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Airway function in healthy and chronic respiratory diseased. An observational cohort study in Rwanda[1]

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Introduction

Spirometry is an important and useful tool in the diagnosis and management of chronic pulmonary diseases (Perez-Padilla *et al.*, 2006). Interpretation of pulmonary function tests is usually based on comparisons of data measured in an individual patient or subject with reference (predicted) values based on healthy subjects (Pellegrino *et al.*, 2005). These references are used to identify abnormal values and, hence, the nature and degree of functional abnormality. Many different studies have established spirometric reference values for various populations but few studies have been conducted in Africa.

Chronic obstructive pulmonary disease (COPD) and asthma are major health problems worldwide and the number of patients with these diseases continues to rise. It is predicted that by the year 2020, COPD will be the third leading cause of death and the fifth leading cause of disability adjusted life years worldwide (Halbert *et al.*, 2003).

Tobacco smoking is by far the major risk factor for COPD and the prevalence of the disease in different countries is related to the rate of smoking and the time of introduction of cigarette smoking (Pauwels *et al.*, 2004). The use of biomass fuel has also been associated with the occurrence of obstructive airways disorders (Bahera *et al.*, 1991).

Prevalence data for asthma are lacking for many countries in Africa including Rwanda, but it is estimated that nearly 50 millions of Africans currently have asthma (Aît-Khaled *et al.*, 2001).

Scope and objectives of the thesis

The overall objective of the present work was to determine the prevalence of atopy, asthma and COPD in Kigali, the capital of Rwanda, and in Huye district, a rural area located in southern Rwanda, but also to establish spirometric reference values for the Rwandan population.

1 This is the report of PhD research carried out at Ghent University, under the supervision of Jan Van Meerbeeck.

Specific objectives were:

- To generate predicted reference equations for the Rwandan population from healthy subjects;
- To measure the prevalence of risk factors of COPD and asthma including socio-economic status, indoor allergens, pollution (outdoor and indoor pollution), work exposure and smoking;
- To compare the prevalence of COPD, asthma and atopy in Kigali and Huye district with that reported in other developing countries;
- To determine the correlation between asthma and atopy in Kigali town and Huye district.

Patients and Methods

Between February 2008 and August 2009, a total of 2138 individuals were randomly recruited in the rural district of Huye and in Kigali town, localized respectively at 1568 m and 1768 m of altitude. In Kigali, the study was performed in Nyarugenge district, which is considered as the gate of the country. This district is based around the city centre of Kigali, it is more polluted and it contains most of the city's businesses. With an urban population of 193000 subjects (Kigali city, 2012) Nyarugenge is known to be representative of the larger population of Kigali in terms of housing, socio-economic status and air quality. Huye district is localized in southern Rwanda and was chosen because it is less polluted and it is the only rural district in the country that has a University Hospital where spirometers could be regularly maintained.

Inclusion criteria were age ≥ 15 years, living in Kigali town or Huye District and being competent and willing to sign the informed consent form after having been given all the details about the study.

Exclusion criteria for the study were age below 15 years or having any mental illness, recent myocardial infarction or history of admission for cardiac illness within the last 5 months, recent thoracic, abdominal or eye surgery (or retinal detachment) and pregnant women. Subjects with active tuberculosis or any acute lung infections were also excluded. Only those who signed the informed consent form participated in the study. These filters left us with 1824 participants for the study on the prevalence of atopy, asthma and COPD in Rwanda.

For producing spirometric reference values, only healthy subjects were included, participants who reported respiratory symptoms such as dyspnoea, chronic cough, phlegm or wheeze, those known to be asthmatic or suffering from chronic bronchitis, COPD and emphysema, active smokers and ex-smokers, subjects with obesity (Body mass index (BMI) >30 kg/m^2) were all excluded. In total 740 healthy subjects were included for generating spirometric reference values for the Rwandan population.

After height and weight were measured, a questionnaire on respiratory symptoms and history of respiratory diseases, smoking history, exposure to various chemical agents and dust was administrated to each participant. For smoking history, non-smokers were defined as those who never had smoked; smokers were those who were currently smo-

king at least one cigarette per day, and ex-smokers those who reported having smoked on a regular basis until ≥ 5 months before the examination. Passive smokers were defined as subjects who were regularly (daily basis) exposed to environmental tobacco smoke at least during the last 12 months. The questionnaires used were a short version of the American Thoracic Society (ATS-DLD, 1978) and the European Community Respiratory Health Survey II questionnaires (ECRHS II, 2002).

Spirometry was performed using a ML 3535 microloop spirometer with a database storage capacity for over 1000 patients (Microloop 3535, SPIDA spirometry, Micromedical limited, UK). The spirometric parameters used were: FEV_1 (Forced Expiratory Volume in one second), FVC (Forced Vital Capacity), FEV_1 /FVC ratio and PEF (Peak Expiratory Flow).

After explanation of the procedures and demonstration by the technician, using local language, participants were asked to perform up to 8 maneuvers to obtain 3 acceptable flow-volume curves. The spirometry with largest value of FVC and FEV was considered as the best and used for analysis. Equipments and procedures were in accordance with the American Thoracic Society for spirometry (American Thoracic Society, 1995). Spirometers were daily calibrated using a 3 liter's syringe.

All the patients were skin prick tested for six common allergen extracts (Laboratoire Stallergène, Waterloo, Belgium): house dust mite, grass pollen mix, cat dander, dog dander, aspergillus and cockroach plus a negative and positive control (Histamine).

Ethical considerations

Ethical approval was obtained from both the Ghent University Hospital Ethics Committee (Belgium) and the Rwanda National Ethics Committee. Only subjects who signed the informed consent form participated in the study.

Statistical methods

Statistical analyses were performed using the statistical package SPSS 12.01 and statistical significance was viewed as P values lower than 0.05. Odds ratios (OR) and 95% confidence intervals (CI) were calculated, the data of height, age and lung function parameters were expressed as means ± SD (Standard deviation). Ratio FEV_1/FVC was expressed as a percentage. A logistic regression model was performed using age, gender, smoking, residential area as independent variables and obstructive lung diseases as dependant variables.

Results

65.2% of participants were below age 45 years and 34.8% above 45 years; this reflects the Rwandan general population distribution where more than 60% of the population is under 40 years and where women are overrepresented (Table 1).

Variables	Kigali	Huye	N
Gender			
Men	502	376	878 (48.1%)
Women	534	412	946 (51.9%)
Age (years)			
15-29	396	308	704 (38.6%)
Male	200	158	358 (40.7%)
Female	196	150	346 (36.5%)
30-44	286	199	485 (26.6%)
Male	134	96	230 (26.2%)
Female	152	103	255 (27.0%)
45-60	249	212	461 (25.3%)
Male	120	96	216 (24.6%)
Female	129	116	245 (25.9%)
>60	105	69	174 (9.6%)
Male	41	33	74 (8.5%)
Female	66	34	100 (10.6%)
Marital status			
Never married	420	378	798 (43.8%)
Married	348	336	684 (37.5%)
Divorced/separated	46	50	96 (5.3%)
Widowed	134	112	246 (13.5%)
Level of education			
None	284	204	488 (26.7%)
Primary school	398	314	712 (39%)
Secondary school	290	151	441 (24.1%)
More than secondary school	112	71	183 (10%)
Body Mass Index (Kg/m²)			
<18.5	42	66	108 (5.9%)
18.5-24.9	640	596	1236 (67.7%)
25-29.9	201	111	312 (17.1%)
>30	76	32	108 (5.9%)

Table 1. Description of the sample according to socio-demographic variables and anthropometric measures

Of the 1824 subjects who performed spirometry, 256 (14%) were classified as having airflow obstruction with a ratio $FEV_1/FVC <$ LLN. All participants with airflow limitation underwent a post bronchodilator spirometry, among them, 174 out of 256 subjects (94 females and 80 males) had a significant improvement of FEV_1 which was greater or equal to 12% predicted and 200 ml.

Asthma was diagnosed in 163 (8.9%) individuals (table 2). Eleven subjects who had a good reversibility after administration of a bronchodilator were not considered as asthmatics since they reported a history of tuberculosis and mentioned that asthma-like symptoms started after tuberculosis treatment. With regard to doctor's diagnosis of asthma, 121 (74.2%) out of 163 individuals who met our criteria for asthma had a doctor's diagnosis of asthma.

	Total	**Age group**	**Men**	**Women**	**P-value**
Atopy	290	< 45	137	153	NS
	194	≥ 45	91	103	NS
Asthma	113	< 45	54	59	NS
	50	≥ 45	22	28	NS
COPD	22	< 45	10	12	NS
	60	≥ 45	50	10	<0.001

Table 2. Prevalence of atopy, asthma and COPD

COPD was diagnosed in 82 (4.5%) subjects who presented a ratio FEV_1/FVC less than the LLN and was more frequently diagnosed in men than in women; the difference was statistically significant. The prevalence of COPD was higher among current (11.2%) and ex-smokers (8.6%) compared to non-smokers (1.9%). 59 (71.9%) subjects with COPD were current smokers or ex-smokers and about one third (28%) were non-smokers. Among 635 individuals aged 45 years and above, COPD was diagnoses in 9.6% of the subjects. 484 participants (26.5%) had a positive skin prick test meaning a wheal at least 3mm greater than the negative control. House dust mites and grass pollen were the main allergens found with respectively 10.7% (13.2% in Kigali versus 7.6% in Huye) and 7.2% (5.8% in Kigali versus 9.1% in Huye) sensitized participants.

Logarithmic prediction equations formula derived from men and women with age and height as independent variables are shown in table 3. Prediction equations for the means were obtained by regressing the natural logarithms of each lung parameter against ln(height) and square age.

Sex	**Equations**	**R^2**	**RSD**
Females			
FVC	Exp (-10.116 + 2.2238 ln(H) - 0.000071A^2)	0.482	0.11
FEV_1	Exp (-8.614 + 1.905 ln(H) - 0.0000821A^2)	0.471	0.11

Sex	Equations	R^2	RSD
FEV_1/FVC	Exp (5.848– 0.268 ln(H) – 0.000839 A)	0.621	0.08
PEF	Exp (-5.631 + 1.416 ln(H) + 0.00086A^2)	0.082	0.17
Males			
FVC	Exp (-12.528 + 2.724 ln(H) – 0.0000564A^2)	0.516	0.12
FEV_1	Exp (-10.668 + 2.334 ln(H) – 0.0000652A^2)	0.447	0.12
FEV_1/FVC	Exp (7.1477 – 0.518 ln(H) – 0.001025A)	0.073	0.06
PEF	Exp (6.142 + 1.612 ln(H) – 0.000216A^2)	0.151	0.24

Table 3. Prediction equations for male and female between 15 and 80 years old (n=740)
(A: age in years, H: Height in centimeters, R^2: fraction of explained variance, RSD: Residual standard deviation, Exp(x)= e^x)

When we compared our spirometric reference values with studies done in white populations, values for FEV_1 and FVC in the current study were lower than those derived from Caucasians at the same age and height. With men, our results for FEV_1 were 9 to 12% lower and FVC was 16 to 18% lower than those from selected studies done with white subjects. With women, FEV_1 was 12 to 23% lower and FVC from 17 to 28% lower. Comparison with African-Americans and black Africans did not show significant differences in the pulmonary function testing values and they were nearly similar to those for black Americans by Hankinson.

Discussion

In developing countries, chronic respiratory diseases represent a challenge to public health because of their frequency, severity, projected trends and economic impact (Ehrlich *et al.*, 2005). The aim of this research was to generate spirometric reference values and to determine the prevalence of asthma, atopy and COPD in Rwanda using questionnaires, spirometry and allergy skin-prick tests. The overall prevalence of COPD was 4.5% and all participants with COPD had a history of smoking. The WHO has published data placing the worldwide prevalence of COPD at 0.8% and Africa having probably the lowest prevalence in the world (Pauwels RA et al. 2004: 613-620). The low prevalence of COPD in Africa is thought to be a reflection of Africa's young population, with 44% under 15 years and only 3.2% over 65 years, and because of the low prevalence of smoking (Behera *et al.*, 1991).

Our prevalence is close to other studies which place the prevalence of COPD substantially higher, at approximately 4 to 6%. The conflicts among published COPD prevalence rates may be due to many factors, including true differences in disease occurrence, differences in defining obstructive lung disease, cultural biases, and whether spirometry was used to confirm the diagnosis (Halbert *et al.*, 2003). This study revealed a prevalence of asthma of 8.9% in Kigali town and Huye district and a significant association to atopy. 26.5% of participants had a positive skin-prick test to at least one allergen. Furthermore, the fact of living in Kigali, the capital, was an important risk factor for having asthma.

Although statistically significant, the difference in asthma prevalence between Huye District and Kigali town was not too large; the magnitude of the urban-rural differences has lessened over recent years due to the relatively greater increase in asthma prevalence in rural communities as they increasingly adopt Western lifestyles (Odhiambo *et al.*, 1998).

In developing regions, asthma prevalence continues to rise sharply with increases in urbanization and westernization (Braman, 2006). The rising prevalence of asthma has been ascribed to a number of factors including a reduction in the prevalence of childhood infections, change in diet and lifestyle, economic development, and increased exposure to various pollutants.

Conclusion

This is the first study which shows the prevalence of atopy, asthma and COPD in Rwanda. Asthma and COPD were respectively diagnosed in 8.9% and 4.5% of the participants. COPD was diagnosed in 9.6% of the subjects aged ≥ 45 years and was higher among current smokers (11.2%). Spirometric reference values in our study were nearly similar to those for black Americans by Hankinson. Considering the similarities of the Great Lake regions inhabitants, the reference equations obtained in Rwanda population can be used in neighbouring countries while waiting for further studies in the region.

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