بسم الله الرحمن الرحيم

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بقسم التوثيق الإلكتروني بمركز الشبكات وتكنولوجيا المعلومات دون أدنى مسئولية عن محتوى هذه الرسالة.

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Ain Shams University
Faculty of Science
Biochemistry Department

Correlation of Phenotype-genotype in Egyptian patients with familial Mediterranean fever

A thesis submitted for the award of M.Sc. degree in Biochemistry

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(B.Sc. in Biochemistry, 2010)

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Approval Sheet

Title of the M.Sc. thesis

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List of Abbreviations

FMF	:	Familial Mediterranean Fever
MEFV	:	Mediterranean fever gene
IL-1	:	Interleukin-1
IL-1β	:	Interleukin-1 beta
AA	:	Amyoloid A
SAA1	:	Serum amyloid A type 1
NSAIDs	:	Non Steroidal Anti-Inflammatory Drugs
ELE	:	Erysipelas-like erythema
MICA	:	Major Histocompatibility Complex class I chain-related gene A

Abstract

Familial Mediterranean fever (FMF) is the most prevalent autosomal recessive disease that affects the ethnic groups living around the Mediterranean basin mainly Jews, Turks, Armenians, Greeks and Arabs. The causative Mediterranean fever (MEFV) gene is located on the short arm of chromosome 16p13.3 with more than 374 gene mutations and polymorphisms. The present study aimed to explore the frequency of common MEFV mutations among patients with FMF in Egypt and associate the phenotyping with genotyping in the FMF Egyptian patients. This study was carried out in Genetic unit in Ain-Shams Hospital (EL-Demerdash) from the period of June 2015 to 2019. A total number of attendant patients enter he unit were 480 patients suspected for FMF and diagnosed according to Tel-Hashomer criteria.A blood sample was withdrawn from each FMF patient for Molecular genetics study using DNA isolation followed by PCR amplification followed by hybridization (This assay covers 12 mutations in the MEFV gene: E148Q, P369S, F479L, M680I (G/C), M680I (G/A), I692deI, M694V, M691V, K695R, V726A, A744S, R761H). The study showed that E148Q, M694I, V726A, M680I and M694V are the most common mutations of MEFV gene, whereas F479L and I692deI mutations were not detected in our study population. The common heterozygous mutations shown in this study were E148Q, M694I, V726A, M694V, and A744S. Meanwhile, the common homozygous mutations were

M694I and M680I. The common compound mutations were M694I / V726A and M680I / V726A.Our results showed complex mutations other than previously recorded. These complexes are E148Q / M694 I / V726A, E148Q / M694I / A744S, E148Q / M680I (G/C) / M694I, and E148Q / M680I(G/A) / V726A. Moreover, we detected a compound homozygous E148Q/M694I. The higher rate of FMF mutations were in Monufia and BeniSuef governorates. Abdominal pain, arthritis, as well as combined presentations are significantly higher in heterozygous than in compound. Conversely, chest pain was significantly higher in compound than heterozygous of E148Q mutation. The combined and arthritis phenotyping were statistically higher in E148Q mutation in comparison with the other mutations. The 5 common FMF mutations were recorded 2.75 times in patients have non-abdominal surgeries than were recorded in patients of abdominal ones. The most sensitive symptoms that predict the mutations were vomiting for V726A, weakness, fatigue, and myalgia for M680I, arthritis and vomiting for E148Q, and vomiting for M694I. These results provided a source for studying the frequency of common MEFV mutations among Egyptian patients with FMF and contribute to a better understanding the association between the phenotyping and genotyping in those patients. Finally, we recommend a larger scale population screening and sequencing of the whole MEFV gene, searching for new and uncommon mutations belong to Egyptian population specifically.