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Effects of comorbidities on asthma control among patients attended to at Chitungwiza Central Hospital in Zimbabwe

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Abstract

Introduction: comorbidity in asthma is the presence of one or more conditions or disorders occurring concurrently with asthma. A comorbid condition with asthma can have adverse effects on the patient´s quality of life as it makes it difficult to control the asthma. The aim of this study was to describe asthma comorbidities among patients attended to at Chitungwiza Central Hospital in Zimbabwe and to determine their effects on asthma control. **Methods:** all the registered 153 asthma patients with comorbidities were enrolled into this unmatched case control study. The demographic and clinical characteristics of these patients were compared to another set of 153 asthma patients without comorbidities. Patient records extracted from electronic databases at the hospital were analysed using SPSS version 25 package. We also computed independent sample test using Mann-Whitney U test, Pearson Chi-square test and the Fisher Exact test. Further analyses were done to determine effects of comorbidities on asthma using ordinal logistic and multiple logistic regression analyses. **Results:** the results indicated that presence of comorbidities affected asthma control. Chronic heart disease, chronic kidney disease, chronic obstructive pulmonary disease, diabetes mellitus, HIV/AIDS, hypertension, tuberculosis and mental illness were the common comorbid conditions among the study participants. One hundred and twenty three (80,4%) of asthma patients with comorbidities adhered to their medications. Over half 102 (66.7%) of patients with comorbid conditions had uncontrolled asthma. The median predicted FEV1% for patients with comorbid conditions was 71% (IQR=40%) compared to 88% (IQR=19%) among those without comorbid conditions. In a multivariate logistic regression, these comorbidities (chronic heart disease, chronic kidney disease, chronic obstructive pulmonary disease, GERD, HIV/AIDS and tuberculosis) were likely to result in inability to perform household tasks and have uncontrolled asthma. Further, the presence of a history of exacerbation of asthma symptoms as a result of comorbidity was associated with a 70% risk of lack of control of asthma. **Conclusion:** we concluded that comorbidities affect asthma control among patients attended to at Chitungwiza Central Hospital, Zimbabwe.

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Introduction

Asthma is defined as a chronic inflammatory condition of the airways that is characterized by recurrent episodes of breathlessness and wheezing. The pathogenesis is linked to genetic, environment and inflammatory immune responses [1,2]. The condition is a major public health problem which affects children and adults of all ages from all regions of the world. Asthma has been shown to co-occur with other ailments some of which make it difficult to control the asthma. The presence of a comorbid ailments (for example, rhinosinusitis, chronic obstructive pulmonary disease (COPD), respiratory infections, diabetes, gastrointestinal reflux disease (GERD), HIV/AIDS, tuberculosis, smoking, cardiovascular diseases and hypertension) with asthma has been shown to have an effect on the patient´s quality of life, treatment options, frequency of asthma-related exacerbations and mortality rates [3]. Comorbidity is defined as either co-existence or interaction of conditions with the latter having a more significant influence on the management of asthma [4]. Asthma is associated with respiratory and extra-respiratory comorbidities. Recognised major respiratory comorbidities are rhinitis and sinusitis [5]. Other comorbid conditions include diabetes, obesity, cardiovascular disease, gastro-oesophageal diseases and chronic obstructive pulmonary diseases (COPD). It has been reported that comorbidities present with additional challenges in asthma management practice [6]. Shenolikar *et al.* found that asthma as a chronic condition almost always occurred with the presence of other health concerns [6]. These comorbidities have been shown to contribute to increased case fatality rates [7]. Furthermore, such comorbidities with asthma result in poorly controlled disease, elevated healthcare costs, reduced work productivity and poor quality of life which puts further strain on already economically burdened families and countries [1,8]. Thus, comorbidities are increasingly recognized as important determinants of asthma management and prognosis [8]. In the elderly, predominantly, the comorbidities are associated with greater mortality, reduced adherence to therapeutic interventions and reduced quality of life [9]. Despite the documented potential ramifications of comorbidities in asthma, these comorbidities have been under-recognised and understudied as demonstrated by lack of attention in the literature and asthma guidelines [5]. The effects of the comorbidities on asthma have not been studied in Zimbabwe and we therefore sought to determine the effects of comorbidities on asthma patients attended to at Chitungwiza Central Hospital in Zimbabwe using a patient record checklist.

Methods

Study design and setting: we conducted an unmatched 1:1 case control study covering the period between January 2008 and January 2018. Two groups of patients were compared with cases comprising asthma patients with comorbidities and controls comprising asthma patients with no documented comorbidities. The study was conducted at Chitungwiza Central Hospital situated in Chitungwiza town about 30 kilometres south east of Harare, Zimbabwe. The hospital has a bed capacity of 500 beds including general, specialised, maternity and emergency care beds. It also has a casualty department which manages patients who present with acute asthmatic attacks. The high dependence unit manages more complex cases of asthma attacks such as status asthmaticus which can occur as a result of comorbidities.

Sample size determination and sampling techniques: a minimum sample size of 146 based on the following: a proportion of 52.5% of asthma only patients with uncontrolled asthma and a proportion of 68.5% of asthma with comorbidity conditions with uncontrolled asthma [10].

$$n = \frac{r+1}{r} X \frac{(p*)(1-p*)\left(Z\beta + \frac{Z\alpha}{2}\right)^2}{(P1-P2)^2}$$

Where: r = Ratio of control to cases; p = Average proportion of exposed = Proportion of exposed cases ± proportion of exposed controls 2; Zβ= Standard normal variate for power (80% power = 0.84); ZÃ/2= Standard normal variate for level of significance (95% = 1.96); PI-P2 = Effect size of difference in proportion expected based on previous studies or estimates; (PI = proportion of cases, while P2 = proportion of controls). Although the calculated sample was 146, we included all available records of asthma patients who presented with comorbidities totalling 153. A further group of 153 patients with asthma and no recorded comorbid conditions was included for comparison of the effect of comorbidity on asthma control.

Inclusion and exclusion criteria: a sampling list with all asthma patients was first developed based on the WHO International Classification of Diseases Version 10. Classification of asthma only and comorbid patients were done from the sampling. All 153 patient records of asthma patients covering January 2008 to January 2018 were included. To be eligible for inclusion in this study, one must have been aged 18 years and above. Records which were identified in the various electronic databases such as the Systems Application Product (SAP), the District Health Information System (DHIS) and the electronic patient management system (ePMS) which showed presence of a comorbid illness with asthma were included in the study. There were the 153 records of HIV/AIDS, sinusitis, mental illness, diabetes mellitus, chronic obstructive pulmonary disease, tuberculosis, chronic kidney disease, chronic heart disease and hypertension and gastroesophageal reflux disease which were included because they are known to affect asthma control.

Data collection: data for both cases and controls were collected from patients´ records using a record checklist. Data collectors were trained on use of KoBoCollect Toolbox for data collection before the actual data collection commenced. The KoBO Collect is an open source platform that is used for collecting data electronically [11]. All available adult asthma patient records that had been reported in the SAP, DHIS and the ePMS (in case of comorbid with HIV and/or tuberculosis) were sampled using WHO International Classification of Diseases Version 10 (ICD10) [12] system for classification of diseases. The system uses codes specific for a disease. In the case of asthma, J459 and J45 identified all asthma cases that were entered into the computer databases. Particular patient records for the asthmatic patients were then picked using the Identification Index Number (IIN) which generated hospital numbers for each patient. All files of asthma patients were extracted and demographic and clinical data for these patients were recorded on the data extraction forms. A spirometry test to determine the predicted (Forced Expiratory Volume at 1 second percentage) FEV1% was conducted and recorded in the patient´s file notes. The predicted FEV1% reading gave an indication of whether asthma was controlled or not.

Data Analysis: SPSS Version 25 package was used for analysing the data. Descriptive statistics on demographic characteristics including gender, employment status and smoking history were generated. We also computed independent sample test using Mann-Whitney U test, Pearson Chi-square test and the Fisher Exact test to ascertain differences between the two groups of patients. Further analysis was done to determine effects of comorbidities on asthma using ordinal logistic and multiple logistic regression analysis.

Ethical Considerations: permission to conduct the study was given by the Biomedical Research Ethics Committee of the University of KwaZulu-Natal (BE613/18) and also by Medical Research Council of Zimbabwe (A/2352). Gatekeepers´

permission was granted by Ministry of Health and Child Care and Chitungwiza Central Hospital. The community advisory board for Chitungwiza allowed the study to be conducted. Data captured through mobile electronic devices did not capture personal identifying information for the patient records and only computer generated codes were used for each participant record.

Results

A total of 306 patient records were reviewed, with 153 patient records comprising asthma patients with comorbid conditions (cases) and 153 records for patients without comorbidity (controls). There were no major differences in the demographic profiles of cases and controls (Table 1). The mean age of the asthma patients with comorbidities was 37.3±15.2 years while that of controls was 42±19.5 and the difference was significant (p=0.009). The majority of the cases 106 (69.3%) and controls 99 (64.7%) were female. With regards medication adherence, more cases 123 (80.4%) were more likely to adhere compared to controls 92 (60.1%) (p<0.001). For both groups, there were more patients who had uncontrolled asthma. However, more controls 65 (42.5%) were more likely to have controlled asthma than cases 51 (33.3%) (p=0.049).

Asthma-related comorbidities at Chitungwiza Hospital: the most commonly reported asthma comorbid conditions amongst the 153 cases at Chitungwiza Hospital included coronary heart disease (CHD), chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), diabetes mellitus (DM), HIV/AIDS, gastrointestinal reflux disease (GERD) hypertension, tuberculosis, sinusitis and mental illness. Table 2 describes asthma control based on the predicted FEV1% for asthma patients with comorbid conditions. We used the following guide to ascertain severity of FEV: normal (FEV1%: >=80%), mild (FEV1%: 60-79), Moderate (FEV1%: 51-59) and severe (FEV1%: <=50). Patients with tuberculosis (85.7%) and COPD (61.6%) had the highest levels of uncontrolled asthma.

Parameter estimates of ordinal logistic regression analysis: we performed an ordinal logistic regression for asthma patients. The results showed that presence of a comorbidity in asthma patients was associated with uncontrolled asthma (p=<0.001). Additionally, we performed ordinal logistic regression of asthma patients by level of asthma control computing against comorbidities, productivity (presentism and absenteeism) and history of smoking. We identified that being a smoker among cases significantly reduced the likelihood of having controlled asthma (p=0.006). However, irrespective of the comorbidity one has, the level of control of asthma was not significantly related to productivity (presentism or absenteeism) (p=0.294) (Table 3).

Multinomial logistic regression for the ability to perform tasks with its covariates: logistic regression analysis to assess the ability of patients with comorbidity condition to perform tasks showed that good (FEV1%: >80) and mild (FEV1%: 60-79) lung function test (asthma control levels) were significantly related with ability to perform tasks (p=0.020) (Table 4). The ability to perform tasks was not significantly influenced by age, sex, comorbidities and history of exacerbation (Table 4).

Discussion

In this study we set out to determine whether comorbidity of asthma with other conditions impacts asthma control. The findings obtained in this study suggest that the presence of comorbid conditions in asthma patients in Chitungwiza, Zimbabwe is associated with uncontrolled asthma. This finding is in line with the observations in other studies [4,13-15]. The findings have implications for both clinical practice and other

broad public health interventions. It is well documented in literature that comorbidities among asthma patients present additional challenges in asthma management [6]. It is therefore imperative to screen for asthma-related comorbidities in clinical practice so that appropriate interventions can be instituted. Additionally, there is need to educate asthma patients on the importance of paying attention to comorbid conditions such as hypertension as they impact negatively on treatment outcomes. Our findings appear to suggest that comorbidity among asthma patients was more prevalent among female patients, thus confirming previous findings by Gershon *et al.* [16]. It must be noted however, that our sample comprised of more women, who in our setting, are more likely to seek healthcare services unlike their male counterparts. Additionally, the composition of women among cases and controls in our study was comparable which resulted in there being no major significant differences. The presence of respiratory infections such as tuberculosis and COPD was linked with uncontrolled asthma among cases in our study. Such a result is in tandem with currently literature which suggests that respiratory infections have potential to cause variable structural changes of the respiratory system which is associated with worsening of asthma symptoms [17].

Results from this study revealed that smoking was significantly associated with having uncontrolled asthma among cases. This is consistent with findings of other studies which showed that lack of control of asthma may be due to high level of irritants, particularly tobacco smoke which is often associated with a marked or unresponsive underlying inflammatory process [18-21]. It should also be noted that smoking increases variable structural changes of the respiratory system and has been linked with the risk of development of COPD [22]. Our study revealed that both cases and controls had relatively good adherence rates to asthma medications and there were no statistically significant differences between the two groups. A plausible explanation for this finding may be that our study may have had a smaller sample size and might not have had sufficient numbers in both groups to be able to detect differences. In this vein, it would be imperative for future studies to use larger sample sizes and use multiple study sites. Our study also explored the economic impact of having a comorbid condition among asthma patients. Cases were more likely to be unable to meet the cost of treatment as compared to controls which is in tandem with previous results reported by Peters *et al.* [23]. Loss of productivity among asthma patient with comorbidities was defined by either presentism or absenteeism [24]. Our results could not establish a significant association between productivity (presentism or absenteeism) and comorbidity.

Conclusion

We concluded that control levels for asthma patients with comorbid conditions is significantly affected by smoking. Uncontrolled asthma compromised performance of tasks by affected patients. We established that comorbidity was related to asthma control. We are however, aware that our sample size was not big enough. We recommend stepping up awareness of the effects of cigarrete smoking on asthma control and the need to improve on adherences to medications as this could reduce risks of uncontrolled asthma.

What is known about the topic

- Asthma co-occur with other ailments some of which make it difficult to control;
- Presence of comorbidities in asthma patients increases the risk of mortality.

What this study adds

- Literature related to effects of comorbidity in African population has been shown in this study to be a significantly affected by smoking;

- We established the need to increase awareness of the effects of cigarrete smoking on asthma control and the need for adherences to asthma medications to reduce the risk of uncontrolled asthma;
- Presents of respiratory comorbidities had a more risk of uncontrolled asthma.

Competing interests

The authors declare no competing interests.

Authors' contributions

PN and MJC conceived the idea. PN with the assistance of MJM designed the protocol and revisions were done by MJC and ENS. PN designed the protocol. PN wrote the first draft of the manuscript and all authors (PN, MJC and ENS) reviewed changes.. All the authors have read and agreed to the final manuscript.

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Tables

Table 1: demographic characteristics of cases and controls

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Table 1: demographic characteristics of cases and controls			
Variable	**Comorbid conditions: n=153**	**Without comorbid conditions: n=153**	**P-value**
Age mean (SD)	**37.2±15.5**	**42±19.5**	**0.009**
Sex			
Women	106(69.3%)	99(64.7%)	0.196
Men	47(30.7%)	54(35.3%)	0.196
Household income status (US$)			
<100	47(30.7%)	43(28.1%)	0.309
100-300	65(45.5%)	52(34.0%)	0.020
301-500	33(21.6%)	37(24.2%)	0.294
>500	8(5.2%)	21(13.7%)	0.006
Employment Status			
Employed	49(32.0%)	58(37.9%)	0.140
Not employed	91(59.5%)	82(53.6%)	0.149
Retired	13(8.5%)	13(8.5%)	0.50
Level of Education			
Did not attend school	10(6.5%)	6(3.9%)	0.153
Primary level	24(15.7%)	22(14.4%)	0.375
Secondary level	106(69.3%)	109(71.2%)	0.358
Tertiary	13(8.5%)	16(10.5%)	0.275
Marital Status			
Co-habiting	5(3.3%)	11(7.2%)	0.063
Married	64(41.8%)	58(37.9%)	0.243
Single	38(24.8%)	38(24.8%)	0.50
Widowed	26(17.0%)	29(19.0%)	0.324
Divorced	20(13.1%)	17(11.1%)	0.296
History of smoking			
Non-smoker	100(65.4%)	89(58.2%)	0.098
Smoker	53(34.6%)	64(41.8%)	0.098
Adherence to asthma medications (Pill count and reported number of puffs taken)			
Yes	123(80.4%)	92(60.1%)	<0.001
No	30(19.6%)	61(39.9%)	<0.001
Asthma control level (FEV_1%≥80%-Controlled; FEV1%<80%-Uncontrolled)			
Controlled	51(33.3%)	65(42.5%)	0.049
Not controlled	102(66.7%)	88(57.5%)	0.049
Lung function test; median(IQR)	Predicted FEV1%: 71% (IQR=40%)	Predicted FEV1%:88(IQR=19%)	<0.001
Ability to meet medical cost			
Yes	84(54.9%)	74(48.4%)	0.128
No	69(45.1%)	79(51.6%)	0.128
History of exacerbation of asthma symptoms			
Yes	118(77.1%)	38(24.8%)	<0.001
No	35(22.9%)	115(75.2%)	<0.001
Ability to perform tasks (household chores)			
Able to perform without limitations	66(43.1%)	90(58.8%)	0.003
Performs with limitations	27(17.7%)	19(12.4%)	0.097
Not able to perform tasks	60(39.2%)	44(28.8%)	0.027

Table 2: level of asthma control according to each comorbidity				
Comorbidity	**Predicted FEV1%; n=153**			
	Normal (FEV1%: ≥80)	**Mild (FEV1%: 60-79)**	**Moderate (FEV1%: 51-59)**	**Severe (FEV1%: ≤50)**
CHD	6(37.5%)	6(31.3%)	4(25%)	1(6.3%)
CKD	6(54.6%)	0(0.0%)	2(18.2%)	3(27.3%)
COPD	0(0%)	0(0%)	4(33.3%)	8(66.7%)
DM	11(57.9%)	3(15.8%)	2(10.5%)	3(15.8%)
GERD	12(42.9%)	6(21.4%)	6(21.4%)	4(14.3%)
HIV/AIDS	7(41.2%)	6(35.3%)	1(5.9%)	3(17.7%)
Hypertension	11(52.4%)	7(33.3%)	1(4.8%)	2(9.5%)
Tuberculosis	2(14.3%)	5(35.7%)	1(7.13%)	6(42.9%)
Mental Illness	1(33.3%)	2(66.7%)	0(0%)	0(0%)
Sinusitis	7(58.3%)	3(25%)	1(8.3%)	1(8.3%)
Totals	63(41.2%)	37(24.2%)	22(14.4%)	31(20.3%)

Table 3: parameter estimates of ordinal logistic regression analysis characterising exposure to comorbidity					
Variable Threshold	**Odds Ratio**	**Std. Error**	**Sig**	**95% C I**	
				Lower bound	**Upper bound**
*Normal FEV1%: ≥80%	0[a]	.	.	.	.
Mild FEV1%: 60-69%	1.23	0.193	.095	0.85	1.61
Moderate FEV1%: 51-59%	2.29	0.228	<0.05	1.84	2.74
Severe FEV1%: ≤50%	3.07	0.26	<0.05	2.56	3.59
Comorbidities					
Asthma	0a	.	.	.	.
CHD	4.55	2.17	0.001	1.79	11.59
CKD	4.67	3.03	0.018	1.31	16.66
COPD	54.89	34.81	0.000	15.84	190.25
Diabetes Mellitus	2.80	1.39	0.037	1.06	7.40
GERD	4.65	1.85	0.000	2.13	10.15
HIV/AIDS	4.27	2.05	0.002	1.67	10.93
HPT	2.70	1.21	0.027	1.12	6.51
Mental illness	3.37	3.24	0.206	0.51	22.17
Sinusitis	2.32	1.37	0.156	-0.73	7.39
Tuberculosis	14.34	7.65	0.000	5.04	40.78
Smoking Status					
Never Smoked	0[a]	0[a]	0[a]	0[a]	0[a]
Smoking	0.52	0.13	0.007	0.33	0.84
Ability to perform household chores					
Able to perform household chores	0[a]	.	.	.	.
Performs with limitations	6.43	2.05	0.000	3.44	12.03
Not able to perform household chores	1.34	0.35	0.254	0.81	2.23
Link function: logit. This parameter is set to zero because it is redundan					

Table 4: parameter estimates of multinomial logistic regression for the ability to perform tasks					
Variable Threshold	**Odds Ratio**	**Std. Error**	**Sig**	**95% CI**	
				Lower bound	**Upper bound**
Normal FEV1%: ≥80%	0[a]	.	.	.	.
Mild FEV1%: 60-79	0.55	0.34		-0.12	1.22
Moderate FEV1%: 51-59	1.74	0.36		1.03	2.44
*Severe FEV1%:≤50%	2.56	0.38		1.81	3.31
*Asthma	0[a]	.	.	.	.
CHD	3.42	1.78	0.018	1.23	9.46
CKD	3.94	2.74	0.049	1.01	15.40
COPD	39.97	25.09	0.000	9.16	141.15
GERD	3.23	1.42	0.008	1.36	7.67
HIV/AIDS	2.76	1.43	0.05	1.0	7.60
Tuberculosis	6.18	3.57	0.002	1.99	19.15
Ability to perform household chores					
Performs with limitation	3.35	1.31	0.002	1.55	7.23
History of exacerbation as a result of comorbidity					
Presence of exacerbation	0.30	0.09	0.000	0.15	0.57
Link function: logit. This parameter is set to zero because it is redundant.					