Serum YKL-40: A POSSIBLE BIOMARKER IN BRONCHIAL ASTHMA?

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Abstract. Background: The evolutionary conserved 18 glycosyl hydrolase family contains chitinases and chitinase like proteins that share amino acid sequence homology with true chitinases but lack enzymatic activity. The chitinase like protein YKL-40, encoded by the chitinase3-like 1 gene (CHI3L1), has been found to be either the cause or a biomarker for asthma. However, its pattern of expression with disease progression has not been evaluated. Interestingly, the C allele of 131 C/G (rs4950928) polymorphism of chitinase3-like 1gene has been shown to associate with elevated serum YKL-40 levels and reduced lung function suggesting that variation in chitinase3-like 1 may influence risk of asthma. The objective of the present study was to investigate whether serum YKL-40 levels were increased in Indian patients with asthma and identify its correlation to mild, moderate and severe asthma conditions. The clinical characteristics of the patients with high serum YKL-40 levels were also evaluated. Furthermore, we aimed to identify possible genetic variants of chitinase3-like 1 gene with prime focus on the association of previously reported rs4950928 and rs880633 variations with bronchial asthma. **Methods:** we quantified serum YKL-40 levels in patients with asthma and in healthy controls by a real time biomolecule interaction analyzer core (BIAcore 2000) technique. The lung function of asthma subjects was measured by Spirometry. Genotyping was done in 100 asthma patients and 45 healthy controls by a polymerase chain reaction based amplification, electrophoresis, purification, sequencing and multiple alignment of the sequences using Genebee clustal W 1.83 software. **Statistical analysis:** Data analysis was done by GraphPad prism6 software(GraphPad software,Inc.,San Diego,CA).Differences in protein level between study groups were compared by using ordinary one way ANOVA and tukey's multiple comparisons test . For single nucleotide polymorphism (snp) analysis, chi square test and fisher's exact test were used. The frequencies of the snp's were evaluated according to the Hardy Weinberg equilibrium. For all tests, a p value of <0.05 was considered significant. **Results:** Serum YKL-40 levels were significantly elevated in patients with asthma as compared with controls (Mean±SD= 3.71±1.65 and 2.60±0.67 respectively).We observed a significant elevation in serum YKL-40 levels of severe asthma group when compared to mild and moderate asthma group. Serum YKL-40 correlated positively with the severity of asthma and inversely with the forced expiratory volume in 1 second (FEV1). In our preliminary findings, we observed 21 snp's associated with chitinase 3 like 1 gene detected mostly in intronic regions. The validated non-synonymous snp rs880633 and the promoter snp rs4950928(C/G) were also observed in our study. In case of rs4950928 variation, we observed high frequency of homozygous G allele in

Indian population which is in contradiction to many previous studies on asthma. Conclusion: YKL-40 was found in increased quantities in the serum of north Indian patients with asthma and its level correlated with disease severity, indicating that increased serum YKL-40 levels may be a biological characteristic of the disease exacerbation with a sentinel role in asthma. This is an ongoing study and in order to confirm the role of observed snp's of chitinase3like-1gene in asthma, a greater in-depth into the study is needed by including more number of subjects.

Keywords: Asthma, snp's, CHI3L1, YKL-40, FEV1