

## Summary

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Asthma is a chronic inflammatory disease, primarily resulting from interactions between genetic and environmental factors, in which immunological mediators and cells play an essential role.

This study was conducted on (69) asthmatic patients (48 females and 21 males) their age ranges between (18-70) years, seen in Al-Diwaniya Teaching Hospital for the period from December 2012 to January 2013. Other (20) healthy subjects (11 females and 9 males) were included as a control group. Blood samples were collected from both groups, genomic DNA was extracted from peripheral blood leukocytes for further molecular study to reveal any association between *ADAM33* polymorphism at V4 SNP and predisposition to bronchial asthma. Polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) technique was used for this purpose and digestion of the amplified DNA products by restriction endonuclease (PstI enzyme) gave fragments with different molecular sizes which express certain genotypes.

Optical density of IgE and IL-4 in serum was detected by ELISA technique and from which IL-4 and IgE concentration were evaluated according to standard curve. Complete blood count was performed to all blood samples to detect eosinophils number (cell/ $\mu$ l) by RUBY system.

The current study showed that 31.9% of the patients were in the age group of (20-35) years and 27.5% of the patients had in the age group of (<20) years, the result also revealed that 69.6% of the patients were females. This study detected that the prevalence rate of single nucleotide polymorphism *ADAM33*-V4 was significantly high among cases of asthma ( $P < 0.001$ ), and found that homozygous mutant GG, heterozygous CG genotypes and mutant G allele carrier frequencies were significantly high in asthmatic patients ( $P < 0.001$ ,  $P = 0.023$  and

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$P < 0.001$  respectively), in contrast homozygous normal CC genotype ( $P = 0.451$ ) and C allele ( $P = 0.6$ ) had no significant association with asthmatic patients. The data showed that 65.2% of asthmatic patients have positive family history and showed that the homozygous mutant genotype GG and mutant allele G were significantly associated with patients who had a family history of asthma (58.70% and 75% respectively) as compared with asthmatic patients without a family history of asthma (21.70% and 47.8%), whereas heterozygous CG, normal homozygous genotypes CC and C alleles not associated with asthmatic patients who had family history (32.6%, 8.7% and 25% respectively). The study showed no statistical significant among the two genotypes GG, GC and level of IL-4 ( $P = 0.47$ ,  $P = 0.41$  respectively), IgE ( $P = 0.33$  and  $P = 0.66$  respectively) and eosinophil count ( $P = 0.1$  and  $P = 0.88$  respectively), in contrast CC genotype has significant association with the increased level of IL-4, IgE and eosinophil count ( $P = 0.023$ ,  $P = 0.019$ ,  $P = 0.039$  respectively).

Serum levels of IL-4 and IgE and eosinophils count in peripheral blood were significantly higher among cases with asthma compared to healthy controls ( $P < 0.001$ ). The study detected a distinct role of IL-4 and eosinophil in cases of asthma compared to healthy controls ( $P < 0.001$ ) and show the gradually high of IL-4 in serum associated with systematic increase in eosinophil count in peripheral blood and also found a significant relationship existed between serum IgE levels and eosinophilia in asthma compared to healthy controls ( $P < 0.001$ ). A significant linear relationship between serum concentration of IL-4 and IgE in asthmatic patients was observed as compared with healthy controls ( $P < 0.001$ ). These results were demonstrated significant association among IL-4, IgE, eosinophils and positive family history in asthmatic patients group

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compared to healthy controls (P=0.04, P=0.022 and P=0.002 respectively).

In conclusion, this study showed that high incidence of bronchial asthma occurred among young adults especially in females and suggested that *ADAM33-V4G/C* polymorphism may contribute to the predisposition of bronchial asthma and there was significant association among G allele, GG genotype and development of the disease. Family history with bronchial asthma is consider as a risk factor especially in patients who have GG genotype and G allele. Immunological markers (IL-4, IgE and eosinophils) were significantly associated with bronchial asthma. Furthermore only protective CC genotype had correlation with these markers in bronchial asthma.