gave me the strength when I thought to give up*

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***Yomna H. Youssef***

## *Abstract*

**Background:** Asparaginase (ASNase) is a key component in the treatment protocols of childhood acute lymphoblastic leukemia (ALL). Asparagine synthetase (ASNS) and the basic region leucine zipper activating transcription factor 5 (ATF5) mediate the anti-leukemic effect of ASNase. Few reports studied the association between polymorphisms in these genes and treatment-related toxicity and response, and the results were controversial. Therefore, the current study aimed to investigate the association of *ASNS* and *ATF5* polymorphisms with the susceptibility to ASNase-related toxicity and disease outcome in a population of childhood ALL Egyptian patients.

**Methods:** In this study, 88 children with ALL were enrolled and genotyped for *ASNS* T629A and *ATF5* C362T polymorphisms using allelic discrimination assay.

**Results:** The studied polymorphisms did not associate with hypersensitivity or thrombosis, while the *ATF5* C362T polymorphism was associated significantly with decreased ASNase-associated pancreatitis (AAP) risk under allelic and dominant models. Patients carrying AA/TA genotypes of *ASNS* T629A polymorphism had a significantly better overall survival (OS) compared to patients with TT genotype, the same tendency was found in *ATF5* C362T polymorphism where patients carrying TT/CT genotypes had a significantly better OS and longer event-free survival (EFS) compared to patients with CC genotype. Multivariate analysis confirmed the independent prognostic value of the *ATF5* C362T dominant model.

**Conclusion:** *ATF5* 362TT and CT genotypes were associated with decreased risk to develop AAP and better disease outcome demonstrating a low risk for events and superior survival.

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