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Title: Risk factors associated with persistent airflow limitation in difficult asthma

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Body: Introduction: The clinical manifestations of difficult asthma are heterogeneous. Some patients with difficult asthma develop irreversible airway obstruction, which is associated with poor outcomes. Objective: the aim of the study is to determine clinical characteristics associated with persistent airflow limitation in difficult asthma. Methods: we retrospectively analyzed 48 patients with difficult asthma between 2005 and 2010. Twenty patients (8 female, 12 male) with persistent airflow limitation (post bronchodilator FEV1/FVC ratio < 70%) were compared to 28 patients (13 female, 15 male) with normal post bronchodilator FEV1/FVC ratio. Patients with chronic obstructive pulmonary disease and bronchiectasis were excluded. Results: there was no significant difference between the two groups in age (51 vs 45 years, p=0,17), sex (p=0,66), age of asthma onset (35 vs 32 years, p=0,07), number of hospitalizations (p=0,39) and frequency of exacerbations (p=0,74). Rhinitis was more frequent in patients with normal FEV1/FVC ratio (15% vs 35%). But, the difference was not significant (p=0,11). Gastroesophageal reflux was found in 25% of patients in both groups. Risk factors associated with persistent airflow limitation were as follows: longer duration of asthma (22 vs 9.5 years, p <0.001), current or past smoking (50% vs 21%, p=0.038) and absence of allergy (69% vs 33%, p=0.026). Dust mite sensitization was significantly more frequent in patients with normal FEV1/FVC ratio (26% vs 61%, p=0,33). Conclusion: Smoking, longer disease duration and absence of sensitization seem to be related to persistent airflow limitation in Tunisian patients with difficult asthma.