Gene polymorphisms of tumor necrosis factor alpha308 and interleukin-101082 among asthmatic Egyptian children

ABSTRACT
Tumor necrosis factor (TNF) alpha308 and interleukin (IL)-101082 have potent inflammatory responses in the process of airway inflammation in asthma. The purpose of this study was to check for association of polymorphisms related to cytokine genes with susceptibility and severity of bronchial asthma in Egyptian children. Blood samples of 69 asthmatic children receiving treatment and follow-up at the Allergy and Respiratory Medicine Unit, Mansoura University Children Hospital, Mansoura, Egypt, were subjected to DNA extraction and amplification using polymerase chain reaction with sequence-specific primers for detection of single nucleotide polymorphisms in the promoter regions of cytokine genes TNF-alpha308(G3A), IL-101082(G3A). Compared with normal controls, Egyptian asthmatic children showed a significant higher frequency of IL-101082 G/G homozygosity genotype (p < 0.001; odds ratio [OR] > 7) with lower frequency of G/A heterozygosity genotype among cases. This finding also was detected in cases with persistent asthma and eczema. These cases showed significant lower frequency of TNF-alpha308 G/A heterozygosity (p < 0.05; OR < 0.44). Also, male cases, cases with positive family history, and those patients with persistent types of asthma showed a higher frequency of TNF-alpha308 G/G homozygosity. IL-101082(G3A) G/G and TNF-alpha308(G3A) G/G may be a contributing factor in susceptibility as well as severity of asthma among Egyptian children. Separate studies should be specified relating these cytokine genotypes to response to various modalities in asthma therapy. This study reports that IL-101082(G3A) G/G and TNF-alpha308(G3A) G/G genotypes may be contributing factors in susceptibility as well as in severity of asthma among Egyptian children. Separate studies may be specified relating these cytokine genotypes to response to various modalities in asthma therapy.

Gene polymorphisms of IL-6(-174) G/C and IL-1Ra VNTR in asthmatic children.

OBJECTIVE: To check for the association of genetic polymorphisms of IL-6(-174)G/C and IL-1RaVNTR with the susceptibility and severity of asthma in Egyptian children.

METHODS: Subjects included 69 asthmatic children and 98 healthy unrelated controls from the Nile Delta of Egypt. Cases consisted of 20 males and 49 females with an age mean +/- SD is 7.5 +/- 2.1 ranging between 2-13 years. DNA amplification using PCR with sequence-specific primers was done for detection of promoter single nucleotide polymorphism of IL-6 gene as well as intron 2 VNTR of IL-1Ra gene. Frequency of
case-genotypes or alleles were compared to controls using Fisher exact test and Odds ratio. RESULTS: Cases showed significant higher frequency of the genotypes: IL-6-174 GG (P<0.05, OR=3.2, 95% CI=1.09-10) that was evident mainly in the uncontrolled asthma subgroup indicative of the possibility of being a severity genotype. All cases as well as case-subgroups showed high significant frequency of IL-1Ra A1A1 (p<0.0001, OR=1.5, 95% CI=1.3-1.8). This may be considered a susceptibility genotype. Cases have also shown significant lower frequency of IL-6(-174) GC and IL-1Ra A1A2 genotypes (P<0.001 and P<0.0001 respectively). CONCLUSION: IL-6 and IL-1Ra polymorphisms can be considered genetic markers for bronchial asthma susceptibility and/or severity among Egyptian children. This may have a potential impact on family counseling and management.

3- Screening for beta thalassemia carriers among school children in Dakahlia, Egypt

4- Prevalence of iron deficiency anemia among the Egyptian population

5- Prognostic cytogenetic markers in childhood acute lymphoblastic leukemia: cases from Mansoura

6- HOW DO EGYPTIAN CHILDREN DESCRIBE ASTHMA SYMPTOMS?

INTRODUCTION
Asthma is a common disease in children that forms a major comorbidity illness. Underdiagnosis of childhood asthma represented one of the pitfalls in the asthma management. History with interpretation of asthma symptoms is still considered the corner stone in asthma diagnosis. The other limb in diagnosis is through the reversibility and variability of pulmonary function tests (PFTs). However, PFTs require patientsâ€™ cooperation that may be not fully feasible in children.(1) Asthma symptoms include wheeze, dyspnea, chest tightness and shortness of breath. Reported wheeze within the last 12 months is considered a surrogate marker for the diagnosis of asthma. This could represent a major difficulty for children in some countries in which no exact equivalent wordings of wheeze exist.(2) The prevalence of asthma and allergies is
increasing in both western and developing countries. Despite a large volume of clinical and epidemiological research within affected populations, the etiology and risk factors of these conditions remains poorly understood. (3) The prevalence of atopic conditions is lower in rural and lessdeveloped areas of the world than that are rapidly urbanizing or modernized. The reasons for these variations are yet to be fully understood. Some researchers have speculated that exposure to infections in early life may have a role in prevention of asthma and atopy in children. (4)

Simple methods for measuring the prevalence of childhood asthma, allergic rhinitis and atopic eczema have been developed by phase one of the International Study of Asthma and Allergies in Childhood (ISAAC). These methods are used for international comparisons and are suitable for different geographical locations and languages. (5) So far, there have been few studies of the epidemiology of asthma in Egypt. One of these studies was conducted in Cairo in 2006 reported the prevalence of asthma in Egypt. One of these studies was conducted in Cairo in 2006 reported the prevalence of asthma to be 9.4% among Cairo citizens. (6) This study was planned to determine the prevalence of bronchial asthma in the Delta region of Egypt through relevant questionnaire. Validation of asthma symptoms was done through evaluation of common Arabic wordings describing wheeze, chest tightness, shortness of breath and dyspnea.

**Eosinophilic cationic protein: is it useful in assessing control of childhood asthma?**
The present study aimed to check for segregation of some oncogenic markers (p53, c-
myc) and DNA ploidy pattern in Egyptian families of children with acute lymphoblastic leukemia (ALL) to determine whether there is an actual risk for cancer among these families. This case-controlled study included 20 Egyptian children with ALL, their median age 6.5 years (interquartiles 2.1-12.5) with males/females 16/4. They were enrolled at presentation to Haematology-Oncology Unit of Mansoura University Children’s Hospital, Egypt. The study included also their first-degree relatives (20 fathers, 20 mothers, 44 healthy sibs) and control group; 20 healthy subjects with median age 6.9 years (interquartiles 3.2-13.1) and sure negative family history of cancer. Blood sampling was done for all persons followed by cell isolation for Flow Cytometric analysis (FCM) of DNA ploidy, apoptosis and other cell cycle parameters. p53 and c-myc protein expression were also assessed by FCM using monoclonal-antibody staining technique. p53 and c-myc showed significantly high values in cases compared to controls and relatives (p

### Increased risk of liver cirrhosis among Egyptian carriers of S and/or Z mutant alleles of Alpha1 anti-trypsin gene.

**Abstract**

Alpha-1-antitrypsin (A1AT) deficiency (Z and S mutations) is the most common inherited metabolic disorder with potential injury to liver and lung. The aim of this study is to determine the frequency of S and Z mutations of A1AT deficiency among Egyptian patients with liver cirrhosis and test their contribution as a risk factor to the development of the disease.

In a cross-sectional study 27 children (< 18 years) and 36 adult patients (> 18 years) suffering from liver cirrhosis in addition to 35 randomly selected, unrelated healthy control subjects were enrolled. Cases were recruited from Hepatology and Tropical Units, Mansoura University Hospitals. S and Z or M (wild) alleles were tested for all included subjects using PCR amplification of specific part of the gene followed by restriction enzyme (Taq1) digestion with analysis of RFLP (Restriction Fragment Length Polymorphism).

Homozygosity for S (SS) and Z alleles (ZZ) were noted among 7.4% and 11.1% of childhood cases and 11.1% and 5.6% of adult cases compared to 8.6% and 0.0% of controls respectively. Heterozygous S (MS) was found among 25.9% of childhood cases, 30.6% of adult cases compared to 8.6% in controls. Compound heterozygotes (SZ) were found with higher frequency among controls (11.4%) than childhood cases (7.4%) and adult cases (0.0%). Gene frequency of S allele was noted higher in childhood and adult cases than controls (24.1%, 26.39%, 18.6%), while the Z allele was higher in childhood cases than adult and controls (14.8%, 6.94%, 8.6%). In addition, significant high relative risk was found among S carries and ZZ homozygotes in both studied groups.

Relative increased frequency of mutant A1AT deficiency alleles within cases of liver cirrhosis may be an actual risk factor taking into consideration the interaction of other genetic or environmental factors as metabolic errors, malnutrition, viral infections like HCV, schistosomiasis and diabetes. Therefore A1AT gene analysis might be an essential diagnostic and/or prognostic parameter among family members of liver cirrhosis cases.

### Detection of Beta-thalassemia Mutations Using Primer-Specific Amplification
Compared to Reversed Dot Blot Hybridization Technique in Egyptian Cases.

Abstract. We aim to evaluate the newly developed Reversed Dot Blot Hybridization (RDBH) technique against the established Amplification Refractory Mutation System (ARMS) in detection of most common Mediterranean mutations of \( \alpha \)-thalassaemia in Egyptian cases from Nile Delta Regions.

Forty patients were enrolled from those presented to Genetic Laboratories in Mansoura University Children’s Hospital, Egypt, for molecular diagnosis of \( \alpha \)-thalassaemia. They comprised 23 males and 17 females with age range 2.4-18 years (mean 7.80.6±). They were subjected to a thorough history stressing on consanguinity and family history, blood sampling for standard haematological testing and DNA extraction. Every DNA sample was tested for 8 common beta thalassaemia mutations using RDBH method (hybridization to 8 chemically-labelled probes fixed on membrane strips, one for mutant and another for normal probe sets) followed by colour detection and interpretation. Mutations were estimated and were compared to that determined via the use of ARMS technique through amplification using sequence specific primers (SSP); one for mutant and another for normal allele with internal control primers. Sensitivity and specificity of RDBH against ARMS method was measured using ROC curve. Considering ARMS results were our gold standard ones, RDBH was found of average sensitivity and specificity in detection of the top three common mutations but when analyzing other mutations it was associated with relatively higher false positive rates. Using both techniques, mutations of highest frequencies were intronic; within IVS I-110, IVS I-6 and IVS I-1 and on the other hand, the least frequent ones were exonic and promoter mutations. We can conclude that common \( \alpha \)-thalassaemia mutations can be simply and reliably detected using ARMS technique rather than by using the ready made strips applied for RDBH.

Diagnostic Significance of Flow Cytometric Analysis of DNA Ploidy and Apoptosis in Children with Lymphadenopathy

Abstract. Lymphadenopathy whether benign or malignant represents a diagnostic dilemma in childhood.
We tried to evaluate flow cytometric analysis of DNA cycle and apoptotic parameters of fine needle aspiration of lymph node (FNA) or peripheral blood lymphocyte (PBL) samples to resolve problematic diagnosis of childhood lymphadenopathy. Seventy nine children with lymphadenopathy were enrolled from Outpatient Clinics, Mansoura University Children’s Hospital; 46 FNA and 50 PBL samples were analyzed using FACS flow cytometer. DNA staining was done with propidium iodide after at least 12 hours ethanol fixation. Apoptosis was measured using the sub-G1 peak analysis. Cases with malignant lymphadenopathy had significantly lower G0/G1 and G2/M peak channels compared to benign cases. Moreover, S-phase and apoptosis percentages were also lower but with statistical insignificant difference. Aneuploidy was significantly higher in PBL samples of malignant cases (P (>3.5%) were the 3 most significant predictors of malignancy. We can conclude that apoptosis percentage and DNA cycle parameters of FNA and PBL samples in addition to other workup investigations can help in the differentiation of malignant from benign lymphadenopathy.

12-

Screening for G6PD Mediterranean mutation among Egyptian neonates with high or prolonged jaundice.

Abstract. Our objective is to determine the frequency of G6PD Mediterranean mutation (Med mut) among neonates with high or prolonged jaundice in Dakahlia province, Egypt. Seventy neonates and infants with definite history of jaundice were enrolled from Neonatal Care Unit in Mansoura University Children’s Hospital; all were subjected to clinical history, laboratory investigations e.g. bilirubin, SGPT, SGOT, Hb and CRP. G6PD assay was done by a qualitative screening test. For detection of G6PD Med mut at nucleotide 563 C-T, DNA was extracted and amplified using the primers published in the literature and applying a specific amplification program. The amplified PCR products were digested and separated by agarose gel electrophoresis; then bands were visualized.

Five cases of G6PD deficiency were detected by screening test and 3 cases in addition were found
having G6PD Med mut, so the minimum frequency of G6PD deficiency among jaundiced Egyptian neonates is 8/70 (11.4%) which is higher than population prevalence in Egypt (7-9.9%), and relatively higher than some countries like Iran (7.5%) but lower than Greece, Turkey and Jamaica. Interestingly, the five qualitatively G6PD deficient cases had no G6PD Med mut, on the other hand the three cases having G6PD Med mut were negative by qualitative screening test. We can conclude that the frequency of G6PD deficiency among jaundiced neonates in Egypt was higher than population prevalence. False negative rate for qualitative test was 4.6%. Absence of G6PD Med mut in the 5 cases diagnosed by qualitative screening test should signify the existence of other mutations.

13-

**Screening of mentally handicapped Egyptian children for Fragile X Syndrome using clinical, cytogenetic and molecular Approaches**

**Abstract**

To screen children with idiopathic mental retardation (MR) using a clinical Ten-Item Checklist (TIC) and to analyze high-risk fragile X syndrome (FXS) cases by cytogenetic and molecular genetic techniques. This study was conducted on 192 children with idiopathic MR enrolled from Pediatric clinics of University Hospitals and MR institutes of Alexandria, Mansoura and Benha Governorates, Nile Delta, Egypt (age range 2-14 years). Clinical scoring for patients was done using TIC according to which patients were categorized either positive checklist with score higher than 5 or negative with score less than 5. Positive cases underwent cytogenetic analysis that provoke expression of fragile sites on chromosome X and molecular genetic analysis for detection of permutation among cases or their 1st degree relatives. Analyzing all cases: IQ ranged from 30 to 80%, family history of MR was found in 28.6% and consanguinity was positive in 26%. Positive checklist cases constituted 23.9% and remainder 76.1% were negative checklist. The most frequent items in positive cases were large prominent ears, hyper-extensible finger joints, hyperactivity, and large narrow face with less common macro-orchidism. A positive linear association was found between laboratory test positivity and TIC score being stronger with cytogenetic analysis compared to polymerase chain reaction (PCR) (P 0.001 and 0.02, respectively). Using TIC, 76.1% cases could be eliminated from the waiting list of genetics laboratories. The relatively weaker association of TIC score to PCR compared to cytogenetic analysis together with areas under receiver operating characteristic curve 0.743 and 0.814 respectively denote the higher accuracy and sensitivity of PCR analysis in final diagnosis of FXS.

14-

**Genetic analysis of rheumatic fever among Egyptian families: Consanguinity pattern, Segregation analysis and Blood group association.**

To assess genetic background of Rheumatic Fever (RF) among Egyptian families and to
test for association to blood group allelic phenotypes. This study was done on 30 Egyptian rheumatic families of which 10 were multiplex; enrolled from Pediatric Cardiology Clinic, Mansoura University Hospital. Subjects included 30 probands and 1142 relatives of different degrees; they were classified clinically into 46 cases with RF, 136 subjects with recurrent Upper Respiratory Infection (URTI) and/or arthralgia and the remainders were irrelevant. Diagnosis of RF was based on Jones criteria. Pedigree analysis with stress on consanguinity, positive family history of RF and definite recurrent URTI. Nine blood group systems were analyzed for probands including; ABO, Rh, MNS, Kell, Lutheran, Lewis, Kidd, Duffy, P1 and individual secretor status. In rheumatic families consanguinity and inbreeding were higher than control (53.3%, 0.015). Segregation analysis suggested multifactorial inheritance for RF with mean heritability (30%) whereas recurrent URTI followed recessive inheritance. Some alleles and phenotypes were of higher incidence in probands compared to control; alleles se (non-secretor), D, Jka+ and phenotypes Lu (a-b-), Le (a-b-) and Fy (a-b-) were of higher frequency, whereas alleles Se (secretor), A, B, Kp a+, Lu b+, Le b+, Fy a+, Fy b+ and phenotypes Fy (a+b+), Sese or SeSe (secretor) were less frequent. Based on the inherited susceptibility to respiratory infection, RF is a genetic disease with multifactorial inheritance. Blood group systems on chromosome 19 could mark hot spots for further linkage and gene mapping.

15-

Montelukast as an episodic modifier for acute viral bronchiolitis: A randomized trial

ABSTRACT

This study was designed to evaluate the effect of once-daily montelukast therapy on the clinical progress and the cytokine profile of patients with acute viral bronchiolitis. A randomized, double-blind, placebo-controlled trial included 85 patients (mean age, 3.5 ± 2.35 months), clinically diagnosed as first-episode acute bronchiolitis in addition to 10 healthy controls of matched age and sex. Patients were randomly assigned to receive either montelukast (4-mg sachets; n = 47) or placebo (n = 38) daily from the time of admission until discharge. The primary outcome measure was the length of hospital stay (LOS), and clinical severity scores (CSs) and changes in plasma levels of interferon gamma and interleukin-4 were secondary outcomes. LOS for the montelukast group was found to be significantly lower than that of the placebo group (p < 0.05). This effect was also found at nonsignificant levels among patients with a positive family history of asthma or allergy. Moreover, cases receiving montelukast showed lower CSs all through the hospital stay that were significant in the first 24 hours (p < 0.05). Montelukast is probably of benefit as an episodic modifier in infants with acute viral bronchiolitis.

**Factor V Leiden and prothrombin gene mutations in Egyptian cases with unexplained recurrent pregnancy**

Background: Thrombophilias have been suggested as a possible cause of recurrent pregnancy loss (RPL).

Objective: Testing for the association of factor V Leiden (FVL) and prothrombin (FII) mutations with RPL among cases from the Nile Delta region of Egypt.

Subjects and methods: Participants included 72 cases having a history of two or more events of unexplained RPL and 70 controls with a good obstetric history. Detection of FVL (G1691A) and FII (G20210A) mutations was carried out using PCR with sequence specific primers.

Results: Cases showed a significantly higher frequency of FVL GA (OR521.38, P,0.0001) and FII GA (OR536.7, P,0.0001) genotypes. Cases with two or more risk factors had significant higher frequency of both mutant genotypes, while no significant difference could be elicited related to primary or secondary infertility, number of fetal losses, or phase of pregnancy loss.

Conclusion: Screening for thrombophilic mutations may help in the prevention of unexplained RPL.


BACKGROUND: Myocardial infarction (MI) can be due to inherited thrombophilia caused by resistance to activated protein C resulting from factor V Leiden (FVL) mutation.

OBJECTIVES: The objectives of this study were to estimate the frequency of FVL mutation among MI cases in various populations and calculate the overall risk related to it.

SUBJECTS AND METHODS: Subjects comprised 7790 cases with MI and 19,276 healthy controls collected from 41 relevant studies in the search databases. The resulting frequency of FVL mutation among cases and the odds ratio were compared and integrated in a meta-analysis format.

RESULTS: Although there was marked variation of the frequency of FVL mutation among different populations including MI and healthy controls, most studies reported a positive risk related to it. Compilation of analyzed studies resulted in an overall frequency of FVL mutation of 6.791% among MI cases, which was significantly higher than that among controls (1.304%, p = 0.0) with an overall odds ratio of 1.608 (95% confidence interval, 1.98-4.44).
CONCLUSION: There is a definite risk related to the carriage of FVL mutation among MI cases. This should have a potential impact on the genetic counseling of family members of affected cases for proper prophylaxis.

18-


Objectives: Many of the signs of hypothyroidism, affect the skin as well as the genital system of affected female cases. The aim of this study is to highlight the presenting dermatologic and gynecologic manifestations of firstly-diagnosed hypothyroid females.

Patients and Methods: This is a case control study that included 150 patients presenting for gynecological consultation. Out of them, 60 were affected with hypothyroidism and 90 were euthyroid based on clinical and laboratory investigation backgrounds. Their gynecologic and dermatologic findings were analyzed and compared statistically.

Results. Compared to euthyroid cases, hypothyroid ones were presenting mostly with amenorrhea (OR=7.76). Other gynecologic manifestations that were prominent in hypothyroid cases were dysparunia, PCO, PMS and Breast tenderness. On the other hand, rate of menstrual irregularities and infertility were non-significantly different in both groups. Hypothyroid women showed also significantly higher frequency of urticaria and puffiness of hands and feet (both were present in 16.7% in hypothyroid vs. 3.3% of euthyroid cases, p =0.007, OR=5.8). Hypothyroid cases showed also significantly higher frequency of yellow ivory skin (OR=5.4) and coarse rough dry skin (OR=3.8). On the other hand, alopecia and periorbital edema were observed only among cases of hypothyroidism and none of euthyroid cases.

Conclusion. A great index of suspicion should be always exerted to the diagnosis of disorders manifesting with subtle manifestations as hypothyroidism in female cases particularly having gynecologic and dermatologic disorders.

19-


Psoriasis is a chronic inflammatory dermatosis that contributes to approximately 1-5% of
all skin
disorders in Saudi Arabia. The genetic basis of psoriasis is supported by family based
investigations;
population based epidemiological studies, association studies with human leucocyte
antigens (HLAs),
genome-wide linkage scans, and candidate gene studies within and outside the major
histocompatibility
complex. Psoriasis represents a complex disease at the cellular, genomic and genetic
levels, with infiltration
of many types of leukocytes into the skin, altered growth and differentiation of skin-
resident cells, and
altered expression of more than 1,300 genes in psoriatic lesions. It is also apparent that
there is considerable
overlap between the molecular pathways that are involved in psoriasis and those that lead
to other
inflammatory or autoimmune diseases in humans. In this Review article, we describe the
immune-genetic
basis of psoriasis, the molecular pathways of pathogenic inflammation and the potential
role of the genes
that confer increased susceptibility to psoriasis.

Incidence of Genetic Polymorphism of IL-1Ra and IL-4 in Egyptian and other
Populations
Cytokines play a key role in immune response and inflammation. IL-1 receptor
antagonist (IL-Ra) is a
naturally occurring structural variant of IL-1 that competitively inhibits receptor binding
of IL-1 induced
pro-inflammatory activity. IL-4 an anti-inflammatory cytokine plays a key role in
activation and differentiation of
B-cells, mast cells. IL-4 is also known to inhibit macrophage activation and therefore may
be involve in cancer. The
two important cytokines genes IL-1Ra and IL-4 of 124 healthy individuals from the Nile
Delta region of Egypt were
compared with the published polymorphism of other populations. Genomic DNA was
isolated from the blood of all
subjects and the variable number of tandem repeat (VNTR) polymorphisms of IL-1Ra
and IL-4 genes was identified
by polymerase chain reaction. It was seen that our population differs from Mediterranean,
European, African and
Asian populations at IL-1Ra (VNTR) and IL-4 (VNTR) genes.

Methylenetetrahydrofolate reductase gene polymorphisms in Egyptian women with
unexplained recurrent pregnancy loss.
Abstract
AIMS:
This work aims at testing for the association of the methylenetetrahydrofolate reductase (MTHFR) gene polymorphisms with unexplained recurrent pregnancy loss (RPL) among Egyptian women.

**SUBJECTS AND METHODS:**
Participants were 70 cases having a history of two or more events of unexplained RPL and 136 controls with a good obstetric history. Detection of MTHFR C677T and A1298C mutations was done by polymerase chain reaction with restriction fragment length polymorphisms assay using restriction enzymes HinfI and MboII respectively.

**RESULTS:**
Compared with controls, cases with unexplained pregnancy loss showed higher frequency of the homozygous mutant MTHFR 677 TT, 1298 CC genotypes, and the mutant haplotype 677T/1298C, although not reaching statistical significance. The frequency of 677 mutant genotypes (TT or TC) combined with either the mutant 1298 (CC or AC) or normal 1298 (AA) genotypes was significantly increased among cases with late-stage pregnancy loss versus those with early-stage pregnancy loss (p=0.001). There was also increased frequency of the 677 mutant genotypes among cases with secondary infertility compared with those with primary infertility and among cases with pregnancy loss >4 times compared with those with ≤4 times but with no statistical significance. Regarding other risk factors, it was noted that the frequency of mutations among cases with no or just one risk factor did not differ significantly from those having two or more risk factors (p=0.98).

**CONCLUSIONS:**
Mutations related to the MTHFR gene are increased but not statistically significant in Egyptian women with unexplained pregnancy loss. Interaction with other genetic variants might be speculated and need to be investigated.

22- Association of cytokine gene polymorphisms with psoriasis in cases from the Nile Delta of Egypt.

**Abstract**
**BACKGROUND:**
Psoriasis is a chronic inflammatory skin disease with an immunogenetic background. This work was planned to check for the association of polymorphisms related to cytokine genes TNF-α(-308) (G/A), IL-10(-1082) (G/A), IL-6(-174) (G/C), and IL-1Ra (VNTR) with psoriasis in cases from Egypt.

**MATERIALS AND METHODS:**
This work included 46 cases with psoriasis recruited from the Dermatology Departments, University Hospitals, Nile Delta region of Egypt. They included 14 males and 32 females with an age mean ± SD of 46.68 ±12.16 years and range of 15-70 years. Their genotypes were compared to 98 healthy controls of matched age and sex from the same locality. Genotyping was done through deoxyribonucleic acid amplification using PCR with sequence specific primers for polymorphic alleles.

**RESULTS:**
Compared to controls, cases showed significant higher frequency of certain genotypes including IL-6(-174) CC (P < 0.001, OR = 6.7), IL-10(-1082) GG (P < 0.05, OR = 5.1), and TNF-308(-)-174) GG (P < 0.05, OR = 3.7). TNF-308(+) GG and IL-10(-1082) GG genotypes were higher among cases with plaque subtype of moderate severity. Combined
heterozygosity for IL-10 GA, IL-6 GC with TNF GA showed a significant low frequency among studied cases.

CONCLUSION:
Genetic polymorphisms related to IL6, IL10, and TNF-α genes showed a particular pattern of association with psoriasis that may have a potential impact on disease counseling and management.

23-

Prevalence of 1-±α-antitrypsin gene mutations in Saudi Arabia.

Abstract
BACKGROUND/AIM:
1-±α-antitrypsin (AAT) deficiency results from mutations of the protease inhibitor (PI). The AAT gene is mapped on chromosome 14 and has been associated with chronic liver disease and chronic obstructive pulmonary disease (COPD).

OBJECTIVE:
To determine the frequency of AAT mutations on S and Z carrier alleles in healthy Saudi individuals from Qassim Province in Saudi Arabia. PATIENTS AND METHODS: A total of 158 healthy, unrelated participants from Qassim Province were recruited. They were genotyped for the two AAT-deficiency alleles, PIFNα01S and PIFNα01Z, using polymerase chain reaction, with primers designed throughout to mediate site-directed mutagenesis.

RESULTS:
Of the 158 subjects, 11.39% were carriers for the S mutation (i.e., had the MS genotype), whereas 2.53% were carriers for the Z mutation (i.e., had the MZ genotype). The SZ genotype was present in 3.8% of subjects, while the homozygous genotype SS was present in 1.9% of subjects. No subjects showed the ZZ mutant genotype. Accordingly, frequency of the mutant S and Z alleles of AAT gene was 9.49% and 3.19%, respectively.

CONCLUSION:
The results obtained showed a high prevalence of the AAT deficiency allele in the Saudi population. This probably warrants adoption of a screening program for at-risk individuals, so that they might initiate adequate prophylactic measures.

24-

Interleukin-1 Receptor Antagonist Gene Polymorphism and Oxidative Stress in Chronic Hepatitis C Virus infection

Cytokines like interleukin-1 receptor antagonist play an important role in defense against viral infection. These cytokines are thought to play a central role in liver metabolism and in the immune response to viral agents. HCV infection is characterized by a systemic oxidative stress that is most likely caused by a combination of chronic inflammation, iron overload, liver damage, and proteins encoded by HCV. This work was planned in order to check for the association of genetic polymorphism of interleukin-1 receptor antagonist (IL-1Ra) gene with chronic hepatitis C infection and its relation to oxidative stress markers.

The polymorphism analyzed, IL-1Ra genotype A1A2 showed lower significant frequencies in HCV patients when compared with controls (52.7% vs. 71.0%, p =0.006, OR=0.4). This means that the genotype A1A2 might be considered a protective genotype.
against HCV infection. On the other hand, the frequency of A2A2 genotypes showed significantly higher in HCV patients than controls (15.5% vs. 8.1%, p= 0.02) and A1A1 genotype frequency was higher in patients than controls but not significantly increase (27.3% vs. 20.2%, p= 0.26). Regarding to oxidative stress markers, in HCV patients showed significantly lower mean level of total antioxidant capacity (TAC) (p< 0.001), while these patients have significantly higher level of malonyldialdehyde (MDA) (p< 0.001). On the other hand, comparing cases-subgroups in terms of their assigned IL-1Ra genotypes, nitric oxide (NO) mean level was significantly higher in patients having the A2A2 genotype than other patients. Finally, the present study suggested that, the patients having the IL-1Ra A2A2 genotype were at higher risk for getting HCV infection and liver complications whereas those with A1A2 genotype seemed to be more protected against such infection. In addition, MDA, TAC and NO levels might be used as monitoring markers for oxidative stress in HCV cases with IL-1Ra A2A2 genotype.

25-

Prognostic cytogenetic markers in childhood acute lymphoblastic leukemia: cases from Mansoura Egypt.

Abstract
The objective of the work was to evaluate children with acute lymphoblastic leukemia (ALL) showing resistance to immediate induction chemotherapy in relation to conventional and advanced cytogenetic analysis. The study was conducted on 63 ALL children (40 males and 23 females) with age range 4.5 months-16 years (mean = 7.76 years). They included 37 cases who attained a true remission and 26 complicated by failure of remission, early relapse or death. They were subjected to history, clinical examination and investigations including CBC, BM examination, karyotyping, FISH for translocations and flowcytometry for immunophenotyping and minimal residual disease diagnosis. Cases aged < 5 years; male sex with organomegaly had better remission although statistically insignificant. Initially low HB < 8 gm/dl, high WBCs and platelet counts >50.000/mm(3) also showed better but non-significant remission rates. Most of our cases were L(2) with better remission compared to other immunophenotypes. About 40 informative karyotypes were subdivided into 15 hypodiploid, 10 pseudodiploid, 8 normal diploid and 7 hyperdiploid cases; the best remission rates were noticed among the most frequent ploidy patterns. Chromosomes 9, 11 and 22 were the most frequently involved by structural aberrations followed by chromosomes 5, 12 and 17. Resistance was noted with aberrations not encountered among remission group; deletions involving chromosomes 2p, 3q, 10p and 12q; translocations involving chromosome 5; trisomies of chromosomes 16 and 21; monosomies of 5 and X and inversions of 5 and 11. Our conclusions were that cytogenetic and molecular characterizations of childhood ALL could add prognostic criteria for proper therapy allocation.