



Allergic sensitization and obstructive airway diseases among an adult rural population in Nepal.

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ABSTRACT

Background: The relevance of the obstructive lung diseases asthma and COPD and IgE-mediated allergy in Nepal is still poorly characterized.

Method: In a cross-sectional study in rural Nepal 199 persons were characterized with a questionnaire, skin prick tests, spirometry and total IgE concentration in serum.

Results: About 20 % of the women and 50 % of the men were current smokers. Half of the study population used biomass fuel at home to cook or to heat and 70 % of the study participants experienced dust-exposure at work or at home. 50% of the women and 30 % of the men had a history of COPD, while 57% of the women and 53% of the men had symptoms of respiratory allergy. 18% of the women and 16% of the men used inhaler devices. 62 % of the women and 66% of the men had a total IgE concentration in serum >100 IU/mL. About 30% of the women had a FEV₁ < 80% and about 10 % had a FEV₁ < 40%, also 30 % of the men had a FEV₁ <80% but none of the men had a FEV₁ <40%. The FEV₁/VC ratio was smaller than 70% in 13 % of the women and 14,6 % of the men. We observed a significant inverse correlation between serum IgE with FEV₁. 14% of study participants had positive prick test for house dust mite, 5% were positive for cat dander and 3 % were positive for mugwort.

Conclusion: In summary this study shows an relevant burden of obstructive pulmonary disorders and IgE-mediated allergy in a rural Nepalese population.

Keywords: Allergy, Bronchial asthma, COPD, Nepal



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INTRODUCTION

Nepal is a low-income country. In 2020 its gross domestic product was 1190 US dollars per capita¹ and only 5.8% (2014) of this was spent on health care². A large proportion (48–69%) of the health care costs comes from the out-of-pocket expenditure of patients or their families³. The scarce resources are focused on acute communicable disease. Less is known on non-communicable diseases like chronic obstructive pulmonary disease (COPD) and asthma.

COPD is common in low- and middle-income countries^{4,5}. In Nepal, COPD was the leading cause of death in 2012, killing 17.2 thousand people¹. In 2014 COPD mortality in Nepal has increased to 13%. Moreover, morbidity due to COPD generates an enormous economic burden due to health care costs and loss of productivity. Thus, COPD alone caused the loss of ca. 800 Disability-adjusted life years (DALYs: sum of years of life lost due to premature mortality and years of healthy life lost due to disability) in Nepal in the year 2012. Therefore, efforts

to control COPD risk factors should be strongly encouraged. While the main risk factor for COPD is tobacco smoking⁴, the use of biomass fuel, very common in Nepal, has also been associated with the occurrence of obstructive airway disorders⁵.

For the past 40 years, the prevalence of asthma has increased in all countries in parallel with that of allergies. The prevalence of asthma is rising in developing countries like Nepal, and appears to be associated with increased urbanization. Allergen sensitization is an important risk factor for asthma. Earlier studies suggest the importance of total serum IgE in the pathophysiology of asthma and the development of airflow obstruction. Moreover, a close association has been reported between the presence of elevated total IgE-levels and asthma symptoms.

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Unfortunately, most of the available information on the burden of chronic lung diseases comes from industrialized countries and data about prevalence of diseases, rate of allergic sensitization, prevalence of risk factors in the developing countries are missing.

To describe the prevalence of obstructive lung disease and allergy in a rural region of Nepal we performed a cross sectional observational study including a questionnaire, spirometry and skin prick tests in a consecutive sample of volunteers and patients attending the Kirtipur Hospital in 2012. In a subset of volunteers we performed a blood test with measurement of total IgE. The study was approved by the Nepal Health Research Council.

PARTICIPANTS AND METHODS

The study included a consecutive sample of ambulatory and in-hospital patients attending the Kirtipur Hospital, $n = 199$, 18 -70 years. Exclusion criteria were uncontrolled allergic diseases, too ill to participate, malignant or infectious diseases.

All subjects gave written informed consent in English or Nepali. A screening questionnaire, developed from different validated questionnaires (CAT and German SF-36) and adapted to local circumstances, was completed during a face-to-face interview.

The questions included level of school education, occupation, respiratory symptoms (cough, sputum, wheezing, shortness of breath), tobacco use, use of biomass fuel, previous tuberculosis, current medication, admissions to hospital and visits to health centers. Age, sex, weight and height were recorded.

All participants underwent spirometry after explanation by a research assistant in Nepalese language. Spirometry was done in the Kirtipur Hospital in accordance with the European Respiratory Society and American Thoracic Society recommendations: at least three acceptable and reproducible blows with the largest and second-largest values for both forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV_1) within 150 mL or no more than 5% difference. The largest values for FVC and FEV_1 were considered the best and used for analysis⁶.

Spirometry was done with the FlowScreen of Jaeger, Germany, reference values of ECCS 1993. A new filter was applied for each measurement to avoid cross-contamination. Spirometers were calibrated every morning with a 1 L syringe and weekly with biological control by a healthy spirometry nurse.

Skin-prick tests have been performed in all participants for 10 common allergen extracts (Novartis Pharma, Switzerland): house dust mite, mugwort, grass pollen mix, birch, chicken feathers, cat dander, swine epithelium, goat epithelium,

cow dander and mold, plus negative (saline) and positive (histamine) controls. After cleaning the forearm, a testing grid was marked on the volar forearm surface. Then, a small drop of each testing solution was placed in the center of each mark. For each allergen, a new lancet was used which was then pressed against the skin in the center of the allergen drop. Then excess solution was blotted with a tissue to avoid cross-contamination. Results were read 15 min later and sensitization was defined as wheal or redness at least 3 mm greater than the negative control.

In a subset ($n=99$) of the volunteers, blood samples were collected for total Immunoglobulin E assay and sent to laboratory. The assay (J. Mitra & Company Private Limited, India) was used to determine total serum IgE. Results were expressed in international units per milliliter (IU/mL).

RESULTS

A total of 199 subjects was enrolled into the study, 194 answered the questionnaire (117 women; 77 men). 182 patients underwent skin prick tests (111 women; 71 men). Blood samples for total IgE count and spirometry measures were performed in 99 study participants (58 women; 41 men).

Smoking prevalence: Among study participants about 20 % of the women and 50 % of the men were current smokers, whereas 80 % of the women and 45% of the men had never smoked (Tab 1). The rate of passive smoking was about 40% for the women and 50% for the men.

Environmental exposure: Half of our study population used biomass fuel at home to cook or to heat (i.e wood, charcoal, agricultural waste and dung) and 70 % of the study participants experienced dust-exposure at work or at home.

Lung Diseases: Based on the questionnaire we found that 50% of the women and 30 % of the men had a history of COPD, while 57% of the women and 53% of the men had symptoms of respiratory allergy.

Use of Asthma Inhaler Devices: 18% of the women and 16% of the men used inhaler devices.

Total IgE Count: In a subset ($n = 99$) of study participants we found that 62 % of the women and 66% of the men had a total IgE in serum >100 IU/mL.

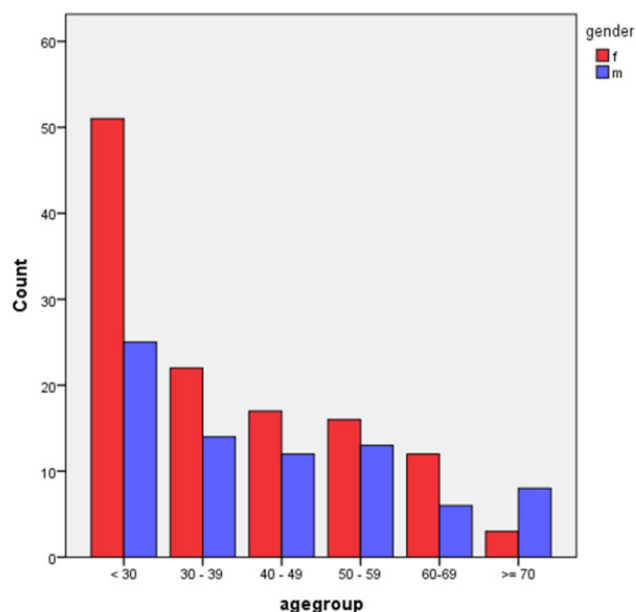
Spirometry FEV_1 : about 30% of the women participating in the study had a $FEV_1 < 80\%$ and about 10 % had a $FEV_1 < 40\%$, also 30 % of the men had a $FEV_1 < 80\%$ but none of the men had a $FEV_1 < 40\%$. The FEV_1/VC ratio was smaller than 70% in 13 % of the women and 14,6 % of the men.

Correlation between Total IgE and Spirometry: We observed a significant inverse correlation between serum IgE

with FEV₁ and with PEF in the study population. When tested separately men and women a significant negative correlation was observed between serum IgE with FEV₁, VC and FVC however only in the women group.

Prick test: 14% of study participants had positive prick test for house dust mite, 5% were positive for cat dander and 3 % were positive for mugwort.

Fig 1: Age of participants.

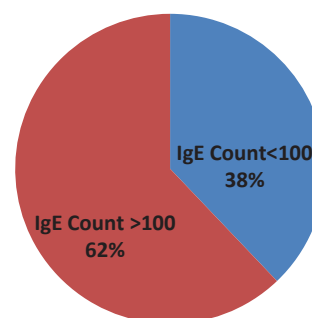


Tab 1: Descriptive statistics of the study population according to smoking history and other types of exposure (mean $\pm$ SD)

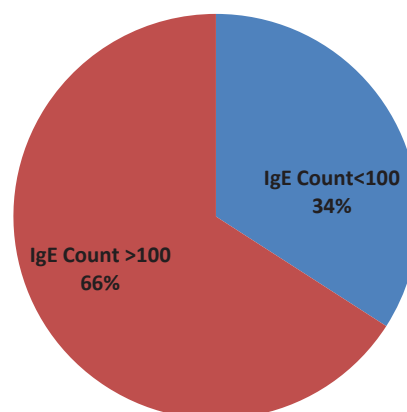
	Female (n=117)	Male (n=77)
Age (Years)	37 ($\pm$ 13)	41 ($\pm$ 15)
Smoking status		
Current smokers	20 (17%)	38 (49%)
Never Smokers	95 (81%)	33 (43%)
Former smokers	2 (2%)	6 (7.8%)
Passive smoking	46 (39%)	36 (47%)
Symptoms		
Dry Cough	31 (26%)	14 (18%)
Productive cough	17 (14%)	12 (15%)
Reduced physical activity	39 (33%)	28 (36%)
Shortness of breath	19 (16%)	19 (25%)
Chronic bronchial symptoms	41 (35%)	28 (36%)
Respiratory allergy	67 (57%)	41 (53%)

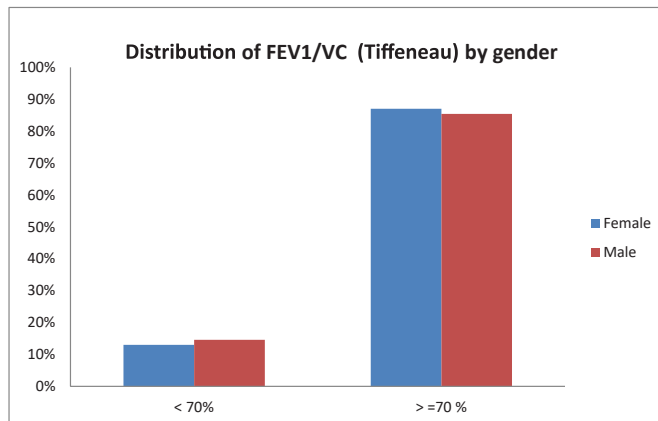
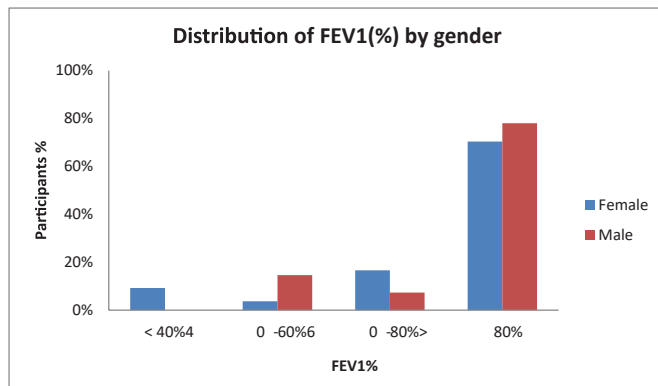
Use of medical resources		
Asthma inhaler	21 (18%)	12 (16%)
Hospital consultation	16 (14%)	9 (12%)
Hospital admission	3 (3%)	5 (6%)
Lung disease		
History of TBC	7 (6%)	6 (8%)
History of COPD	59 (50%)	25 (32%)
Environmental Exposure		
Biomass fuel use	59 (50%)	36 (47%)
Dust exposure	85 (73%)	56 (73%)

IgE concentration in serum in women (n= 58)



IgE concentration in serum in men (n=41)





Allergen Extract	Positive skin reaction		
	Female	Male	Total
house dust mite	16 (14%)	10 (14%)	26(14%)
cat dander	6 (5,4%)	3 (4,2%)	9 (5%)
mugwort	1 (0,9%)	5 (7%)	6 (3%)
grass pollen mix	1 (0,9%)	2 (2,8%)	3 (2 %)
swine epithelium	4 (3,6%)	0	4 (2%)
goat dander	2 (1,8%)	1 (1,4%)	3 (2 %)
cow dander	0	2 (2,8%)	2 (1%)
birch	1 (0,9%)	1 (1,4%)	2 (1%)
mold	1 (0,9%)	1 (1,4%)	2 (1%)
chicken feathers	1 (0,9%)	0	1 (0,5%)

Tab 3: Inverse correlation between Total IgE, FEV₁ and Total IgE and PEF

Pulmonary function parameters	Correlation Coefficient [R]	Alfa Sig 2 teill	N=
FEV ₁ Basis	-,219*	,033	95
FEV ₁ % Soll	-,223*	,030	95
PEF Basis	-,198*	,049	99
PEF % Soll	-,214*	,034	99

DISCUSSION:

The aim of this study was to describe the prevalence of obstructive lung diseases and atopy in a rural population of Nepal using questionnaires, spirometry, allergy skin prick tests and total serum IgE levels. Spirometry in Nepal does not belong to routine medical examination due to lack of specialized personal as well as equipment making it difficult to diagnose obstructive lung diseases. At the same time the burden of NCD and particularly of COPD and asthma are increasing in Nepal. Therefore, it seems particularly important to collect data about obstructive lung diseases.

We collected medical history, performed lung function tests, skin prick tests and measured total IgE in adults visiting the Kirtipur Hospital. We observed a very high prevalence of environmental risk factors for lung health, specifically active and passive smoking as well as exposure to indoor air pollution mainly due to use of biomass as fuel. Prevalence of current smoking was 49 % in men and 17% in women. This prevalence is very high compared to the general prevalence of smoking in Nepal. The tobacco atlas reports a prevalence of smoking of 37.6% for the men and 16.7% for the women¹⁰. In another study about prevalence of risk factors for non-communicable diseases in Nepal, the overall prevalence for smoking was 20%¹¹, men smoked more often than women (27% vs.10%) with higher prevalence among older men (29%) and among rural population. However, in a study about prevalence of cardiovascular risk factors among industrial workers (n= 494) the prevalence of current smoking for men aged 20–59 years was about 40.2%¹². A possible explanation for the discrepancy is, that we performed a survey among patients accessing the hospital. It is known that smokers and former smokers have higher odds of hospitalization compared to never smokers¹³. Our study population was a rural population; in this group is the prevalence of smoking is higher as in the urban population.

About the half (women 50%, men 47%) of the study participants used coal or biomass (wood, animal dung and crop residues) to cook or heat. It is known that in Nepal 2/3 of the households still use biomass fuel to heat or cook^{14,15}. In a study assessing indoor air quality in Nepal and its health effects was found that solid biomass fuels are the main sources of indoor air pollution affecting health. Significant associations were observed between biomass smoke pollution and respiratory symptoms such as cough, phlegm, breathlessness, wheezing and chronic respiratory diseases such as COPD and asthma¹⁶. The indoor air pollution, resulting from incomplete combustion of solid fuels for cooking and/or heating is a major global public health concern because it contains many harmful pollutants including known human carcinogens and is a major contributor to the global burden of disease¹⁷. In one survey conducted in Nepal in 2007 was shown that household air pollution was over 18-folds higher than the WHO recommended guidelines¹⁸. Particularly women and children living in rural regions are exposed to indoor air pollution. In our small population women showed a poor

respiratory health comparable to men, that were on average older and smoked more than women. Interestingly in our sample population 50% of the women had a history of COPD compared to 30 % of men. Likewise, more women (57%) than men (53%) had symptoms of respiratory allergy.

The access to medical care and the use of asthma medication were comparably low in men and women, confirming the observation of Mendis et al.²⁰. In their study about availability of medication in the public and private sector in different middle- and low-income countries, they observed that in Nepal inhaled corticosteroid (ICS) inhalers were rarely available. Moreover, Saito et al.²¹ found that the poor in Nepal tend to use health care facilities far less than the rich. Particularly surprising was the finding, that poor do not even use the public facilities. Their proposed explanation for this finding was that financial barriers due to high out-of-pocket payments may explain the limited access to both private and public facilities²¹.

More than 60% (62% women, 66% men) of the study participants tested for IgE, had a total IgE greater than 100IU/mL. While total serum-IgE is a well-established marker of atopy²²⁻²³, there are other conditions that are known to cause increased IgE levels and specifically: parasitic infections (especially by helminths)²⁴, immunodeficiencies (e.g. Wiskott-Aldrich syndrome)²⁵ and some neoplasms²⁶. Furthermore, in a study of young European adults IgE levels were dependent on gender and smoking status, with men and smokers having slightly higher IgE level²⁷. It is possible that parasitic infections could contribute to the high IgE values in our patient sample. In fact, there is a small study reporting a very high prevalence of parasitic infection in women in Nepal²⁸. However, there was a weak inverse correlation between the IgE concentrations and FEV₁ and PEF values (Tab. 3). When tested by gender the correlation persisted only in the women group. Given the small sample size it is difficult to speculate about the relevance of this finding. However, an inverse correlation between serum IgE and FEV₁ seems biological plausible, since total IgE is a marker of atopy and has been found to correlate with childhood asthma. Moreover, there is growing scientific evidence that exposure to air pollution might play a role in modulating atopy and IgE levels²⁹⁻³⁰.

We found that ca. 20% of study participants had at least one positive prick test. The most common positive test was house dust mite (14 %) followed from cat dander (5%). Although the prevalence of allergic respiratory disorders seems to be high in Nepal, we were not able to find other studies about the prevalence of positive prick test in the adult population in Nepal. The only one was a study of children aged 5 to 15 that showed a prevalence of positive prick test of ca. 20%³¹.

In summary we observed that more than 30 % of the study participants showed an obstructive respiratory disorder and about 20 % of the subjects had positive skin-prick test for at least one of the allergens tested. We found elevated total IgE

level in about 60% of the samples. In the questionnaires we found a very high prevalence of respiratory symptoms and at the same time a very low use of medications and hospital or doctor consultation. We also observed a very high prevalence of environmental pollutants since about the half of the participants used organic fuel to cook and heat and a high prevalence of smoking habit.

Some limitations of this study need to be mentioned. First the study was performed on a consecutive sample of patients accessing the Kirtipur hospital. So that it might not be representative for the general population. We did not test the reversibility of airflow obstruction so we are not able to separate Asthma from COPD. Nevertheless, our observations point out the need for a better awareness of lungs health in rural Nepal.

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