



Original Article

Fungal asthma among Ugandan adult asthmatics

Richard Kwizera^{1,2,*}, Felix Bongomin^{3,4}, Ronald Olum⁴, David B. Meya^{1,4}, William Worodria^{4,5}, Freddie Bwanga⁶, Stephen J. Fowler⁷, Robin Gore⁸, David W. Denning⁷ and Bruce J. Kirenga^{2,4,5}

¹Infectious Diseases Institute, College of Health Sciences, Makerere University, P.O. Box 22418, Kampala, Uganda, ²Makerere University Lung Institute, College of Health Sciences, Makerere University, P.O. Box 7749, Kampala, Uganda, ³Department of Medical Microbiology, Faculty of Medicine, Gulu University, P.O. Box, 166, Gulu, Uganda, ⁴Department of Medicine, School of Medicine, College of Health Sciences, Makerere University, P.O. Box 7072, Kampala, Uganda, ⁵Division of Pulmonology, Mulago National Referral Hospital, P.O. Box 7051, Kampala, Uganda, ⁶Department of Medical Microbiology, School of Biomedical Sciences, College of Health Sciences, Makerere University, P.O. Box 7072, Kampala, Uganda, ⁷Manchester Fungal Infection Group, Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, M13 9PL, UK and ⁸Cambridge University Hospitals NHS Foundation Trust, Cambridge, CB2 0QQ, UK

*To whom correspondence should be addressed. Richard Kwizera, Department of Research, Infectious Diseases Institute, College of Health Sciences, Makerere University, P.O. Box 22418, Kampala, Uganda; E-mail: kwizerarichard@gmail.com

Received 17 February 2021; Revised 19 March 2021; Accepted 29 March 2021; Editorial Decision 26 March 2021

Abstract

Fungal sensitization is associated with poor asthma control. We aimed to determine the prevalence and factors associated with fungal asthma among Ugandan adults. Individuals aged ≥ 18 years with a new diagnosis of asthma in the last 12 months participating in the African Severe Asthma Program constituted the study population. Skin prick test results, clinical and demographic data were retrieved from the database, and serum *Aspergillus fumigatus* specific antibodies and total IgE were measured in stored blood. We enrolled 374 patients, median (IQR) age 34 (25–45) years, 286 (76.5%) females and 286 (76.5%) with severe asthma. Prevalence of *Aspergillus fumigatus* sensitization was 42.0% (95% CI: 37.1–47.0%), allergic bronchopulmonary aspergillosis (ABPA) 3.2% (1.8–5.5%), severe asthma with fungal sensitization (SAFS) 16% (12.7–20.1%) and allergic bronchopulmonary mycosis (ABPM) 2.9% (1.7–5.2%). Older age (55–64 years) (crude odds ratio (cOR) = 2.6), sensitization to at least one allergen (cOR = 9.38) and hypertension (cOR = 1.99) were significantly associated with *Aspergillus* sensitization, whereas tertiary education level (cOR = 0.29), severe depression (cOR = 0.15) and strong emotions (cOR = 0.47) were not. High occupational exposure to *Aspergillus* (cOR = 4.26) and contact with moulds (cOR = 14.28) were significantly associated with ABPA. Palpitations (cOR = 5.54), uncontrolled asthma (cOR = 3.54), eczema/dermatitis (cOR = 3.07), poor lung function (cOR = 2.11) and frequent exacerbations (cOR = 1.01) were significantly associated with SAFS. Eczema/dermatitis (cOR = 1.55) was significantly associated with ABPM, but cold weather trigger (cOR = 0.24) was not. Fungal asthma is a significant problem among Ugandans with asthma and should be particularly considered in individuals who remain uncontrolled despite optimal standard of care for asthma, as it is responsive to available and affordable oral antifungal therapy.

Lay Summary

This study showed that fungal asthma is a significant problem among Ugandans with asthma with a high prevalence. Fungal asthma should be considered in patients with uncontrolled asthma despite receiving optimal standard of care. This is the first modern attempt to define these endotypes of asthma in Africa.

Key words: asthma, *Aspergillus* sensitization, allergic bronchopulmonary aspergillosis, allergic bronchopulmonary mycosis, severe asthma with fungal sensitization.

Introduction

Asthma is one of the commonest non-communicable diseases with an estimated global prevalence of over 300 million people.^{1,2} It is among the top 20 chronic diseases for global ranking of disability adjusted life years in children.² In Africa, asthma carries a high burden and is considered a neglected disease.³ National estimates range from 2 to 53% among individuals aged 2 to 64 years.^{4–11} In Uganda, asthma is also common (prevalence, ~11%) and is associated with other allergic diseases, smoking, urbanization and biomass smoke exposure.¹²

Fungal sensitization, mainly due to *Aspergillus fumigatus* is associated with poor asthma control by causing exacerbations¹³ and bronchiectasis.^{14–16} Allergic bronchopulmonary aspergillosis (ABPA) and severe asthma with fungal sensitization (SAFS) are the usual clinical phenotypes of asthma linked to *A. fumigatus* sensitization.¹⁴ Both these distinctive patterns of asthma are responsive to antifungal therapy, which is available and affordable in Africa, for many at least, unlike the new biologics which are not.¹⁷ However, patients may also suffer from allergic bronchopulmonary mycosis (ABPM), due to sensitization to non-*fumigatus* *Aspergillus* species and other molds.^{18,19} The term ‘fungal asthma’ encompasses a spectrum of closely related and often overlapping clinical syndromes ranging from fungal-IgE sensitized asthma, SAFS, serological ABPA and ABPA with bronchiectasis.²⁰ Fungal asthma is a common problem in patients with severe asthma or those with poorly controlled disease using conventional pharmacological approaches.¹⁴

Fungal asthma is estimated to complicate more than 10 million cases of adult asthmatics globally.²¹ However, there is a paucity of published data on this problematic disease entity in sub-Saharan Africa. A systematic review and meta-analysis²² attempted to estimate the burden of fungal asthma in Africa. In this review, approximately 4 074 000 (23.3%) adult asthmatics had fungal sensitization, 437 000 (2.5%) were estimated to have ABPA and 577 000 (3.3%) SAFS in Africa, based on outdated or data outside Africa. Data were lacking on ABPM and factors associated to fungal asthma. Therefore, fungal asthma is a significant and yet an under-recognized problem in Africa.

It is important that country-level epidemiology and associated complications of fungal asthma is described across the continent. The last survey of ABPA prevalence in Africa was published in 1980 and no surveys of SAFS or ABPM have been done.²³ In the current study, we therefore aimed to determine the prevalence and factors associated with fungal asthma among Ugandan adults.

Materials and methods

Study design and population

This was a cross-sectional study, with the aim of investigating the prevalence of *Aspergillus* sensitization, ABPA, SAFS and ABPM among Ugandan asthmatics, while detailing factors associated

with fungal asthma in this population. This study was nested under the African Severe Asthma Program (ASAP) clinical study (*ClinicalTrials.gov Identifier: NCT03065920*)^{24–26} at the Makerere University Lung Institute. ASAP is a clinical study whose primary objective is to identify and characterize severe asthma in Uganda, Kenya and Ethiopia in order to understand its determinants.^{25,26} Between November 2015 and May 2018, ASAP prospectively recruited 821 participants regardless of severity status for the Ugandan site alone. Of these, 50% (412/821) were adults (≥ 18 years) and were eligible for inclusion in this fungal asthma study.

Informed consent for the ASAP study was inclusive enough to cover the current study. All participants in the current study were adults (≥ 18 years) enrolled in ASAP at the Ugandan site having a ‘current/previous doctor diagnosis of asthma or clinical/treated asthma or wheezing/whistling breath in the last 12 months’. Participants were included in this study regardless of severity status at baseline. Patients with an alternative lung disease likely to confound assessment of asthma, patients unable to perform study tests and procedures and pregnant women were excluded. Each patient was followed up for 12 months.

Sample size calculation

With actual prevalence of *Aspergillus* sensitization among adult asthmatics in different African countries not exceeding 41.8%,^{23,27–34} we used the Leslie Kish formula³⁵ to estimate sample size with a precision/absolute error of 5% and at a 95% confidence level to obtain a sample size of 374.

Study samples and assays

Samples used for this study were stored baseline serum samples from the ASAP study population at the Ugandan site (stored at -80°C). Simple random sampling using computer generated numbers was used to select 374 of the 412 stored baseline samples of those ASAP participants eligible for this study (i.e., ≥ 18 years) regardless of severity status. Their respective clinical and demographic data were also retrieved from the ASAP database.

Samples were shipped to the Mycology Reference Centre Manchester, UK and testing performed via ImmunoCAP® (ThermoFisher, previously Phadia) for levels of *Aspergillus fumigatus*-specific IgG (Asp IgG), *Aspergillus fumigatus*-specific IgE (Asp IgE) and total serum IgE (TIgE) antibodies.

Assay cut-offs

We used cut-offs of 40 mg/l for the ImmunoCAP *Aspergillus*-specific IgG and 0.35 kUA/l for *Aspergillus*-specific IgE as recommended by the manufacturer. We used a cut-off of 113.9 kU/l for total IgE as recommended by the manufacturer and a cut-off of 1000 kU/l as a screen for ABPA.³⁶ A cut-off of 500 cells/ul for eosinophil was used to screen for ABPA.³⁷

Table 1. Case definition for fungal asthma.

Aspergillus sensitization	Positive AF SPT or AF IgE
ABPA	Positive TIgE > 1000 IU/ml and Positive AF SPT or Asp IgE and AEC > 500 cells/μl
SAFS	Severe asthma and Fungal sensitization (Positive Asp SPT or Asp IgE) and Positive TIgE < 1000
ABPM	Severe asthma and Negative Asp IgE and Asp SPT and Positive TIgE < 1000 Positive MM SPT

Data presented are case definitions for fungal asthma. ABPA = Allergic bronchopulmonary aspergillosis, SAFS = Severe asthma with fungal sensitization, ABPM = Allergic bronchopulmonary mycosis, AF = *Aspergillus fumigatus*, SPT = skin prick test, Asp = *Aspergillus*, IgG = Immunoglobulin G, IgE = Immunoglobulin E, TIgE = total Immunoglobulin E, AEC = absolute eosinophil count, MM = Mold mix.

Skin prick test procedures

Skin prick testing (SPT) (Immunospec (Pty) Ltd, Johannesburg, Gauteng, South Africa) was performed at baseline for all enrolled patients in the ASAP study, and the tests were performed and interpreted according to international guidelines.³⁸ We used a panel of 12 allergens that included only two fungal allergens (*Aspergillus fumigatus* and Mould mix IV [*Penicillium brevicompactum*, *Penicillium expansum*, *Penicillium notatum*]). Normal saline served as a negative control while histamine was the positive control, with a mean wheal diameter of at least 3 mm being positive, read after 15 min of allergen application. A comprehensive clinical history was obtained to ensure that the patients had not been taking oral steroids or anti-histamines in the last 7 days prior to the SPT. A second reader was called upon for reactions that were not clear.

Case definitions

Asthma severity was assessed using the severity grading based on the National Asthma Education and Prevention Program/National Heart, Lung and Blood Institute Expert Panel Report (EPR 3) guideline.³⁹ We defined non-severe asthma as (intermittent or mild) and severe asthma as (moderate persistent or severe persistent). Level of asthma control was assessed using the asthma control questionnaire (ACQ)⁴⁰ with ACQ cut off of 1.5. A variable named ‘occupational risk’ was generated by categorizing patients’ occupations according to their risk of exposure to *Aspergillus* spores into low, moderate and high risk. For this study, the term fungal asthma was used to refer to ABPA, SAFS and ABPM and included *Aspergillus* sensitization.²² *Aspergillus* sensitization was defined as ‘a positive SPT (mean wheal diameter $\geq$ 3 mm) against *Aspergillus fumigatus* antigen’ or ‘an elevated *Aspergillus fumigatus* specific IgE antibody level greater than 0.35 kUA/l’. In the current study, we adopted and used the case definition for SAFS, ABPA and ABPM as proposed by Agarwal et al. for the ABPA complicating asthma ISHAM

working group.³⁷ Table 1 summarizes the criteria used for the case definition of fungal asthma.

Data analysis

Data were analyzed using STATA version 16 (StataCorp LLC, College Station, TX, USA). All analyzed data were collected at baseline visit. Descriptive statistics were used to summarize baseline characteristics of participants; categorical variables as frequencies (percentages) and numerical variables as median (interquartile range). To compare the differences in asthma severity and baseline demographics, chi-square or Fisher’s exact ($n \leq 5$) tests were performed for categorical variables and Mann-Whitney U tests for continuous variables. To compare *Aspergillus*-specific antibody titers and baseline demographics, Mann-Whitney U (for variables with 2 categories) or Kruskal-Wallis (for variables with 3 or more categories) tests were performed. Our primary data analysis aimed at establishing the prevalence or proportions of asthmatics with fungal asthma (*Aspergillus* sensitization, ABPA, SAFS and ABPM) and the factors associated with fungal asthma. The prevalence estimates were calculated as proportion of patients with *Aspergillus* sensitization, ABPA, SAFS and ABPM and presented as percentages at 95% confidence interval. The number of cases was obtained by extrapolating prevalence to total estimated numbers in Uganda. A binary logistic regression was performed to assess the association between fungal asthma and baseline demographics. At all levels of hypothesis testing, a p -value < 0.05 was considered statistically significant.

Ethical statement

Participants provided written informed consent to participate in the ASAP study (MHREC 875). Ethics approval for this sub-study was received from the School of Biomedical Sciences research and ethics committee (SBS 598), the Uganda National

Table 2. Baseline characteristics of the study population.

Characteristic	Overall (N = 374)		Intermittent and mild asthma (N = 88)		Moderate persistent and severe persistent asthma (N = 286)		P-value
	N	n (%) or median (IQR)	N	n (%) or median (IQR)	N	n (%) or median (IQR)	
Current age in years	369	34 (25–45)	88	29 (23–41)	281	35 (26–46)	0.013
Age when first diagnosed with asthma	372	25 (15–36)	87	23 (15–33)	285	25 (15–36)	0.650
Male gender	374	88 (23.5)	88	20 (22.7)	286	68 (23.8)	0.839
Overall BMI	374	24.8 (21.6–29.5)	88	23.7 (20.9–28.9)	286	25.7 (21.6–29.7)	0.104
Marital status	374		88		286		
Single		131 (35)		35 (39.8)		96 (33.6)	0.031
Married		188 (50.3)		44 (50)		144 (50.3)	
Separated		27 (7.2)		8 (9.1)		19 (6.6)	
Mean ACQ	372						
Well controlled		94 (25.3)	88	46 (52.3)	284	48 (16.8)	0.000
Not well controlled		278 (74.7)		42 (47.7)		236 (82.5)	
Pre-measurements			88		286		
FVC	374	2.9 (2.2–3.4)		3.3 (2.9–3.6)		2.7 (2.1–3.2)	0.000
FVC%	374	100 (83–112)		110 (103–120)		95.5 (78–109)	0.000
FEV1	374	2.1 (1.6–2.7)		2.6 (2.3–3.0)		1.97 (1.4–2.5)	0.000
FEV1%	374	88 (65–105)		103 (91.5–115.5)		79 (60–100)	0.000
FEV1/FVC ratio	374	0.76 (0.66–0.84)		0.82 (0.74–0.88)		0.73 (0.63–0.83)	0.000
Post-measurement			9		117		
FVC	126	2.6 (2.2–3.4)		3.1 (2.8–3.6)		2.62 (2.2–3.4)	0.050
FVC %	126	99.5 (80–112)		117 (111–120)		97 (80–111)	0.002
FEV1	126	1.8 (1.3–2.3)		2.3 (2.1–2.5)		1.73 (1.29–2.2)	0.010
FEV1%	126	73.5 (56–89)		98 (92–103)		71 (56–87)	0.000
FEV1/FVC ratio	126	0.65 (0.56–0.71)		0.74 (0.7–0.76)		0.64 (0.56–0.71)	0.006
Skin prick, at least one allergen positive	331		71		260	(0)	
Yes		310 (93.7)		67 (94.4)		243 (93.5)	1.000
No		21 (6.3)		4 (5.6)		17 (6.5)	
Eosinophil count	374	210 (110–390)		200 (110–410)		215 (100–390)	0.984
Patient uses ICS	370	34 (9.2)	87	3 (3.4)	283	31 (11)	0.034
History of smoking	374		88		286		
Current smoker		1 (0.3)		0 (0)		1 (0.3)	0.569
Former smoker		22 (5.9)		7 (8)		15 (5.2)	
Never		351 (93.9)		81 (92)		270 (94.4)	
Patient uses inhaler medication	370	108 (29.2)	87	13 (14.9)	283	95 (33.6)	0.001

Data presented are percentages (%), medians and interquartile ranges (IQR). The *P*-values compare severe vs non-severe in a given variable using Mann-Whitney U test for continuous variables, chi-square or Fisher's for categorical variables.

FVC = Forced vital capacity, FEV = Forced Expiratory Volume ICS = Inhaled Corticosteroids, PHQ = Patient Health Questionnaire.

Council for Science and Technology (HS 2532) and the Uganda National Drug Authority (9464).

Results

Study population characteristics

Of the 374 asthma patients included in the study, 286 (76.5%) were females, and the median age was 34 years (IQR = 25–45; *n* = 369). Overall, 74.7% of the participants had poorly controlled asthma, 286 (76.5%) of whom were in the severe asthma group. Cough (45.5%), wheezing

(40.6%), chest pain (31.8%) and shortness of breath (28.1%) were the commonest symptoms. Rhinosinusitis (30.7%) and gastroesophageal reflux disease (24.1%) were the commonest co-morbidities reported in this population (Table 2 and Supporting Information 1). Family history of asthma was reported in 222/372 (59.7%) participants. HIV prevalence was 7.5%.

S1.pdf: Extended baseline characteristics of the study population.

Using skin prick test, 310 (93.7%) participants had reaction to at least one allergen. The median eosinophil count was

Table 3. Summary of *Aspergillus fumigatus*-specific antibody titers and total serum IgE.

Characteristic	N	Overall		Intermittent and mild asthma		Moderate persistent and severe persistent asthma	P-value
		n (%) or median (IQR)	N	n (%) or median (IQR)	N	n (%) or median (IQR)	
Asp IgG	356	9.46 (5.4–17.3)	86	10.35 (6.38–18)	270	9.14 (5.19–17.2)	0.104
Asp IgE	374	0.03 (0.01–0.08)	88	0.03 (0.01–0.09)	286	0.03 (0.01–0.08)	0.911
Total IgE	374	385.2 (107.5–1013.3)	88	283.1 (91.5–899.0)	286	388.1 (107.9–1021.7)	0.513
Pos Asp-SPT	374	143 (38.2)	88	33 (37.5)	286	110 (38.5)	0.871
Pos Asp-SPT and Asp-IgE	374	13 (3.5)	88	3 (3.41)	286	10 (3.5)	1.000

Data presented are percentages (%), medians and interquartile ranges (IQR). The *P*-values compare severe vs non-severe in a given variable using Mann-Whitney U test for continuous variables, chi-square or Fisher's for categorical variables.

Asp = *Aspergillus*, IgG+ = Immunoglobulin G, IgE = Immunoglobulin E, Pos = positive, SPT = skin prick test.

210 cells/ul (IQR = 110 – 390). Only 9.2% (34/370) were using inhaled corticosteroids (ICS) at baseline.

Antibody levels

The median *Aspergillus*-specific IgG (Asp-IgG) antibody level was 9.46 mg/l (IQR = 5.4–17.3; *n* = 356) and 16/374 (4.3%) participants had elevated Asp-IgG levels. The median *Aspergillus*-specific IgE (Asp-IgE) antibody level was 0.03 kUA/l (IQR = 0.01–0.08; *n* = 374) and 27/374 (7.2%) participants had elevated Asp-IgE levels. The median total IgE (T-IgE) antibody level was 385.2 kU/l (IQR = 107.5–1013.3; *n* = 374) and 275/374 (73.5%) participants had elevated T-IgE levels. 95/374 (25.4%) participants had T-IgE levels greater than 1000 kU/l, yet stool microscopy for helminths using formol-ether concentration method was negative for all patients. There was no significant difference in antibody levels between the severe and non-severe asthmatics (Table 3).

When examining the differences between *Aspergillus*-specific antibody titers and baseline demographics, we found gender, chest pain, level of asthma control, lung function and eosinophil count significantly associated with *Aspergillus*-specific IgE titers; while age, level of asthma control, HIV status and use of ICS were significantly associated with *Aspergillus*-specific IgG titers (Table 4).

Prevalence and factors associated with *Aspergillus* sensitization

The prevalence of *Aspergillus* sensitization in this population was 41.9% (157/374, 95% CI: 37.1–47.0%). Using the Global Health Data Exchange tool (GHDx) (<http://ghdx.healthdata.org/gbd-results-tool>) and 'asthma' as the cause, we took the '15–49 years' group to represent the population of adult asthmatics in Uganda. If there were 691 442 cases of adult asthma in the year 2019, with a prevalence of *Aspergillus* sensitization of 41.9%, we estimated that approximately 289 714 adult asthmatics had *Aspergillus* sensitization in Uganda in the same year. Patients

aged 55–64 years (crude odds ratio (cOR): 2.60, *P* = 0.018), at least one allergen positive on SPT (cOR:9.38, *P* = 0.003) and hypertension (cOR:1.99, *P* = 0.037) were more likely to have *Aspergillus* sensitization. However, patients with secondary education (cOR:0.23, *P* = 0.019), tertiary education (cOR = 0.29, *P* = 0.048), severe depression (cOR:0.15, *P* = 0.043) and those triggered by strong emotions (cOR:0.47, *P* < 0.001) were less likely to have *Aspergillus* sensitization (Table 5 and Supporting Information 2).

S2.pdf: Extended factors associated with fungal asthma.

Prevalence and factors associated with ABPA

The prevalence of ABPA in this population was 3.2% (12/374, 95% CI: 1.8–5.5%). Similarly using the GHDx, with a prevalence of ABPA of 3.2%, we estimated that approximately 22 126 adult asthmatics had ABPA in Uganda in 2019. Patients with high occupational risk (cOR:4.26, *P* = 0.046) and those in contact with molds (cOR:14.28, *P* = 0.003) were more likely to have ABPA (Table 5 and Supporting Information 2).

Prevalence and factors associated with SAFS

The prevalence of SAFS in this population was 16.0% (60/374, CI: 12.7– 20.1%). Similarly using the GHDx, with a prevalence of SAFS of 16%, we estimated that approximately 110 630 adult asthmatics had SAFS in Uganda in 2019. Patients with palpitations (cOR:5.54, *P* = 0.018), uncontrolled asthma (cOR:3.54, *P* = 0.005), eczema/dermatitis (cOR:3.07, *P* = 0.015), poor lung function (cOR:2.11, *P* = 0.010) and frequent exacerbations (cOR:1.01, *P* = 0.043) were more likely to have SAFS (Table 5 and Supporting Information 2).

Prevalence and factors associated with ABPM

The prevalence of ABPM due to *Penicillium* species in this population was 2.9% (11/374, CI: 1.7– 5.2%). Similarly using the GHDx, with a prevalence of ABPM of 2.9%, we estimated that approximately 20 051 adult asthmatics had ABPM

Table 4. Differences in Aspergillus-specific antibody titers and selected baseline demographics.

Characteristic	N	Asp IgE		Asp IgG	
		Median (IQR)	P	Median (IQR)	P
Gender					
Male	88	0.05 (0.03–0.13)	0.000	8.12 (5.19–13.15)	0.193
Female	286	0.02 (0.01–0.07)		9.09 (5.03–17.80)	
BMI					
Underweight	22	0.04 (0.01–0.14)	0.073	6.00 (4.3–12.6)	0.218
Normal	168	0.04 (0.01–0.09)		8.3 (4.92–15.25)	
Overweight	103	0.02 (0.01–0.07)		10.7 (5.18–17.8)	
Obese	81	0.02 (0.01–0.06)		11.0 (5.35–18)	
Occupational exposure to Asp					
Low	200	0.03 (0.01–0.08)	0.302	8.4 (5.0–15.7)	0.175
Moderate	123	0.03 (0.01–0.08)		10.4 (5.4–20.9)	
High	50	0.04 (0.02–0.09)		7.6 (4.8–14.0)	
Cough					
Yes	170	0.03 (0.01–0.08)	0.778	8.03 (4.8–16.1)	0.176
No	204	0.03 (0.01–0.09)		9.36 (5.34–16.90)	
Wheezing					
Yes	152	0.03 (0.01–0.08)	0.910	7.87 (4.8–16.1)	0.161
No	222	0.03 (0.01–0.09)		9.36 (5.18–10.9)	
Shortness of breath					
Yes	105	0.02 (0.01–0.07)	0.079	7.63 (4.8–14.6)	0.142
No	269	0.03 (0.01–0.09)		9.66 (5.17–16.9)	
Chest pain					
Yes	119	0.02 (0.01–0.07)	0.050	7.97 (4.39–17.8)	0.393
No	255	0.03 (0.01–0.09)		9.12 (5.17–16.3)	
Level of asthma control					
Well controlled	94	0.02 (0.01–0.07)	0.039	11.15 (5.71–20.70)	0.032
Not well controlled	278	0.03 (0.01–0.09)		8.40 (4.92–15.40)	
Contact with molds					
Yes	7	0.02 (0.01–0.05)	0.647	12.00 (3.24–35.60)	0.397
No	367	0.03 (0.01–0.08)		8.69 (5.05–16.50)	
Rhinosinusitis					
Yes	115	0.04 (0.01–0.10)	0.148	8.87 (5.35–14.50)	0.822
No	259	0.03 (0.01–0.08)		8.55 (4.88–17.30)	
HIV					
Yes	28	0.04 (0.02–0.09)	0.570	4.72 (3.25–7.99)	0.0003
No	346	0.03 (0.01–0.08)		9.36 (5.31–17.20)	
Eczema/dermatitis					
Yes	23	0.05 (0.02–0.11)	0.180	7.90 (3.79–14.00)	0.293
No	351	0.03 (0.01–0.08)		8.75 (5.08–16.90)	
Lung function					
Normal	201	0.02 (0.01–0.07)	0.001	9.27 (5.25–17.2)	0.273
Poor	173	0.04 (0.02–0.09)		8.24 (4.92–16.30)	
Methacholine challenge test					
Positive	23	0.03 (0.02–0.09)	0.359	10.30 (6.49–15.20)	0.533
Negative	338	0.03 (0.01–0.08)		8.64 (4.99–16.90)	
At least one allergen positive					
Yes	310	0.03 (0.01–0.09)	0.653	8.45 (5.03–16.20)	0.313
No	21	0.02 (0.01–0.07)		13.00 (4.49–22.30)	
Eosinophilic count					
AEC < 500	310	0.02 (0.01–0.08)	0.004	8.56 (4.97–16.90)	0.995
AEC ≥ 500	64	0.05 (0.02–0.12)		10.25 (5.28–15.45)	
Patient uses ICS:					
Yes	34	0.02 (0.01–0.05)	0.103	6.38 (4.62–10.80)	0.036
No	336	0.03 (0.01–0.09)		9.36 (5.11–17.25)	

Data presented are medians and interquartile ranges (IQR). The *P*-values compare categories in a given variable using Mann-Whitney U (for variables with 2 categories) or Kruskal-Wallis (3 categories and above).

BMI = body mass index, HIV = human immunodeficiency virus, AEC = absolute eosinophil count, ICS = Inhaled Corticosteroids.

Table 5. Factors associated with fungal asthma.

Variables	Aspergillus sensitization				ABPA				SAFS				ABPM			
	N	n (%)	COR (95% CI)	P	N	n (%)	COR (95% CI)	P	N	n (%)	COR (95% CI)	P	N	n (%)	COR (95% CI)	P
Prevalence	374	157 (41.9)			374	12 (3.2)			374	60 (16.0)			374	11 (2.9)		
Current age	155				11				59				11			
18–24		31 (20)	1.00			3	1.00			9	1.00			1	1.00	
25–34		40	1.14	0.655		(27.3)	1.13	0.876		(15.3)	1.83	0.166		2	(18.2)	0.667
35–44		(25.8)	(0.63–2.07)		4	(36.4)	(0.25–5.19)			18	(0.78–4.32)			4	(36.4)	
45–54		34	1.26	0.471			0.69	0.691		(30.5)	1.76	0.217		2	(18.2)	0.192
55–64		(21.9)	(0.67–2.34)		2	(18.2)	(0.11–4.25)			14	(0.72–4.33)			2	(18.2)	
65+		23	1.57	0.215		0 (0)	NA	0.624		(23.7)	1.43 (0.5–4.1)	0.511		0 (0)	3.62	0.299
		(14.8)	(0.77–3.20)		2	(18.2)	1.58			7	2.75				(0.32–40.95)	
		22	2.60	0.018		2	(0.25–9.88)			9	(0.99–7.63)	0.052			4.86	0.203
		(14.2)	(1.18–5.73)		0 (0)	(18.2)	NA			2	1.9				(0.43–55.31)	
		5 (3.2)	1.48	0.545		0 (0)				(15.3)	(0.35–10.21)	0.454			NA	
			(0.42–5.24)							(3.4)						
Gender	157				12				60				11			
Male		40	1.00			5	1.00			14	1.00			3	(27.3)	1.00
Female		(25.5)	0.83	0.450		(41.7)	0.42	0.143		(23.3)	1.01	0.969		8	(72.7)	0.767
		117	(0.51–1.34)		7	(58.3)	(0.13–1.35)			46	(0.53–1.95)				(0.21–3.14)	
		(74.5)								(76.7)						
Asthma	157				12				60				10			
control		38	1.00			3	1.00			6	1.00			3	(30)	1.00
controlled		(24.2)	1.10	0.686		(25)	1.01	0.983		(10)	3.54	0.005		7	(70)	0.728
Not		119	(0.69–1.77)		9	(75)	(0.27–3.83)			54	(1.47–8.51)				(0.2–3.09)	
controlled		(75.8)								(90)						
Asthma	157				12				60				11			
severity		167 (0)	0.94	0.794		11	3.48 (0.44–	0.236		60	NA			11	(0)	NA
moderate		50 (0)	(0.58–1.52)			(91.7)	27.34)			(100)				0	(0)	
and severe			1.00			1	1.00			0						
persistent						(8.3)										
Intermittent																
and mild																
Lung function	157				12				60				11			
Normal		82	1.00			5	1.00			23	1.00			7	(63.6)	1.00
Poor		(52.2)	1.11	0.617		(41.7)	1.65	0.398		(38.3)	2.11	0.010		4	(36.4)	0.66
		75	(0.74–1.68)		7	(58.3)	(0.52–5.31)			37	(1.2–3.71)				(0.19–2.28)	0.507
		(47.8)								(61.7)						

Table 5. Continued.

Variables	Aspergillus sensitization					ABPA			SAFS			ABPM		
	N	n (%)	COR (95% CI)	P	N	n (%)	COR (95% CI)	P	N	n (%)	COR (95% CI)	P	n (%)	COR (95% CI)
MCT	151				12				58				11	
Positive		9 (6)	1.00	0.786		2 (16.7)	1.00	0.158		3 (5.2)	1.00	0.684		0 (0)
Negative		142 (94)	1.13 (0.47–2.68)			10 (83.3)	0.32 (0.07–1.56)			55 (94.8)	1.3 (0.37–4.51)			11 (100)
At least 1 allergen pos	156	154 (98.7)	9.38	0.003	12	12 (100)	NA		60	60 (100)	NA		11 (100)	NA
Yes		2 (1.3)	(2.15– 40.95)			0 (0)				0 (0)			0 (0)	
No			1.00											
Eosinophilic count	157	133 (84.7)	1.00	0.426	12	0 (0)	NA		60	52 (86.7)	1.00	0.398	11 (100)	NA
AEC ≤ 500		24 (15.3)	0.80 (0.46–1.39)			12 (100)				8 (13.3)	0.71 (0.32–1.58)		0 (0)	
AEC > 500														
Patient uses ICS	154	14 (9.1)	0.98	0.956	12	0 (0)	NA		59	6 (10.2)	1.14 (0.45–2.9)	0.776	2 (18.2)	2.27 (0.47–10.97)
Yes		140 (90.9)	(0.48–2.01)			12 (100)				53 (89.8)	1.00		9 (81.8)	1.00
No			1.00											
History of smoking	157				12				60				11	
Current smoker		1 (0.6)	1.00	0.722		0 (0)	1.00	0.718		0 (0)	1.00	0.748		0 (0)
Former smoker		10 (6.4)	1.17 (0.49–2.78)			1 (8.3)	1.47 (0.18–11.95)			3 (5)	0.81 (0.23–2.84)		0 (0)	NA
Never		146 (93)	NA			11 (91.7)	NA			57 (95)	NA		11 (100)	
Use of inhaler					12				59				11	
Yes		47 (30.5)	1.12 (0.71–1.76)	0.635	12	1 (8.3)	0.21 (0.03–1.67)	0.141		22 (37.3)	1.56 (0.87–2.79)	0.138	3 (27.3)	0.91 (0.24–3.49)
No		107 (69.5)	1.00			11 (91.7)	1.00			37 (62.7)	1.00		8 (72.7)	1.00
Episodes of exacerbations	157	8 (3–20)	1.00 (1.00–1.01)	0.295	12	8 (4.5–20)	1.00 (0.98–1.02)	0.971	60	10 (3–20)	1.01 (1.00–1.02)	0.043	5 (3–20)	1.00 (0.98–1.02)
AQL score	157	128 (111–153)	1.00 (0.99–1.01)	0.957	12	125 (116.5–149.5)	1.00 (0.98–1.02)	0.987	60	126 (107.5–147.0)	1.00 (0.99–1.00)	0.263	127 (112–155)	1.00 (0.98–1.02)

Data presented are percentages (%), crude odds ratios (cOR) and 95% confidence intervals (CI).

AEC = absolute eosinophil count, MCT = Methacholine challenge test, AQL = Asthma quality of life.

in Uganda in 2019. Patients with eczema/dermatitis (cOR:1.55, $P = 0.683$) were more likely to have ABPM. Asthma triggered by cold weather appeared to be protective for ABPM (cOR:0.24, $P = 0.043$) (Table 5 and Supporting Information 2).

Discussion

Asthma is a common chronic respiratory disorder in Africa.⁴ However, currently, there is a paucity of population-based epidemiological data on the burden of fungal asthma and its associated complications among Africans living with asthma.²² In the present study, the prevalence of *Aspergillus* sensitization was 41.9% (~289 000 cases), SAFS 16% (~110 000 cases), ABPA 3.2% (~22 000 cases) and ABPM 2.9% (~20 000 cases). These findings are in keeping with a recent systematic review which showed that about 3–52% of Africans with asthma have fungal sensitization.²² We also previously demonstrated a 32% prevalence of *Aspergillus* sensitization in the same Ugandan population.⁴¹ We also observed a large discordance between the proportion of patients reported to be *Aspergillus* sensitized by SPT (42%) and the proportion with a raised IgE to *Aspergillus* (7%). More studies are needed to investigate this discordance. Fungal sensitization is associated with worse asthma control, leading to asthma attacks,¹³ additional need for corticosteroids, hospitalization⁴² and increased rates of bronchiectasis (especially due to *A. fumigatus*).^{14–16} However, other studies have similarly demonstrated a weak association between *Aspergillus* sensitization and asthma severity.⁴³ SAFS in our study was significantly associated with un-controlled asthma, poor lung function and frequent episodes of exacerbations, unlike ABPA and ABPM.

Compared to previously published studies from African countries, the prevalence of fungal sensitization ranged from 2.9 to 51.9%.^{23,27,29–31,33,34,44–47} Three studies from Egypt reported a prevalence of 2.9,²⁷ 38.4³⁴ and 51.9%.⁴⁷ Comparatively, the prevalence of fungal sensitization among South Africans with asthma ranged between 4.8 and 26.7%.^{23,29,31} Oluwole and colleagues reported a prevalence of fungal sensitization of 10.9% among Nigerians.⁴⁵ A study from Sudan reported a much higher prevalence at 40.0%.⁴⁴ Compared to the above studies, we report a much higher prevalence of fungal sensitization (42%) among the Ugandan cohorts.

The high prevalence of SAFS in our cohort could be related to the very high prevalence of severe asthma (76.5%) among our participants. This is partly because we used data of patients from the ASAP study, which mainly had patients with severe asthma, and thus may not truly reflect the prevalence of the disease among the general population of individuals with asthma in Uganda. Besides, we defined severe asthma using the severity grading based on EPR3³⁹ i.e., non-severe asthma = (intermittent or mild) while severe asthma = (moderate persistent or severe persistent). This could have overestimated the prevalence of

severe asthma in this population. Our estimate of the prevalence of SAFS in Uganda may be too high for this reason.

Consistently, the global burden of ABPA is estimated to range between 0.7 and 3.5%,⁴⁸ and in this study was 3.2%. The only other estimate from Africa is from 1980 in South Africa and was 2.5%.²³ The prevalence of ABPA varies with the diagnostic criteria or case definition used. A recent study revealed that the new diagnostic criteria, compared with existing criteria, showed better sensitivity and specificity for diagnosing ABPA/ABPM.¹⁹ We likely overdiagnosed some patients as ABPA since we used only a single criterion.

Our study reports for the first time the prevalence of ABPM due to *Penicillium* species in Africa. Patients with eczema/dermatitis were three times more likely to have ABPM while those whose asthma is triggered by cold weather were 76% less likely to have ABPM. Studies have shown fungal sensitization in severe asthma to be associated with the isolation of *Aspergillus fumigatus* in sputum.⁴⁹ However, in our study, we did not culture sputum because other previous studies showed that it is not a reliable test in this population, and hence not included in most case definitions.⁵⁰ Besides, good quality sputum is difficult to obtain. However, sputum culture might be useful in patients with ABPM, given the range of fungi linked with ABPM.

Fungal asthma has a complex clinical presentation, diagnosis is challenging, treatment is poorly defined and long-term complications such as chronic pulmonary aspergillosis (CPA) complicates prognosis.²⁰ CPA is a well-known complication of ABPA and SAFS; the burden of this debilitating disease among Ugandans with fungal asthma remains unknown and is a subject for future research. ABPA, ABPM and SAFS do not respond clinically to conventional asthma therapy.⁵¹ Antifungal therapy, typically oral itraconazole may be considered in patients with SAFS or ABPA.⁵² An open-label randomized trial showed that prednisolone was superior (100%) to itraconazole (88%) in terms of reducing the number of asthma exacerbations and % decline in IgE after treatment, but with more adverse events.⁵³ There are no data on fungal asthma treatment and treatment outcomes among Africans.

However, the strength of our study lies in its inclusion of a large sample size and a diverse population of patients with asthma in Uganda. We robustly evaluated fungal allergy through skin prick and serological tests. Therefore, we likely captured all cases of fungal sensitization. Also, we were able to assess the impact of fungal sensitization on lung function of the affected participants. Our study provides baseline data for future epidemiologic studies on fungal asthma in Uganda. Importantly, future studies evaluating chest CT findings, particularly among patients suspected of ABPA may be more informative. Of equal importance are studies on the efficacy and safety of antifungal therapy among Ugandans with SAFS and ABPA.

In other limitations of the study; we are not certain of the accuracy of the figures in the GHDx. However, from a public health

perspective, we only used it to extrapolate and estimate the number of individuals who could be suffering from fungal asthma cross-sectionally. Formol-ether concentration used to detect stool helminths has a sensitivity that ranges from 53 to 81%.⁵⁴ The 25% participants that had T-IgE levels greater than 1000 kU/l, could be entirely due to fungal allergy rather than false negative stool microscopy or reduced sensitivity of the method used for stool analysis. We lacked radiological studies for our patients, so a direct comparison to determine the presence of infiltrates or bronchiectasis is not possible and needs to be done in a follow up study. In most developing countries, computed tomography (CT) scans are costly. In the current study, we did not perform chest CT scans, which are a key investigative tool specially to demonstrate bronchiectasis and hyper-attenuated mucous plugging, which are of diagnostic and prognostic significance in ABPA. Besides, ASAP study excluded patients with known bronchiectasis. The skin prick test panel used did not include other relevant fungal allergens such as *Alternaria* and *Cladosporium* species. The mould mix too was composed of three *Penicillium* species only (*P. brevicompactum*, *P. expansum*, *P. notatum*). This could have underestimated the prevalence of ABPM.

In conclusion, the prevalence of fungal asthma among Ugandans, most of whom had severe asthma was high. Fungal asthma is a neglected, yet significant clinical problem among Ugandans with asthma and should be considered in individuals with uncontrolled asthma despite optimized standard asthma care. Diagnosis of fungal asthma provides a therapeutic option for these patients (oral antifungal therapy) which can be life changing. There is also need to advocate for translational research into developing more fungal diagnostics to address the local disease burden.⁵⁵

Supplementary material

Supplementary data are available at [MMYCOL](https://academic.oup.com/mmy/advance-article/doi/10.1093/mmy/myab023/6264697) online.

Acknowledgments

We would like to acknowledge all our participants and their families. We especially thank the ASAP team for patient care. We thank IDI research department for providing the PhD student with office space, internet access, printing services, research peer support, health insurance and salary support during the period of study. We thank Prof Malcolm Richardson for helping get the assay done at Manchester. David Denning is partially funded by the Manchester NIHR Biomedical Research Centre. This work was supported by the DELTAS Africa Initiative grant # DEL-15-011 to THRiVE-2. The DELTAS Africa Initiative is an independent funding scheme of the African Academy of Sciences (AAS)'s Alliance for Accelerating Excellence in Science in Africa (AESA) and supported by the New Partnership for Africa's Development Planning and Coordinating Agency (NEPAD Agency) with funding from the Wellcome Trust grant # 107742/Z/15/Z and the UK government. ASAP (ClinicalTrials.gov Identifier: NCT03065920) under the Makerere University Lung Institute provided study participants, clinical data and samples to the student. ASAP provided clinical support, asthma medication and paid for all clinical

and some general laboratory procedures. ASAP was funded by the Glaxo-SmithKline (GSK) African Non-Communicable Disease (NCD) Open Lab (Project number: 8019) to Dr Bruce Kirenga. Funders had no role in data collection, analysis or decision to publish. Authors retained control of the final content of the publication.

Authors' contributions

R.K. conceived the study. R.K. designed concept/protocol. R.K., W.W., D.W.D., and B.J.K. participated in getting project funding. R.K. collected data. R.K., R.O. reviewed, curated and analyzed data. R.K., F.B. participated in initial manuscript drafting. R.K., F.B., R.O., D.B.M., W.W., S.J.F., D.W.D., R.G., B.J.K. participated in critical revisions for intellectual content. B.J.K. participated in project administration. D.B.M., W.W., F.B., S.J.F., R.G. participated in supervision.

Availability of data and materials

All data generated or analyzed during this study are available upon reasonable request. Data used in this manuscript is fully available in hard paper copy and soft copy data files at Makerere University Lung Institute without restriction.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and the writing of the paper.

References

- Masoli M, Fabian D, Holt S, Beasley R, Global Initiative for Asthma P. The global burden of asthma: executive summary of the GINA Dissemination Committee report. *Allergy*. 2004; 59: 469–478.
- Asher I, Pearce N. Global burden of asthma among children. *Int J Tuberc Lung Dis*. 2014; 18: 1269–1278.
- van Gemert F, van der Molen T, Jones R, Chavannes N. The impact of asthma and COPD in sub-Saharan Africa. *Primary Care Respiratory Journal: Journal of the General Practice Airways Group*. 2011; 20: 240–248.
- Adeloye D, Chan KY, Rudan I, Campbell H. An estimate of asthma prevalence in Africa: a systematic analysis. *Croat Med J*. 2013; 54: 519–531.
- Nriagu J, Robins T, Gary L et al. Prevalence of asthma and respiratory symptoms in south-central Durban, South Africa. *Eur J Epidemiol*. 1999; 15: 747–755.
- Georgy V, Fahim HI, El Gaafary M, Walters S. Prevalence and socioeconomic associations of asthma and allergic rhinitis in northern Africa. *Eur Respir J*. 2006; 28: 756–762.
- Pearce N, Ait-Khaled N, Beasley R et al. Worldwide trends in the prevalence of asthma symptoms: phase III of the International Study of Asthma and Allergies in Childhood (ISAAC). *Thorax*. 2007; 62: 758–766.
- Weinberg EG. Urbanization and childhood asthma: an African perspective. *J Allergy Clin Immunol*. 2000; 105: 224–231.
- Esamai F, Ayaya S, Nyandiko W. Prevalence of asthma, allergic rhinitis and dermatitis in primary school children in Uasin Gishu district, Kenya. *East Afr Med J*. 2002; 79: 514–518.
- Anandan C, Nurmatov U, Van Schayck O, Sheikh A. Is the prevalence of asthma declining? Systematic review of epidemiological studies. *Allergy*. 2010; 65: 152–167.
- Masjedi M, Ainy E, Zayeri F, Paydar R. Assessing the prevalence and incidence of asthma and chronic obstructive pulmonary disease in the Eastern Mediterranean region. *Turk Thorac J*. 2018; 19: 56–60.
- Kirenga BJ, de Jong C, Katagira W et al. Prevalence and factors associated with asthma among adolescents and adults in Uganda: a general population based survey. *BMC Public Health*. 2019; 19: 227.
- Bush RK, Prochnau JJ. *Alternaria*-induced asthma. *J Allergy Clin Immunol*. 2004; 113: 227–234.

14. Denning D, O'driscoll B, Hogaboam C, Bowyer P, Niven R. The link between fungi and severe asthma: a summary of the evidence. *Eur Respir J*. 2006; 27: 615–626.
15. Menzies D, Holmes L, McCumiesky G, Prys-Picard C, Niven R. Aspergillus sensitization is associated with airflow limitation and bronchiectasis in severe asthma. *Allergy*. 2011; 66: 679–685.
16. Fairs A, Agbetele J, Hargadon B et al. IgE sensitization to *Aspergillus fumigatus* is associated with reduced lung function in asthma. *Am J Respir Crit Care Med*. 2010; 182: 1362–1368.
17. Rapeport WG, Ito K, Denning DW. The role of antifungals in the management of patients with severe asthma. *Clinical and Translational Allergy*. 2020; 10: 46.
18. Chowdhary A, Agarwal K, Kathuria S, Gaur SN, Randhawa HS, Meis JF. Allergic bronchopulmonary mycosis due to fungi other than *Aspergillus*: a global overview. *Crit Rev Microbiol*. 2014; 40: 30–48.
19. Asano K, Hebisawa A, Ishiguro T et al. New clinical diagnostic criteria for allergic bronchopulmonary aspergillosis/mycosis and its validation. *J Allergy Clin Immunol*. 2020; S0091-6749: 31240–31249.
20. Agarwal R, Sehgal IS, Dhooria S, Aggarwal AN. Challenging cases in fungal asthma. *Med Mycol*. 2019; 57: S110–S117.
21. Bongomin F, Gago S, Oladele RO, Denning DW. Global and multi-national prevalence of fungal diseases—estimate precision. *J Fungi*. 2017; 3: 57.
22. Kwizera R, Musazizi J, Meya DB et al. Burden of fungal asthma in Africa: a systematic review and meta-analysis. *PLoS One*. 2019; 14: e0216568.
23. Benatar SR, Keen GA, Du Toit Naude W. Aspergillus hypersensitivity in asthmatics in Cape Town. *Clin Allergy*. 1980; 10: 285–291.
24. Kirenga B. African Severe Asthma Program (ASAP). 2017. A Research Network for Characterisation of Severe Asthma in Africans. Available at: <https://clinicaltrials.gov/ct2/show/NCT03065920>. Accessed 14/08/2018, 2018.
25. Kirenga B, Muttamba W, Mugenyi L et al. A prospective cohort study of severe asthma and its determinants in an African population: the African Severe Asthma Program. Paper presented at: AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE 2018.
26. Kirenga B, Chakaya J, Yimer G et al. Phenotypic characteristics and asthma severity in an East African cohort of adults and adolescents with asthma: findings from the African severe asthma project. *BMJ Open Respir Res*. 2020; 7: e000484.
27. Alshishtawy MM, Abdella AM, Gelber LE, Chapman MD. Asthma in Tanta, Egypt: serologic analysis of total and specific IgE antibody levels and their relationship to parasite infection. *Internat Arch Allerg Appl Immunol*. 1991; 96: 348–354.
28. Anderson HR. The epidemiological and allergic features of asthma in the New Guinea Highlands. *Clin Allergy*. 1974; 4: 171–183.
29. Baatjes R, Lopata AL, Sander I et al. Determinants of asthma phenotypes in supermarket bakery workers. *Eur Respir J*. 2009; 34: 825–833.
30. Badiane AS, Ndiaye D, Denning DW. Burden of fungal infections in Senegal. *Mycoses*. 2015; 58: 63–69.
31. Benatar SR. Aspergillus infection in the Western Cape. *South African Medical Journal = Suid-Afrikaanse tydskrif vir geneeskunde*. 1977; 51: 297–305.
32. Bezjak V, Farsey SJ. Prevalence of skin sensitivity to histoplasmin and coccidioidin in various Ugandan populations. *Am J Trop Med Hyg*. 1970; 19: 664–669.
33. Chekir-Talbi M, Denning DW. [The burden of fungal infections in Algeria]. *Journal de Mycologie Medicale*. 2017; 27: 139–145.
34. el-Hefny A, Mohamed HA. Mould sensitivity in asthmatic children and adults in Cairo. *J Egypt Med Assoc*. 1967; 50: 354–359.
35. Cochran WG. *Sampling Techniques* - 3. ed.: New York, N.Y. (USA): Wiley; 1977.
36. Tillie-Leblond I, Tonnel AB. Allergic bronchopulmonary aspergillosis. *Allergy*. 2005; 60: 1004–1013.
37. Agarwal R, Chakrabarti A, Shah A et al. Allergic bronchopulmonary aspergillosis: review of literature and proposal of new diagnostic and classification criteria. *Clinical and Experimental Allergy: Journal of the British Society for Allergy and Clinical Immunology*. 2013; 43: 850–873.
38. Dreborg S. The skin prick test in the diagnosis of atopic allergy. *J Am Acad Dermatol*. 1989; 21: 820–821.
39. National Asthma Education and Prevention Program. Expert Panel Report 3 (EPR-3): Guidelines for the Diagnosis and Management of Asthma-Summary Report 2007. *J Allergy Clin Immunol*. 2007; 120: S94.
40. Juniper EF, O'Byrne PM, Guyatt GH, Ferrie PJ, King DR. Development and validation of a questionnaire to measure asthma control. *Eur Respir J*. 1999; 14: 902–907.
41. Kwizera R, Wadda V, Mugenyi L et al. Skin prick reactivity among asthmatics in East Africa. *The World Allergy Organization Journal*. 2020; 13: 100130.
42. O'Driscoll BR, Hopkinson LC, Denning DW. Mold sensitization is common amongst patients with severe asthma requiring multiple hospital admissions. *BMC Pulmon Med*. 2005; 5: 4.
43. Agarwal R, Noel V, Aggarwal AN, Gupta D, Chakrabarti A. Clinical significance of Aspergillus sensitization in bronchial asthma. *Mycoses*. 2011; 54: e531–e538.
44. Hasnain SM, Al-Frayh AR, Subiza JL et al. Sensitization to indigenous pollen and molds and other outdoor and indoor allergens in allergic patients from Saudi Arabia, United Arab Emirates, and Sudan. *World Allergy Organization J*. 2012; 5: 59–65.
45. Oluwole O, Arinola OG, Falade GA et al. Allergy sensitization and asthma among 13–14 year old school children in Nigeria. *Afr Health Sci*. 2013; 13: 144–153.
46. Faini D, Maokola W, Furrer H et al. Burden of serious fungal infections in Tanzania. *Mycoses*. 2015; 58: 70–79.
47. Sabry MK, Shahin RY, Sheha DS, Saleh AM, Yassin AA. Suspected allergic bronchopulmonary aspergillosis cases in adult bronchial asthma patients attending a tertiary care clinic. *Egypt J Immunol*. 2016; 23: 31–37.
48. Denning DW, Pleuvry A, Cole DC. Global burden of allergic bronchopulmonary aspergillosis with asthma and its complication chronic pulmonary aspergillosis in adults. *Med Mycol*. 2013; 51: 361–370.
49. Farrant J, Brice H, Fowler S, Niven R. Fungal sensitization in severe asthma is associated with the identification of *Aspergillus fumigatus* in sputum. *J Asthma*. 2016; 53: 732–735.
50. Kousha M, Tadi R, Soubani AO. Pulmonary aspergillosis: a clinical review. *Eur Respir Rev*. 2011; 20: 156–174.
51. Knutsen AP. Allergic bronchopulmonary aspergillosis in asthma. *Exp Rev Clin Immunol*. 2017; 13: 11–14.
52. Moss RB. Treatment options in severe fungal asthma and allergic bronchopulmonary aspergillosis. *Eur Respir J*. 2014; 43: 1487–1500.
53. Agarwal R, Dhooria S, Singh Sehgal I et al. A randomized trial of itraconazole vs prednisolone in acute-stage allergic bronchopulmonary aspergillosis complicating asthma. *Chest*. 2018; 153: 656–664.
54. Nikolay B, Brooker SJ, Pullan RL. Sensitivity of diagnostic tests for human soil-transmitted helminth infections: a meta-analysis in the absence of a true gold standard. *Int J Parasitol*. 2014; 44: 765–774.
55. Kwizera R, Mande E, Omali D et al. Translational research in Uganda: linking basic science to bedside medicine in a resource limited setting. *J Transl Med*. 2021; 19: 76.

S1: Extended baseline characteristics of the study population

	Overall (N=374)		Intermittent & mild asthma (N=88)		moderate persistent & severe persistent asthma (N=286)		
Characteristic	N	n (%) or median (IQR)	N	n (%) or median (IQR)	N	n (%) or median (IQR)	P-value
Current age in years, median	369	34 (25 - 45)	88	29 (23 - 41)	281	35 (26 - 46)	0.013
Age when first diagnosed with asthma	372	25 (15 - 36)	87	23 (15 - 33)	285	25 (15 - 36)	0.650
Categories of current age in years	367		87		280		
18 - 24		86 (23.4)		24 (27.6)		62 (22.1)	0.234
25 - 34		102 (27.8)		31 (35.6)		71 (25.4)	
35 - 44		82 (22.3)		15 (17.2)		67 (23.9)	
45 - 54		49 (13.4)		8 (9.2)		41 (14.6)	
55 - 64		37 (10.1)		7 (8)		30 (10.7)	
65+		11 (3)		2 (2.3)		9 (3.2)	
Male Gender	374	88 (23.5)	88	20 (22.7)	286	68 (23.8)	0.839
Overall BMI	374	24.8 (21.6 - 29.5)	88	23.7 (20.9 - 28.9)	286	25.7 (21.6 - 29.7)	0.104
Underweight		22 (5.9)		5 (5.7)		17 (5.9)	
Normal		168 (44.9)		50 (56.8)		118 (41.3)	0.040
Overweight		103 (27.5)		15 (17)		88 (30.8)	
Obese		81 (21.7)		18 (20.5)		63 (22)	
Marital Status	374		88		286		
Single		131 (35)		35 (39.8)		96 (33.6)	0.031
Married		188 (50.3)		44 (50)		144 (50.3)	
Separated		27 (7.2)		8 (9.1)		19 (6.6)	
Widowed		28 (7.5)		1 (1.1)		27 (9.4)	
Highest level of education	374		88		286		
None		14 (3.7)		2 (2.3)		12 (4.2)	0.001
Primary		118 (31.6)		16 (18.2)		102 (35.7)	
Secondary		133 (35.6)		46 (52.3)		87 (30.4)	
Tertiary		109 (29.1)		24 (27.3)		85 (29.7)	
Occupational risk	373		88		285		

Low		200 (53.6)		45 (51.1)		155 (54.4)	0.347
Moderate		123 (33.0)		34 (38.6)		89 (31.2)	
High		50 (13.4)		9 (10.2)		41 (14.4)	
Cough	374	170 (45.5)	88	31 (35.2)	286	139 (48.6)	0.028
Duration in days	170	7 (5 - 30)	31	7 (7 - 30)	139	7 (5 - 30)	0.716
Wheezing	374	152 (40.6)	88	24 (27.3)	286	128 (44.8)	0.004
Duration in days	152	7 (5 - 25.5)	24	10.5 (7 - 22)	128	7 (4 - 25.5)	0.267
Chest Pain	374	119 (31.8)	88	18 (20.5)	286	101 (35.3)	0.009
Duration in days	118	7 (7 - 14)	18	10.5 (7 - 16)	100	7 (3 - 14)	0.157
Shortness of breath	374	105 (28.1)	88	14 (15.9)	286	91 (31.8)	0.004
Duration in days	105	7 (3 - 14)	14	14 (7 - 30)	91	7 (3 - 14)	0.081
Blocked Nose	374	32 (8.6)	88	6 (6.8)	286	26 (9.1)	0.505
Duration in days	32	8.5 (5 - 30)	6	10.5 (5 - 30)	26	8.5 (5 - 30)	0.942
Running nose	374	22 (5.9)	88	8 (9.1)	286	14 (4.9)	0.144
Duration in days	22	12 (7 - 30)	8	7 (7 - 30)	14	14 (7 - 30)	0.422
Sputum production	374	22 (5.9)	88	3 (3.4)	286	19 (6.6)	0.312
Duration in days	21	7 (41760)	3	7 (11140)	18	7 (41760)	0.627
Sore throat	374	4 (1.1)	88	0 (0)	286	4 (1.4)	0.577
Duration in days	4	5 (2.5 - 18.5)	0		4	5 (2.5 - 18.5)	NA
Level of asthma control	372						
Well controlled		94 (25.3)	88	46 (52.3)	284	48 (16.8)	0.000
Not well controlled		278 (74.7)		42 (47.7)		236 (82.5)	
Currently comorbidities	374		88		286		
Rhino sinusitis		115 (30.7)		33 (37.5)		82 (28.7)	0.117
Gastroesophageal reflux disease		90 (24.1)		15 (17)		75 (26.2)	0.078
Hypertension		42 (11.2)		7 (8)		35 (12.2)	0.266
HIV		28 (7.5)		3 (3.4)		25 (8.7)	0.109
Eczema/dermatitis		23 (6.1)		3 (3.4)		20 (7)	0.311
Obstructive sleep apnea		10 (2.7)		1 (1.1)		9 (3.1)	0.463
Depression or other psychiatry illness		3 (0.8)		0 (0)		3 (1)	1.000
Heart failure		1 (0.3)		0 (0)		1 (0.3)	1.000
Nasal polyps		0 (0)		0 (0)		0 (0)	NA
COPD		0 (0)		0 (0)		0 (0)	NA
None of the above		171 (45.7)		42 (47.7)		147 (51.4)	0.385

Pre-measurements			88		286		
FVC	374	2.9 (2.2 - 3.4)		3.3 (2.9 - 3.6)		2.7 (2.1 - 3.2)	0.000
FVC%	374	100 (83 - 112)		110 (103 - 120)		95.5 (78 - 109)	0.000
FEV1	374	2.1 (1.6 - 2.7)		2.6 (2.3 - 3.0)		1.97 (1.4 - 2.5)	0.000
FEV1%	374	88 (65 - 105)		103 (91.5 - 115.5)		79 (60 - 100)	0.000
FEV1/FVC ratio	374	0.76 (0.66 - 0.84)		0.82 (0.74 - 0.88)		0.73 (0.63 - 0.83)	0.000
Lung function	374						
Normal		201 (53.7)		76 (86.4)		125 (43.7)	0.000
Poor		173 (46.3)		12 (13.6)		161 (56.3)	
Post-measurement			9		117		
FVC	126	2.6 (2.2 - 3.4)		3.1 (2.8 - 3.6)		2.62 (2.2 - 3.4)	0.050
FVC %	126	99.5 (80 - 112)		117 (111 - 120)		97 (80 - 111)	0.002
FEV1	126	1.8 (1.3 - 2.3)		2.3 (2.1 - 2.5)		1.73 (1.29 - 2.2)	0.010
FEV1%	126	73.5 (56 - 89)		98 (92 - 103)		71 (56 - 87)	0.000
FEV1/FVC ratio	126	0.65 (0.56 - 0.71)		0.74 (0.7 - 0.76)		0.64 (0.56 - 0.71)	0.006
Methacholine challenge test	361		85		277		
Positive		23 (6.4)		2 (2.4)		21 (7.6)	0.190
Negative		338 (93.4)		83 (97.6)		255 (92.1)	
Skin prick, at least one allergen positive	331		71		260	(0)	
Yes		310 (93.7)		67 (94.4)		243 (93.5)	1.000
No		21 (6.3)		4 (5.6)		17 (6.5)	
Eosinophilic count	374						
AEC<500		310 (82.9)		72 (81.8)		238 (83.2)	0.761
AEC>=500		64 (17.1)		16 (18.2)		48 (16.8)	
Eosinophil count	374	210 (110 - 390)		200 (110 - 410)		215 (100 - 390)	0.984
Total BHQ score	374	72 (49 - 98)	88	61.5 (32.5 - 78.5)	286	77.5 (53 - 102)	0.000
Patient uses ICS	370	34 (9.2)	87	3 (3.4)	283	31 (11)	0.034
History of smoking	374		88		286		
Current smoker		1 (0.3)		0 (0)		1 (0.3)	0.569
Former smoker		22 (5.9)		7 (8)		15 (5.2)	
Never		351 (93.9)		81 (92)		270 (94.4)	
Secondary smoker	374	20 (5.3)	88	4 (4.5)	286	16 (5.6)	1.000
Relatives who have asthma	372		87		285		
Yes		222 (59.7)		50 (57.5)		172 (60.4)	0.149

No		89 (23.9)		27 (31)		62 (21.8)	
Don't know		61 (16.4)		10 (11.5)		51 (17.9)	
Exposed to firewood/ charcoal smoke	374	344 (92)	88	76 (86.4)	286	268 (93.7)	0.027
Use of kerosene for lighting or cooking	374	374 (100)	88	12 (13.6)	286	37 (12.9)	0.865
Depression status according to total PHQ-9 score	374		88		286		
No depression		15 (4)		9 (10.2)		6 (2.1)	0.000
Minimal depression		96 (25.7)		27 (30.7)		69 (24.1)	
Mild depression		113 (30.2)		32 (36.4)		81 (28.3)	
Moderate depression		92 (24.6)		11 (12.5)		81 (28.3)	
Moderately severe depression		47 (12.6)		9 (10.2)		38 (13.3)	
Severe depression		11 (2.9)		0 (0)		11 (3.8)	
Patient uses inhaler medication	370	108 (29.2)	87	13 (14.9)	283	95 (33.6)	0.001
Asthma triggers	374		88		286		
Upper respiratory infection		371 (99.2)		87 (98.9)		284 (99.3)	0.514
Exposure to household pets such as cats, dogs or poultry		13 (3.5)		4 (4.5)		9 (3.1)	0.514
Smoking or exposure to tobacco smoke		356 (95.2)		81 (92)		275 (96.2)	0.115
Strong emotions such as anger, excitement, anxiety		223 (59.6)		45 (51.1)		178 (62.2)	0.063
Cold weather		341 (91.2)		82 (93.2)		259 (90.6)	0.448
Drugs such those treating high blood pressure and pain killers like aspirin		1 (0.3)				1 (0.3)	1.000
Exercise		116 (31)		21 (23.9)		95 (33.2)	0.097
Dust		359 (96)		83 (94.3)		276 (96.5)	0.361
Strong smells or perfumes		315 (84.2)		74 (84.1)		241 (84.3)	0.969
Exposure at work		13 (3.5)		2 (2.3)		11 (3.8)	0.741
Other		5 (1.3)		2 (2.3)		3 (1)	0.336
None of the above		0 (0)		0 (0)		0 (0)	NA

S2: Extended factors associated with fungal asthma

Variables	Aspergillus Sensitisation				ABPA				SAFS				ABPM			
	N	n (%)	COR (95% CI)	P	N	n (%)	COR (95% CI)	P	N	n (%)	COR (95% CI)	P	N	n (%)	COR (95% CI)	P
Overall prevalence	374	157 (58.0)			374	12 (3.2)			374	60 (16.0)			374	11 (2.9)		
current age in years	155				11				59				11			
18 - 24		31 (20)	1.00			3 (27.3)	1.00			9 (15.3)	1.00			1 (9.1)	1.00	
25 - 34		40 (25.8)	1.14 (0.63 - 2.07)	0.655		4 (36.4)	1.13 (0.25 - 5.19)	0.876		18 (30.5)	1.83 (0.78 - 4.32)	0.166		2 (18.2)	1.7 (0.15 - 19.08)	0.667
35 - 44		34 (21.9)	1.26 (0.67 - 2.34)	0.471		2 (18.2)	0.69 (0.11 - 4.25)	0.691		14 (23.7)	1.76 (0.72 - 4.33)	0.217		4 (36.4)	4.36 (0.48 - 39.84)	0.192
45 - 54		23 (14.8)	1.57 (0.77 - 3.20)	0.215		0 (0)	NA			7 (11.9)	1.43 (0.5 - 4.1)	0.511		2 (18.2)	3.62 (0.32 - 40.95)	0.299
55 - 64		22 (14.2)	2.60 (1.18 - 5.73)	0.018		2 (18.2)	1.58 (0.25 - 9.88)	0.624		9 (15.3)	2.75 (0.99 - 7.63)	0.052		2 (18.2)	4.86 (0.43 - 55.31)	0.203
65+		5 (3.2)	1.48 (0.42 - 5.24)	0.545		0 (0)	NA			2 (3.4)	1.9 (0.35 - 10.21)	0.454		0 (0)	NA	
Gender	157				12				60				11			
Male		40 (25.5)	1.00			5 (41.7)	1.00			14 (23.3)	1.00			3 (27.3)	1.00	
Female		117 (74.5)	0.83 (0.51 - 1.34)	0.450		7 (58.3)	0.42 (0.13 - 1.35)	0.143		46 (76.7)	1.01 (0.53 - 1.95)	0.969		8 (72.7)	0.82 (0.21 - 3.14)	0.767
BMI	157				12				60				11			
Underweight		7 (4.5)	0.69 (0.27 - 1.77)	0.437		0 (0)	NA			4 (6.7)	1.56 (0.48 - 5.04)	0.461		0 (0)	NA	
Normal		68 (43.3)	1.00			5 (41.7)	1.00			21 (35)	1.00			5 (45.5)	1.00	
Overweight		42 (26.8)	1.01 (0.61 - 1.67)	0.961		6 (50)	2.02 (0.60 - 6.78)	0.257		19 (31.7)	1.58 (0.81 - 3.11)	0.183		4 (36.4)	1.32 (0.35 - 5.02)	0.687
Obese		40 (25.5)	1.43 (0.84 - 2.45)	0.185		1 (8.3)	0.41 (0.05 - 3.55)	0.416		16 (26.7)	1.72 (0.84 - 3.51)	0.135		2 (18.2)	0.83 (0.16 - 4.35)	0.821
Marital Status	157				12				60				11			
Single		48 (30.6)	1.00			4 (33.3)	1.00			15 (25)	1.00			2 (18.2)	1.00	
Married		80 (51)	1.28 (0.81 - 2.03)	0.290		6 (50)	1.05 (0.29 - 3.78)	0.945		31 (51.7)	1.53 (0.79 - 2.96)	0.210		6 (54.5)	2.13 (0.42 - 10.7)	0.360
Separated		12 (7.6)	1.38 (0.60 - 3.20)	0.448		0 (0)	NA			7 (11.7)	2.71 (0.98 - 7.47)	0.054		1 (9.1)	2.48 (0.22 - 28.38)	0.465
Widowed		17 (10.8)	2.67 (1.16 - 6.18)	0.021		2 (16.7)	2.44 (0.43 - 14.04)	0.317		7 (11.7)	2.58 (0.94 - 7.08)	0.066		2 (18.2)	4.96 (0.67 - 36.84)	0.117

S2: Extended factors associated with fungal asthma

Highest education	157				12				60				11			
None		10 (6.4)	1.00			0 (0)	NA			2 (3.3)	1.00			0 (0)	NA	
Primary		52 (33.1)	0.32 (0.09 - 1.06)	0.063		5 (41.7)	2.37 (0.45 - 12.46)	0.309		27 (45)	1.78 (0.38 - 8.45)	0.468		6 (54.5)	2.87 (0.57 - 14.51)	0.203
Secondary		49 (31.2)	0.23 (0.07 - 0.78)	0.019		5 (41.7)	2.09 (0.40 - 10.99)	0.384		14 (23.3)	0.71 (0.14 - 3.48)	0.669		3 (27.3)	1.23 (0.2 - 7.52)	0.819
Tertiary		46 (29.3)	0.29 (0.09 - 0.99)	0.048		2 (16.7)	NA			17 (28.3)	1.11 (0.23 - 5.4)	0.898		2 (18.2)	1.00	
Occupational risk	157				12				60				11			
Low		84 (53.5)	1.00			4 (33.3)	1.00			35 (58.3)	1.00			6 (54.6)	1.00	
Moderate		51 (32.5)	0.98 (0.62 - 1.54)	0.924		4 (33.3)	1.65 (0.40 - 6.71)	0.486		15 (25.0)	0.65 (0.34 - 1.26)	0.203		3 (27.3)	0.81 (0.20 - 3.29)	0.767
High		22 (14.0)	1.09 (0.58 - 2.03)	0.798		4 (33.3)	4.26 (1.03 - 17.67)	0.046		10 (16.7)	1.18 (0.54 - 2.58)	0.681		2 (18.2)	1.35 (0.26 - 6.88)	0.720

S2: Extended factors associated with fungal asthma

Symptoms	157				12				60				11			
Cough		64 (40.8)	0.72 (0.48 - 1.09)	0.122		5 (41.7)	0.85 (0.27 - 2.74)	0.789		28 (46.7)	1.06 (0.61 - 1.84)	0.837		6 (54.5)	1.46 (0.44 - 4.86)	0.541
Sputum production		9 (5.7)	0.95 (0.40 - 2.29)	0.917		0 (0)	NA			4 (6.7)	1.17 (0.38 - 3.6)	0.778		0 (0)	NA	
Wheezing		65 (41.4)	1.06 (0.70 - 1.60)	0.799		2 (16.7)	0.5 (0.11 - 2.33)	0.380		28 (46.7)	1.34 (0.77 - 2.34)	0.301		6 (54.5)	1.78 (0.53 - 5.95)	0.347
Shortness of breath		47 (29.9)	1.17 (0.74 - 1.85)	0.496		2 (16.7)	0.5 (0.11 - 2.33)	0.380		19 (31.7)	1.23 (0.68 - 2.23)	0.500		3 (27.3)	0.96 (0.25 - 3.69)	0.952
Chest Pain		45 (28.7)	0.78 (0.50 - 1.21)	0.266		2 (16.7)	0.42 (0.09 - 1.94)	0.266		19 (31.7)	0.99 (0.55 - 1.8)	0.978		3 (27.3)	0.8 (0.21 - 3.07)	0.743
Palpitations		5 (3.2)	2.35 (0.55 - 9.97)	0.248		0 (0)	NA			4 (6.7)	5.54 (1.35 - 22.78)	0.018		0 (0)	NA	
Body swelling		1 (0.6)	1.38 (0.09 - 22.31)	0.818		0 (0)	NA			1 (1.7)	5.31 (0.33 - 86)	0.240		0 (0)	NA	
Reduced urine output		1 (0.6)	NA			0 (0)	NA			1 (1.7)	NA			0 (0)	NA	
Running nose		8 (5.1)	0.78 (0.32 - 1.90)	0.583		1 (8.3)	1.48 (0.18 - 11.98)	0.715		3 (5)	0.82 (0.23 - 2.85)	0.752		1 (9.1)	1.63 (0.2 - 13.33)	0.649
Vomiting		0 (0)	NA			0 (0)	NA			0 (0)	NA			0 (0)	NA	
Abdominal pain		1 (0.6)	0.23 (0.03 - 1.89)	0.170		0 (0)	NA			0 (0)	NA			0 (0)	NA	
Yellow body/ eyes		0 (0)	NA			0 (0)	NA			0 (0)	NA			0 (0)	NA	
Seizures		1 (0.6)	NA			0 (0)	NA			1 (1.7)	NA			0 (0)	NA	
Limb weakness		1 (0.6)	0.69 (0.06 - 7.67)	0.762		0 (0)	NA			1 (1.7)	2.64 (0.24 - 29.63)	0.430		0 (0)	NA	
Headaches		4 (2.5)	0.68 (0.20 - 2.31)	0.540		0 (0)	NA			3 (5)	1.78 (0.47 - 6.79)	0.396		0 (0)	NA	
Memory problems		0 (0)	NA			0 (0)	NA			0 (0)	NA			0 (0)	NA	
Skin rashes		0 (0)	NA			0 (0)	NA			0 (0)	NA			0 (0)	NA	
Sore throat		3 (1.9)	4.21 (0.43 - 40.83)	0.215		0 (0)	NA			2 (3.3)	5.38 (0.74 - 38.96)	0.096		0 (0)	NA	
Joint swellings		2 (1.3)	1.38 (0.09 - 22.31)	0.818		0 (0)	NA			1 (1.7)	5.31 (0.33 - 86)	0.240		0 (0)	NA	
Blocked Nose		2 (1.3)	0.60 (0.28 - 1.31)	0.202		2 (16.7)	2.21	1.766		2 (3.3)	0.33 (0.08 - 1.4)	0.133		1 (9.1)	1.07 (0.13 - 8.64)	0.949
Facial pain		0 (0)	NA			0 (0)	NA			0 (0)	NA			0 (0)	NA	

S2: Extended factors associated with fungal asthma

[illegible]

Current					12				60				11			
comorbidities		41 (26.1)	0.68 (0.43 - 1.07)	0.099		2 (16.7)	0.44 (0.1 - 2.04)	0.295		15 (25)	0.71 (0.38 - 1.34)	0.294		4 (36.4)	0.71 (0.38 - 1.34)	0.294
Rhino sinusitis		35 (22.3)	0.85 (0.52 - 1.37)	0.496		5 (41.7)	2.33 (0.72 - 7.52)	0.158		9 (15)	0.51 (0.24 - 1.08)	0.077		4 (36.4)	0.51 (0.24 - 1.08)	0.077
GERD		24 (15.3)	1.99 (1.04 - 3.82)	0.037		1 (8.3)	0.71 (0.09 - 5.66)	0.748		10 (16.7)	1.76 (0.82 - 3.81)	0.150		1 (9.1)	1.76 (0.82 - 3.81)	0.150
Hypertension		12 (7.6)	1.04 (0.48 - 2.26)	0.922		1 (8.3)	1.13 (0.14 - 9.07)	0.910		5 (8.3)	1.15 (0.42 - 3.16)	0.786		1 (9.1)	1.15 (0.42 - 3.16)	0.786
HIV		13 (8.3)	1.87 (0.80 - 4.38)	0.150		1 (8.3)	1.4 (0.17 - 11.38)	0.750		8 (13.3)	3.07 (1.24 - 7.6)	0.015		1 (9.1)	3.07 (1.24 - 7.6)	0.015
Eczema/dermatitis		9 (5.7)	1.04 (0.43 - 2.53)	0.933		0 (0)	NA			3 (5)	0.87 (0.25 - 3.04)	0.821		1 (9.1)	0.87 (0.25 - 3.04)	0.821
Other diseases		5 (3.2)	1.39 (0.40 - 4.90)	0.604		0 (0)	NA			3 (5)	2.31 (0.58 - 9.19)	0.235		0 (0)	NA	
Obstructive sleep apnea		2 (1.3)	2.79 (0.25 - 31.01)	0.404		0 (0)	NA			1 (1.7)	2.64 (0.24 - 29.63)	0.430		0 (0)	NA	
		1 (0.6)	NA			0 (0)	NA			0 (0)	NA			0 (0)	NA	
Depression/psychiatry illness		0 (0)	NA			0 (0)	NA			0 (0)	NA			0 (0)	NA	
		0 (0)	NA			0 (0)	NA			0 (0)	NA			0 (0)	NA	
Heart failure		63 (40.1)	1.00 (0.66 - 1.52)	0.995		4 (33.3)	0.74 (0.22 - 2.5)	0.628		21 (35)	0.77 (0.43 - 1.37)	0.379		4 (36.4)	0.77 (0.43 - 1.37)	0.379
Nasal polyps																
COPD																
None of the above																
Lung function	157				12				60				11			
Normal		82 (52.2)	1.00			5 (41.7)	1.00			23 (38.3)	1.00			7 (63.6)	1.00	
Poor		75 (47.8)	1.11 (0.74 - 1.68)	0.617		7 (58.3)	1.65 (0.52 - 5.31)	0.398		37 (61.7)	2.11 (1.2 - 3.71)	0.010		4 (36.4)	0.66 (0.19 - 2.28)	0.507
Methacholine challenge test	151				12				58				11			
Positive		9 (6)	1.00			2 (16.7)	1.00			3 (5.2)	1.00			0 (0)	NA	
Negative		142 (94)	1.13 (0.47 - 2.68)	0.786		10 (83.3)	0.32 (0.07 - 1.56)	0.158		55 (94.8)	1.3 (0.37 - 4.51)	0.684		11 (100)		

[illegible]

S2: Extended factors associated with fungal asthma

Exposed to firewood smoke	157				12				60				11			
Yes		145 (92.4)	1.09 (0.51 - 2.34)	0.819		12 (100)	NA			58 (96.7)	2.84 (0.66 - 12.25)	0.162		10 (90.9)	0.87 (0.11 - 7.02)	0.895
No		12 (7.6)	1.00			0 (0)				2 (3.3)	1.00			1 (9.1)	1.00	
Use of kerosene	157				12				60				11			
Yes		17 (10.8)	0.7 (0.37 - 1.32)	0.269		1 (8.3)	0.59 (0.08 - 4.71)	0.623		5 (8.3)	0.56 (0.21 - 1.47)	0.238		2 (18.2)	1.49 (0.31 - 7.13)	0.615
No		140 (89.2)	1.00			11 (91.7)	1.00			55 (91.7)	1.00			9 (81.8)	1.00	
Depression status	157				12				60				11			
No depression		9 (5.7)	1.00			0 (0)	1.00			1 (1.7)	1.00			0 (0)	1.00	
Minimal depression		42 (26.8)	0.52 (0.17 - 1.57)	0.246		4 (33.3)	2 (0.22 - 18.41)	0.541		18 (30)	3.23 (0.4 - 26.19)	0.272		4 (36.4)	0.98 (0.17 - 5.54)	0.980
Mild depression		41 (26.1)	0.38 (0.13 - 1.14)	0.085		1 (8.3)	0.41 (0.03 - 6.71)	0.532		14 (23.3)	1.98 (0.24 - 16.24)	0.525		4 (36.4)	0.83 (0.15 - 4.67)	0.828
Moderate depression		44 (28)	0.61 (0.2 - 1.86)	0.385		6 (50)	3.21 (0.37 - 27.47)	0.287		19 (31.7)	3.64 (0.45 - 29.48)	0.225		1 (9.1)	0.25 (0.02 - 2.8)	0.259
Moderately severe depression		19 (12.1)	0.45 (0.14 - 1.48)	0.190		1 (8.3)	NA			7 (11.7)	2.45 (0.28 - 21.71)	0.421		2 (18.2)	1.00	
Severe depression		2 (1.3)	0.15 (0.02 - 0.94)	0.043		0 (0)	NA			1 (1.7)	1.4 (0.08 - 25.14)	0.819		0 (0)		
Use of inhaler medication					12				59				11			
Yes		47 (30.5)	1.12 (0.71 - 1.76)	0.635		1 (8.3)	0.21 (0.03 - 1.67)	0.141		22 (37.3)	1.56 (0.87 - 2.79)	0.138		3 (27.3)	0.91 (0.24 - 3.49)	0.887
No		107 (69.5)	1.00			11 (91.7)	1.00			37 (62.7)	1.00			8 (72.7)	1.00	

S2: Extended factors associated with fungal asthma

Asthma triggers	157				12				60				11			
Upper respiratory infection		154 (98.1)	NA			12 (100)	NA			60 (100)	NA			11 (100)	NA	
Exposure to household pets		6 (3.8)	1.19 (0.39 - 3.62)	0.756		0 (0)	NA			2 (3.3)	0.95 (0.21 - 4.4)	0.948		0 (0)	NA	
Smoking/exposure to tobacco		149 (94.9)	0.9 (0.35 - 2.33)	0.828		12 (100)	NA			59 (98.3)	3.38 (0.44 - 25.87)	0.241		11 (100)	NA	
Strong emotions		77 (49)	0.47 (0.31 - 0.71)	0.000		6 (50)	0.67 (0.21 - 2.11)	0.492		33 (55)	0.8 (0.46 - 1.39)	0.426		9 (81.8)	3.13 (0.67 - 14.71)	0.148
Cold weather		138 (87.9)	0.5 (0.24 - 1.03)	0.061		10 (83.3)	0.47 (0.1 - 2.23)	0.341		53 (88.3)	0.68 (0.28 - 1.66)	0.399		8 (72.7)	0.24 (0.06 - 0.95)	0.043
BP drugs & pain killers		1 (0.6)	NA	0.154		0 (0)	NA			0 (0)	NA			0 (0)	NA	
Exercise		55 (35)	1.38 (0.89 - 2.14)	0.367		3 (25)	0.73 (0.2 - 2.76)	0.648		21 (35)	1.24 (0.69 - 2.22)	0.467		4 (36.4)	1.28 (0.37 - 4.46)	0.698
Dust		149 (94.9)	0.62 (0.22 - 1.75)	0.947		11 (91.7)	0.44 (0.05 - 3.67)	0.450		59 (98.3)	2.75 (0.36 - 21.34)	0.332		11 (100)	NA	
Strong smells or perfumes		132 (84.1)	0.98 (0.56 - 1.72)	0.409		11 (91.7)	2.1 (0.27 - 16.57)	0.482		47 (78.3)	0.62 (0.31 - 1.24)	0.175		10 (90.9)	1.9 (0.24 - 15.14)	0.544
Exposure at work		4 (2.5)	0.6 (0.18 - 2)	0.928		0 (0)	NA			1 (1.7)	2.42 (0.72 - 8.13)	0.153		1 (9.1)	2.93 (0.35 - 24.73)	0.324
Other		2 (1.3)	0.92 (0.15 - 5.57)			0 (0)	NA			1 (1.7)	1.31 (0.14 - 11.96)	0.809		0 (0)	NA	
None of the above		0 (0)	NA			0 (0)	NA			0 (0)	NA			0 (0)	NA	

S2: Extended factors associated with fungal asthma

Current/ recent	157				12				60				11			
medication		2 (1.3)	0.69 (0.12 - 3.8)	0.667		0 (0)	NA			1 (1.7)	1.05 (0.12 - 9.13)	0.967		0 (0)	NA	
Aspirin		0 (0)	NA			0 (0)	NA			0 (0)	NA			0 (0)	NA	
NSAIDs		3 (1.9)	2.09 (0.35 - 12.68)	0.421		1 (8.3)	8.14 (0.84 - 78.91)	0.071		1 (1.7)	1.31 (0.14 - 11.96)	0.809		0 (0)	NA	
ACE inhibitors		3 (1.9)	NA			0 (0)	NA			1 (1.7)	2.64 (0.24 - 29.63)	0.430		0 (0)	NA	
Beta blockers		2 (1.3)	1.39 (0.19 - 9.95)	0.745		0 (0)	NA			0 (0)	NA			0 (0)	NA	
Estrogens		9 (5.7)	0.95 (0.4 - 2.29)	0.917		0 (0)	NA			5 (8.3)	1.59 (0.56 - 4.48)	0.382		2 (18.2)	3.81 (0.77 - 18.82)	0.101
Herbs		0 (0)	NA			0 (0)	NA			0 (0)	NA			0 (0)	NA	
Supplements		31 (19.7)	1.06 (0.63 - 1.78)	0.837		2 (16.7)	0.83 (0.18 - 3.89)	0.818		12 (20)	1.06 (0.53 - 2.11)	0.872		3 (27.3)	1.6 (0.41 - 6.18)	0.497
Others		114 (72.6)	0.94 (0.59 - 1.5)	0.809		10 (83.3)	1.86 (0.4 - 8.62)	0.430		43 (71.7)	0.91 (0.49 - 1.68)	0.761		6 (54.5)	0.43 (0.13 - 1.43)	0.166
None of the above																
Episodes of exacerbations; median (IQR)	157	8 (3 - 20)	1.00 (1.00 - 1.01)	0.295	12	8 (4.5 - 20)	1.00 (0.98 - 1.02)	0.971	60	10 (3 - 20)	1.01 (1.00 - 1.02)	0.043	11	5 (3 - 20)	1.00 (0.98 - 1.02)	0.935
Asthma quality of life score; median (IQR)	157	128 (111 - 153)	1.00 (0.99 - 1.01)	0.957	12	125 (116.5 - 149.5)	1.00 (0.98 - 1.02)	0.987	60	126 (107.5 - 147.0)	1.00 (0.99 - 1.00)	0.263	11	127 (112 - 155)	1.00 (0.98 - 1.02)	0.877