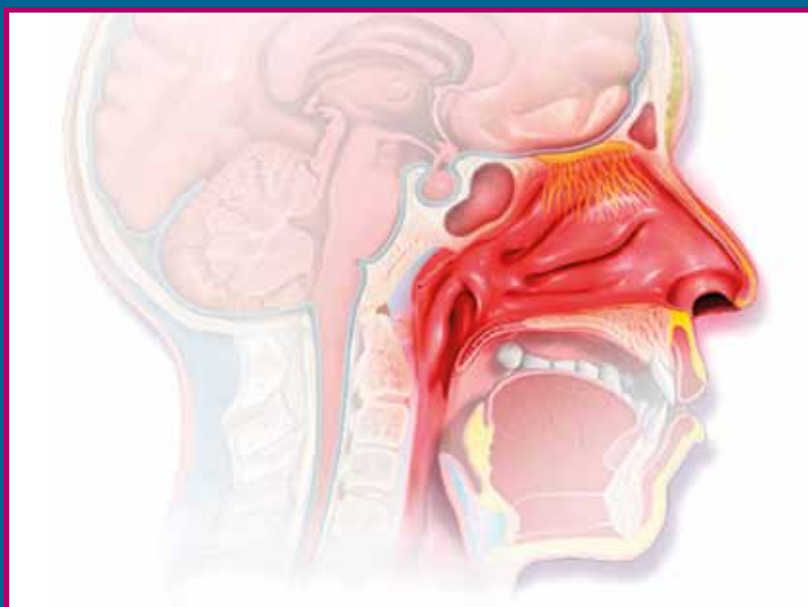


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Knowledge, attitudes, and practice survey about antimicrobial resistance and prescribing among physicians in a hospital setting in Nairobi, Kenya

Risk factors for pulmonary tuberculosis treatment failure in rural settings in Benin, West Africa: A cohort study



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First word

The relationship between infections and asthma has been recognised for over a century. Osler noted that every 'fresh cold' could induce a paroxysm of disease.¹ Stachan, an epidemiologist, proposed that lower incidence of infection in early childhood can be responsible for increase in allergic disease.² It is also well known that viral infections have been implicated in asthma exacerbations and they also contribute to asthma inception in high-risk young children with susceptible genetic background. Therefore, a history of wheeze associated with viral infections early in life is one of the risk factors for the development of asthma in childhood. It has also been discovered that the more severe the asthma is, the more the likelihood of isolating viruses from the respiratory tract. Studies by Gbadero et al have shown that the viral inciters are one of the triggers for asthma in children.³

In this edition of the *African Journal of Respiratory Medicine*, Gobir et al found that a significant proportion of asthmatic children had co-existent allergic rhinitis and that the presence of allergic rhinitis is associated with poorer control. This confirms previous work that allergies not only trigger asthma but also may worsen exacerbations. Most allergies are viral in origin and the relationship between allergic rhinitis and asthma is pretty well established. Doctors must keep this in mind when evaluating and treating asthma.

Prescribing antibiotics has been a problematic issue in Africa where regulations are poor, there are numerous fake drugs, and almost every disease has only one solution – antibiotics. This has led to increasing antibiotic resistance. Health practitioners should be aware of this impending danger and hospitals should have a rational approach to prescribing antibiotics. Pharmacodynamics, pharmacokinetics, and the local microbiologic spectrum and antibiotic resistance pattern must be considered. Government should also put policies in place to control this problem. Futuristically, to circumvent this bizarre way of prescribing antibiotics, scientific thrust should be directed towards development of vaccines.

Prof Gregory Erhabor, Co-Editor, AJRM

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Knowledge, attitudes, and practice survey about antimicrobial resistance and prescribing among physicians in a hospital setting in Nairobi, Kenya

E K Genga, L Achieng, F Njiri, and M S Ezzi

Abstract

Antimicrobial resistance (AMR) is an increasing threat to global health security, potentially compromising gains made in public health worldwide. Resistance has been reported for entire classes of antibiotics, and untreatable multi-drug resistant bacteria are increasingly documented. This study, using a Knowledge, Attitude and Practice (KAP) survey, aimed to describe AMR and antimicrobial prescribing among medical doctors from the Kenyatta National Teaching and Referral Hospital in Nairobi, Kenya. A total of 160 questionnaires were distributed to the four departments of Internal Medicine, Paediatrics, Obstetrics, and Surgery. A total of 107 of the 160 questionnaires were completed (response rate, 66.88%). All the participants agreed that knowledge about antibiotics and their appropriate use is important in their daily work and 64.5% declared that they prescribed antibiotics more than once a day. Participants strongly agreed that AMR is a problem worldwide (97.2%), locally (93.4%), and in daily practice (75.9%). About one third of the participants (33.6%) agreed that they had difficulties choosing an antibiotic. Overall, 85.9% of the study participants had had fewer than four lectures on antibiotic use as part of academic activities within their departments during the previous year. The majority of the participants also identified that antibiotics are being overused in hospitals across Kenya (91.5%) and in local communities (93.4%) as a whole. Patient demand for antibiotics in outpatient practice was perceived by 88.8% of the participants to contribute to their overuse. Half of the participants (52.4%) suspected that some antibiotics available in their hospital are of poor quality and for that reason do not work. The awareness of AMR as a

worldwide and national problem was very high among the participants. The present KAP survey has shown that there is a clear need to carry out research on local AMR rates, to promote confidence in the quality of locally available AMs, and to expand the current residency curriculum to include AM use in greater detail. The lack of standard implementation of local AM guidelines is another issue that should be addressed.

Introduction

Antibiotics are the most important tool we have to control many life-threatening bacterial diseases once infection has occurred, yet increasing levels of resistance are compromising the effectiveness of these antibiotics. Antimicrobial resistance (AMR) is an increasing threat to global health security, potentially compromising gains made in public health worldwide.¹ AM-resistant bacterial infections now account for much of the problem of emerging infectious disease worldwide.²⁻⁶ AMR is a complex problem driven by many interconnected factors, therefore single, isolated interventions have little impact and coordinated action is required. Underlying factors that have accelerated the emergence and spread of AMR in middle- and low-income countries include: lack of a comprehensive and coordinated response; weak or absent AMR surveillance and monitoring systems; inadequate systems to ensure quality and uninterrupted supply of medicines; inappropriate use of AM medicines, including in animal husbandry; poor infection prevention and control practices; insufficient diagnostic, prevention and therapeutic tools.⁷

AMR can lead to many infectious diseases becoming untreatable and uncontrollable, which could derail the progress made towards reaching the health-related United Nations Millennium Development Goals for 2015. Therefore, knowledge about the driving forces behind AM prescription is needed, and such information can be obtained by means of Knowledge, Attitudes and Practice (KAP) surveys. KAP surveys on AMR have been conducted among medical doctors in the community setting. This study used a KAP survey about AMR and antibiotic prescribing among medical doctors from the Kenyatta National Teaching and Referral Hospital in Nairobi, Kenya.

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Methods

This was a cross-sectional survey of residents and specialist doctors from the Kenyatta National Hospital (the largest public teaching and referral hospital in Nairobi, Kenya) carried out between September and November 2015. A self-administered questionnaire was distributed among residents (i.e. physicians in training) and attending physicians (i.e. staff physicians after completion of training and specialisation). Medical doctors from psychiatry, radiology, ophthalmology and anaesthesiology were not included as they do not routinely prescribe AMs. Questionnaires were distributed on-site during working hours and participants were asked to respond immediately. There was no incentive for subjects to participate and no reminders were given. The questionnaire was based on previous surveys carried out in the United States and in Peru.⁸ This tool was modified to suit the Kenyatta National Hospital setting by a team of infectious disease experts from the University of Nairobi. The 35-item questionnaire addressed the professional profile of the participants and frequency of antimicrobial prescription, their awareness about the current scope of AMR, sources of information and continuing education about antimicrobials, confidence and factors influencing decisions around AM prescription. Questions used a 4- or 5-point Likert scale (which included answers ranging from 'strongly agree' to 'strongly disagree', from 'very useful' to 'not useful at all' and from 'always' to 'never'). The study tool had seven questions that assessed basic knowledge about the clinical indications, spectrum, administration and pharmacology of AMs.

The survey had three case-based questions that looked into the choice of AMs for treating an upper respiratory tract infection, acute diarrhea, and sepsis in a patient with impaired renal function, three questions looked into the spectrum of AMs and their ability to cross the blood- brain barrier and a question on safety of AMs during pregnancy.

The study was approved by the Department of Medicine, University of Nairobi and Kenyatta National Hospital Ethical Committee. As the nature of the study was anonymous, informed consent was not sought.

Data analysis. The survey targeted residents and specialists in Internal Medicine, Paediatrics, Obstetrics, and Surgery. In each department, 40 doctors were targetted, giving a total of 160. Proportions were calculated for categorical variables and their significance assessed by the Chi-square method. Means and standard deviations were calculated as continuous variables. Unless otherwise stated, Likert items were used by combining the data into two categories, 'strongly agree/agree', 'very useful/ useful' and 'very confident/ confident' versus the remaining options of the scale. The data were verified, cleaned, and entered into a Microsoft database access and analysed using SPSS version 21.0.

Results

Demographics and professional profiles. A total of 107 of the 160 questionnaires were completed and returned successfully by the study participants (response rate, 66.88%). The majority of the doctors (59.9%) had worked for more than five years.

The participants were mainly residents (91.6%) with Internal Medicine and Surgery predominating at 35.5% and 32.7%, respectively. All the participants agreed that knowledge about AMs and their adequate use are important in their daily work and 64.5% declared that they prescribe AMs more than once a day.

Knowledge on AM use. The majority of the participants agreed that there was no need to start AM for the two case-based questions on acute diarrhoea (81%) and upper respiratory tract infection (54.2%). However, 36.4% of the participants would start amoxicillin for the upper respiratory tract infection. The last case-based question assessed knowledge of when to adjust the dose of AM in a patient with severe renal failure due to sepsis. The patient was prescribed ceftriaxone and gentamicin. About half (n=51.0, 47.7%) correctly identified that the dose of these two AMs would have to be adjusted in the setting of renal failure. There were two questions on choice of antibiotics with regard to anaerobes and methicillin-resistant *Staphylococcus aureus* (MRSA). The majority correctly identified metronidazole (94.4%) as a target for anaerobes and that MRSA is not susceptible to cephalosporins (81%). Amoxicillin was the preferred drug of choice in pregnancy (n=101, 94.4%). A total of 79 (73.8%) participants correctly identified ceftriaxone as the drug with the best blood-brain barrier penetration.

Medical rank		n	%
Consultant physician		8	7.5
Internal medicine Resident		38	35.5
Obstgyn consultant		1	9
Obstgyn resident		7	6.5
Paediatric Resident		18	16.8
Surgery Resident		35	32.7
Since leaving medical school, how many years have you worked in a hospital?	≤1 year or less	3	2.8
	2 years	5	4.7
	3 years	19	17.8
	4 years	16	15.0
	5 years	19	17.8
	6 years	11	10.3
	≥7 years	34	31.8

Table 1: Medical rank of study participants and years worked

Awareness about the current scope of AMR. A total of 104 participants (97.2%) agreed that AMR is a worldwide problem. The majority agreed that AMR is a problem both locally and in daily practice (93.4% and 75.9% combined agreed and strongly agreed, respectively, for both settings). Most of the study participants disagreed (77.2%, disagree and strongly disagree combined) that AMR is not a significant problem in their local hospital.

Confidence and seeking of inputs. Nearly all the residents (81.3%) were confident about the optimal use of antibiotics. About one third of the participants (33.6%) agreed they had difficulties choosing an antibiotic. With regard to seeking reviews with a senior colleague, 3.7% replied 'never', 82.2% 'sometimes', 1.9% 'most', and 7.5% 'half the time'.

Sources of information and continuing education about AMs.

Overall, 85.9% of the resident doctors in the study had received fewer than four lectures about AM use as part of academic activities within their departments during the previous year. The majority (95.6%) attended less than four training courses on AM over the past year yet, surprisingly, most (95.5%) would have wanted to attend these courses. Regarding sources of information, the majority found senior colleagues, same-rank colleagues, and the internet to be the most useful sources (82.3%, 86% and 85.9% respectively, 'very useful' and 'useful' combined). Most of the residents (72%) disagreed that antibiotic guidelines and antibiotic committees are an obstacle rather than a help to clinical care. The majority of the participants (96.2%) agreed that the development of local guidelines would be more useful than international guidelines. About four in 10 were not familiar with the Kenyatta National Hospital guidelines. Of those who were familiar, 39.8% found them useful. The Sanford Guidelines were not familiar to 59.8% of the residents.

Factors influencing decisions around AM prescription. Over half of the residents (53.2%) reported that they 'never knew the antibiotics available at Kenyatta National Hospital because of the frequent formulary changes'. The majority of the participants identified that antibiotics were being overused in hospitals across Kenya and in the local community as a whole (91.5% and 93.4% respectively, 'agree' and 'strongly agree' combined). Patients' demands for antibiotics in outpatient practice was perceived by 88.8% of the participants to contribute to their overuse. This contrasted with inpatient care where half of the participants (51.4%) disagreed that patient demands for antibiotics contributed to their overuse. Half of the participants (52.4%) suspected that some of the antibiotics available in their hospital are of poor quality and for that reason do not work.

Discussion

The present study describes the results of a KAP survey among 107 medical doctors (both residents in training and attending physicians) practicing in the Kenyatta National Teaching hospital in Nairobi, Kenya. The departments included were Internal Medicine, Paediatrics, Surgery, and Obstetrics and Gynecology. Overall, the participants scored well on theoretical knowledge about AMs, including indications, administration, and side effects. However, it is important to note that about one third of the participants would have treated the upper respiratory tract infection with an antibiotic and that just under half the participants were able to identify the need to adjust the dose of antibiotics in the sepsis patient. This suggests that knowledge of AMs – including indications, administration, and side effects – is a potential target for intervention. The awareness of AMR as a global and national problem was very high among the participants. This contrasts with a study from Peru where doctors were aware of the problem worldwide but failed to identify it in the local setting.⁸ Research from the United States among general

		n	%
When you are in the emergency room, outpatient clinic or in the wards, how frequently do you review your decision to prescribe antibiotics with a senior colleague?	About half the time	7	6.5
	Always	1	9
	Most of the time	16	15.0
	Never	14	13.1
	Sometimes	68	63.6
If you ask a senior colleague, how frequently does he/she recommend a different antibiotic to you?	About half the time	8	7.5
	Most of the time	2	1.9
	Never	4	3.7
	Sometimes	88	82.2
How confident do you feel about the optimal use of antibiotics?	Somewhat confident	80	74.8
	Somewhat unconfident	7	6.5
	Unconfident	2	1.9
	Very confident	18	16.8

Table 2: Choice of antibiotics

practitioners showed that most of the physicians interviewed were aware that inappropriate use of AMs in their own practice contributes to increasing AMR.⁹ Approximately nine in ten of the participants identified that patient demand for AMs plays a major role in their overuse in the local community and hospital. The pressure from patients has been found to influence prescription patterns in middle- and low-income settings. This is despite the fact that the majority of participants identified that prescribing AMs can cause some harm to patients who do not need them. A study among parents and paediatricians in Venezuela revealed that the majority (87%) of doctors felt pressured by parents into prescribing AMs; 48% of parents said that they had requested AMs and 33% revealed that they had obtained a prescription.¹⁰ The high expectation about AM use from patients is probably due to their minimal understanding of AMR and AM side effects. This can be addressed by educational forums targeting the community setting. The participants identified guidelines and education as key areas to help tackle AMR. About four in 10 were not familiar with the Kenyatta National Hospital guidelines. Of these, an equally low number (39.8%) found them useful. The Sanford Guidelines were not familiar to 59.8% of the residents. In addition to this, half of the residents (53.2%) reported that they never knew which antibiotics were available at Kenyatta National Hospital because the formulary always changes. The need for local guidelines is paramount in the fight against AMR. The residents should be encouraged to consult their colleagues (senior and same rank) as this was found to be beneficial in passing on information about AM use and AMR. An increase in the number of classroom lectures about AMR and AM prescribing was welcomed by the vast majority of participants, suggesting a gap in knowledge about infectious diseases, microbiology, and AM prescribing in university teaching curriculums. Other influences on AMR included poor quality of the AM. This is similar to other studies in low- and middle-income countries like Peru and Columbia.^{11,12} Studies need to be done to potentiate the efficacy of these AM drugs. There should be strict policies on

vetting and testing of these drugs before and after they enter the local market. Efforts should be made by the Kenya Ministry of Health to instill confidence in AMs. In conclusion, this survey has presented some vital information on the prescribing attitudes and practices of medical doctors from a major public hospital of a middle-income country. The key message is that AMR is an emerging problem in healthcare in Kenya and steps should be put in place to tackle it. Simple steps would include increasing AMR educational fora, dissemination of information about local AMR rates, and the importance of renewing public confidence in the quality of locally available AMs. Furthermore, the study highlights that local guidelines should be revised to suit a Kenyan setting. Local infectious diseases services and AM stewardship programmes should take these data into account when planning and executing their activities. A key step to minimise AMR in Kenya would be the development of a healthcare policy on infection prevention and control.

Study limitations

1. KAP surveys are limited by the fact that participants may tend to give socially desirable answers rather than expressing their true opinions.
2. The present setting was a teaching hospital, and this may not reflect the knowledge and attitudes towards community infections of clinicians in the general community.

The following recommendations can be made from the results of the survey:

1. Inclusion of more formal lectures in the teaching curriculum in the various residential programmes with emphasis on AM use, AMR, and side effects.
2. Local guidelines on AM use should be produced.
3. More local studies on patterns of AMR are needed.
4. There should be strict policies on the vetting and testing of these drugs before and after they enter the local market.

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Author declaration

Competing interests: none.

Any ethical issues involving humans or animals: none.

Was informed consent required: yes.

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		n	%
1. A 40-year-old woman went to the Emergency room complaining of four days of diarrhoea (three unformed stools per day). No history of fever. What treatment would you recommend?	Ceftriaxone	1	9
	Ciprofloxacin	7	6.5
	Metronidazole	9	8.4
	No need of antibiotic use.	87	81.3
	Oral rehydration		
2. A 32-year-old male went to the clinic complaining of fever (37.6°C), nasal discharge and throat pain for three days. Which antibiotic will you recommend?	Amoxicillin	39	36.4
	Cefuroxime	4	3.7
	Clarithromycin	5	4.7
	No need of antibiotic use	58	54.2
3. During your stay in the ward, you have seen two patients with impaired kidney function. Patient A is a 68 year-old male with cellulitis in the lower limb. He received clindamycin. Patient B is a 64 year-old woman with diabetes who received empirically treatment. Which treatment should be adjusted?	Neither patient A nor patient B	3	2.8
	Patient A	18	16.8
	Patient A and B	28	26.2
	Patient B	51	47.7
4. Which one of the following antibiotics may be safe during pregnancy?	Amoxicillin	101	94.4
	Ciprofloxacin	1	9
	Doxycycline	1	9
	Gentamicin	1	9
5. Which one of the following antibiotics has the best activity against anaerobes?	Ceftriaxone	1	9
	Ciprofloxacin	2	1.9
	Metronidazole	101	94.4
	Trimethoprim-sulfamethoxazole	1	9
6. Methicillin resistant- <i>Staphylococcus aureus</i> is susceptible to:	Cefalotin	6	5.6
	Ceftriaxone	11	10.3
	Cefuroxime	5	4.7
	None of these antibiotics	81	75.7
7. Which one of the following antibiotic is more effective to cross the blood-brain barrier?	Ceftriaxone	79	73.8
	Clindamycin	2	1.9
	Vancomycin	22	20.6

Table 3: Case based questions and responses

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Risk factors for pulmonary tuberculosis treatment failure in rural settings in Benin, West Africa: a cohort study

AC Dovonou, AA Kpangon, SA Amidou, S Dansou, CA Attinssounon, R Keke, MJ Hounnougba, HB Lawin, G Agodokpessi, CL Yehouenou, DM Zannou, and YS Anagonou

Abstract

Tuberculosis (TB) remains a public health issue particularly in the north-east of Benin where there is a high frequency of TB treatment failure. The aim of our study was to identify the risk factors of TB treatment failure in rural north-east settings, Bembèrèkè, Benin (West Africa). This was a retrospective cohort study. We included smear-positive pulmonary TB patients who began TB treatment between 1 January 2007 and 31 January 2011 as extracted from the TB registry. The outcomes of TB treatment were defined according to 2007 the World Health Organization (WHO) guidelines. Failure was defined as remaining smear positive at month five or later during TB treatment for smear-positive pulmonary TB cases. Treatment successes was defined as being either smear negative (cured) at month five or later of treatment or having completed TB treatment in situations where sputum smear microscopy was not done. Those who died for any reason during TB treatment were also recorded. For reasons of analysis, we also defined composite outcome (failure or death). After univariate analysis, multivariate analysis with 0.05 as the level of significance was carried out, focusing on socio-demographic variables, HIV status, and acid-fast bacilli score at baseline.

Of the 270 pulmonary TB patients, 264 were included in the final analysis. The median age was 35 years (interquartile range, 28–46 years); 23 patients failed on TB treatment with a frequency of 8.6% (5.5–12.6%). In the multivariate analysis, positive HIV status (OR, 10.38; 95% CI, 1.77–60.91; $p=0.01$) and male gender (OR, 4.34; 95% CI, 1.03–18.28; $p=0.046$) were each significantly associated with increased risk of TB treatment failure. Only positive HIV status (OR, 12.86; 95% CI, 4.27–8.27; $p<0.0001$) remained significantly associated with composite

outcome. In conclusion, positive HIV status and male gender are the potential risks factors of TB treatment failure. The association between positive HIV status and composite outcome confirmed the deadly association between TB and HIV. There is a need to truly integrate HIV and TB activities in all levels of the health system.

Introduction

Tuberculosis (TB) is one of the oldest preventable and curable diseases.¹ However, TB remains an important public health problem in the world, as evidenced by the 10.4 million new TB cases and the 1.4 million deaths from the disease in 2015,² the majority of cases occurring in resource-limited settings. Benin Republic (West Africa) has a low TB burden, with 32 cases per 100 000 inhabitants and a death rate of 5% for smear-positive pulmonary TB cases (PTB+).³ The treatment of PTB+ cases in Benin Republic is free of charge and is based on a four-drug regimen according to the World Health Organization (WHO) TB treatment guidelines 2010.⁴

The whole country has achieved the WHO minimum acceptable threshold for treatment success which was 85% for PTB+;⁵ the high rate of treatment failure of about 8% in two areas of north-east Benin could be a factor in the emergence of multidrug resistant (MDR) TB in these settings.⁶ Those authors reported a 12% occurrence of MDR strains among retreatment cases.⁷

Many approaches have been proposed to increase TB treatment success and reduce failure, such as Directly Observed Treatment Short course (DOTS),^{5,8} which is implemented nationwide in Benin.^{9,10} Many factors (such as age ≥ 35 years, body mass index (BMI) ≤ 18.5 , diabetes, MDR TB,¹¹ and non-conversion of sputum smear after intensive phase) have been reported to be significantly associated with TB treatment failure.¹² However, it is unknown to what extent these or other factors contribute to treatment failure in north-east Benin and in West African rural settings.

We present the results of a study designed to assess risk factors for anti-TB treatment failure in PTB+ cases in north-east Benin.

Materials and methods

We conducted a retrospective cohort study of PTB+ cases in order to assess risk factors for treatment failure. The study was carried out at the Evangelic Hospital of Bembèrèkè (EHB), a rural setting situated in north-east Benin about 700 km away from the capital city of Cotonou. We selected Bembèrèkè because it has a much higher TB treatment failure rate than the rest of Benin. EHB is an intermediary referral hospital for all patients

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Variables	Overall	TB treatment success	TB treatment failure	Died	P-value ³
	n=264	n=205	n=23	n=36	
Ages (years) ¹	38.0 (±14.3)	37.2 (±14.2)	41.3 (±15.3)	40.9 (14.2)	0.19
Male gender	67.80%	65.4%	87.0%	69.4%	0.11
HIV positive	08.71%	5.0%	13.6%	30.3%	<0.001
Benin resident	72.26%	73.7%	52.2%	77.8%	0.068
AFB smear (++ or +++) ²	80.70%	86.3%	95.7%	88.9%	0.485

¹ Data expressed as mean (±SD).

² AFB result at baseline.

³ T-tailed unadjusted p-value based on one-way analysis of variance (for age) or Pearson's chi-square test.

Table 1: Characteristics of tuberculosis treatment outcome group

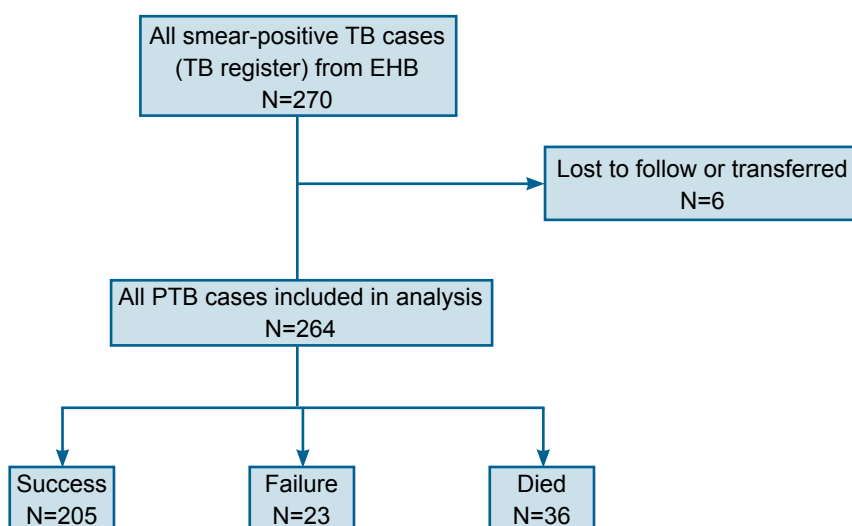


Figure 1: Flow chart of new pulmonary tuberculosis-positive cases registered in EHB between 2007-2011

Variables	Success vs failure		
	OR ¹	95% CI	p value ³
Ages (years)	1.15	0.83–1.58	0.40
Male gender	4.34	1.03–18.28	0.046
HIV positive	10.38	1.77–60.91	0.010
Resident	0.43	0.17–1.11	0.080
AFB (++ or +++) ²	6.26	0.66–39.23	0.11

¹ Adjusted odd ratio.

² AFB result at baseline.

³ Adjusted p value.

Table 2: Logistic regression of TB treatment failure vs TB treatment success

from the upper north-east of Benin and to residents of neighbouring Niger and Nigeria.

Using the EHB registry of TB patients, we identified all new cases of PTB+ occurring between 1 January 2007 and 31 December 2011, among individuals aged 10 years of age or older.

We defined PTB+ as the presence of cough and fever (temperature $\geq 39^{\circ}\text{C}$) for more than 2 weeks, loss of body weight, and the presence of acid-fast bacilli (AFB) sputum. Prior to 2010, three smear sputum samples were required to diagnose PTB+. The patient was considered positive for PTB+ if two or more of the samples were positive for AFB. After 2010, only two smears sputum were required, and patients were considered positive for PTB+ if at least one smear sputum sample was positive for AFB.

For the purposes of analysis, we excluded five patients who were lost to follow-up and one patient who transferred to a different facility for treatment before the six-months follow-up interval was completed, leaving a final analysis sample of 264 individuals (Figure 1). The study was approved by the ethics panel of Parakou University in Benin.

Study definitions. We used the EHB TB registry to abstract treatment outcomes. Consistent with WHO guidelines¹³ the following definitions were used: 'TB treatment failure' - patients who were initially smear positive and who remained smear positive at month 5 or later during treatment; 'TB treatment cure' - patients who were initially smear positive and who were smear negative in the last month of treatment and on at least one previous occasion; 'TB treatment completed' - patients who completed treatment but did not meet

the criteria for cure or failure; 'TB treatment success' - either TB treatment cure or TB treatment completed. 'Deaths' were patients who died from any cause during treatment. For the purposes of this analysis, we also define a 'composite adverse outcome' as the occurrence of either anti-TB treatment failure or death in first six months of treatment. Potential predictor variables for TB treatment failure and the composite adverse outcome include: socio-demographic factors (age, sex, country of residence Benin or not), HIV-related factors (HIV status), AFB result at baseline.

Statistical methods. We conducted separate analyses for TB treatment failure and the composite adverse outcome. For the former we excluded the 36 patients who died during the study (Figure 1). We used one-way ANOVA and Pearson chi-square tests to compare the baseline characteristics of patients in the three treatment outcome groups (TB treatment success, TB treatment failure, and deaths), and multiple logistic regression analysis to assess risk factors for TB treatment failure and for the composite adverse outcome. Analyses were conducted using Stata, version 12, and all reported p values are two-sided with a significance level <0.05 .

Variables	Success vs composite outcome		
	OR ¹	95% CI	p value ³
Ages (years)	1.21	0.96–1.57	0.11
Male gender	2.20	0.98–4.94	0.56
HIV positive	12.86	4.31–38.27	<.001
Resident	0.71	0.35–1.44	0.34
AFB (++) or (+++) ²	3.17	0.95–10.57	0.060

¹ Adjusted odd ratio.
² AFB result at baseline.
³ Adjusted p value.

Table 3: Logistic regression of composite outcome vs TB treatment success

Results

General and socio-demographic characteristics of the study population. Of the 264 PTB+ cases, 23 (8.71%) had TB treatment failure, 36 (13.64%) died, and 205 (77.65%) had TB treatment success (Figure 1). The mean age of the cohort was 38.4 (±14.3) years, the majority were male (179, 67.80%). There were 23 (8.71%) HIV positive cases, 91 (72.6%) patients resided in Benin, and 213 (80.70%) had had high positivity of AFB (Table 1).

Univariate analysis. Positive HIV status was strongly associated with treatment outcome, accounting for 13.6% of TB treatment failures and 30.3% of deaths; only 5% of those successfully treated for TB were HIV positive. Although not significantly different, in our sample TB treatment failures were considerably more likely to be male and to not live in Benin. Of the 72 non-Benin residents attending EHB for treatment, 70 were from Nigeria and 2 were from Niger. They were also somewhat more likely to have higher initial AFB scores (Table 1).

Multivariate logistic regression models. Positive HIV status (OR, 10.38; 95%CI, 1.77–60.91) and male gender (OR, 4.34; 95%CI, 1.03–18.28) were each significantly associated with increased risk of TB treatment failure with respectively $p=0.01$ and $p=0.046$. An increased baseline AFB score was also associated with increased risk of TB treatment failure (OR, 6.26; 95%CI, 0.66–39.23) but this was not statistically significant ($p=0.11$). Finally, the data were suggestive of a reduced risk of TB treatment failure for Benin residents (OR, 0.43; 95%CI, 0.17–1.11), but this was not statistically significant ($p=0.08$) (Table 2).

Positive HIV status was significantly associated with composite outcome (OR, 12.86; 95%CI, 4.27–38.27; $p<0.0001$) with increased risk of the composite adverse outcome of treatment failure or death (Table 3). Increased baseline AFB score was also just significantly associated with composite outcomes (OR, 3.17; 95%CI, 0.95–10.57; $p=0.06$). Being resident in Benin appeared to be a protective factor against composite outcome, without statistical significance (OR, 0.71; 95%CI, 0.35–1.44; $p=0.34$).

Discussion

Positive HIV status was the first predictor of TB treatment failure. Male gender was the second predictor of TB treatment failure. These findings reinforce the necessity of HIV test screening in

order to reach 100% of TB patients and to give further attention to those who are male and/or HIV positive in TB clinics. Perriens et al¹⁴ in Zaire, found an association between HIV and TB treatment failure among PTB+ patients with a risk ratio (RR) of 2.6, 95%CI of 1.4–4.9, $p=0.002$. Sanchez et al¹⁵ found in a study in Brazil, that the risk of occurrence of unfavourable outcomes during TB treatment was 3.09 times higher among HIV-co-infected vs HIV-negative patients and underlined the necessity of screening TB patients for HIV. In Cameroon, Pefura Yone et al¹⁶ found that, being HIV positive was associated with an increased, but non-significant, risk of failure/defaulting of TB treatment (RR, 1.19; 95%CI, 0.88–1.59). The difference between these results and our study could be explained by the fact that their study included 1467 TB cases with 73.8% of them PTB+. In the same study, Pefura Yone et al found that ignorance of HIV status was associated with a statistically significant increased risk of failure/default (RR, 2.30; 95%CI, 1.65–3.21).¹⁶ The role of HIV in TB treatment failure is linked to the active replication of HIV in the presence of Mycobacterium tuberculosis strains.^{17,18} This active replication of HIV, induced lymphocyte T4 depletion in gut mucosae. This has been shown to cause chronic enteropathy and malabsorption of anti-TB drugs in PTB+ individuals co-infected with HIV.^{19–21} The role of HIV in TB treatment failure could be attenuated by antiretroviral therapy (ART)²² and many authors have shown the advantages of early initiation of ART after starting TB treatment.^{23,24} In other study, HIV among TB patients was associated with low adherence to TB treatment.²⁵ In the current study, HIV also had a role in composite outcomes (i.e. treatment failure or death), with one third of PTB+ patients who died being HIV positive, and an increase in OR from treatment failure (OR, 10.38) to composite outcome (OR, 12.86). Male gender has also been shown to be a risk factor for unsuccessful TB treatment outcomes in a study in Malaysia.²⁶ In another study, Pefura Yone et al in Cameroon showed that TB treatment failure rates (28% among patients with Mycobacterium tuberculosis strains) were high among those with positive sputum cultures after the intensive phase of TB treatment.¹² The high failure rate in this study could be due to the fact that the test used to assess TB treatment outcomes among patients who remained positive for AFB after the intensive phase of TB was more sensitive than the AFB technique used in the current study.

There were several limitations to the current study. The retrospective data were incomplete and therefore it was not possible to assess the role of diabetes in TB treatment failure; this non-communicable disease is a public health problem in West Africa. In fact the role of diabetes in TB treatment failure is unclear; some authors, for example Jiménez-Corona et al,²⁷ have shown that diabetes is associated with a higher probability of TB treatment failure (OR, 2.93; 95%CI, 1.18–7.23; $p=0.022$), also a study from Guangzhou in China by Fengling et al²⁸ reported a risk ratio (RR) of 4.46, 95%CI 1.46–10.98. In contrast, studies such as those by Duangrithi,²⁹ Dooley et al,³⁰ and Prasad et al³¹ did not find any association between diabetes and TB treatment failure ($p=0.51$). However, the role of diabetes in increased risk of failure and death combined, was underlined in a meta-analysis by Baker et al.³² (RR, 1.69; 95%CI, 1.36–2.12). Another limitation of the current study was a selection bias due to the AFB technique

used for PTB+ diagnosis and TB treatment failure assessment; AFB positivity did not mean the presence of Mycobacterium tuberculosis in every case.³³ Finally, the number of failures and deaths reported in the study limited the power of multivariate analysis, but the use of composite outcomes improved this.

Conclusion

In summary we have shown that risk factors for PTB+ treatment failure were co-infection with HIV and being of male gender; this suggests that national guidelines must emphasize the integration of HIV and TB clinics at all levels of the health system in order to enable collaborative activity. The fact that HIV remains a predictor risk of composite outcome (failure or death) confirms the deadly association between HIV and TB, and suggests that further studies are required in this area.

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Author declaration

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Any ethical issues involving humans or animals: none.

Was informed consent required: not required.

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Obstructive sleep apnoea risk and excessive daytime sleepiness among intercity commercial drivers in Benin City, Nigeria

A R Isara and A Q Aigbokhaode

Abstract

The objective of this descriptive cross-sectional study was to assess the prevalence of obstructive sleep apnoea (OSA) and excessive daytime sleepiness (EDS) risk among intercity commercial drivers in Benin City, Nigeria. The Berlin Questionnaire and Epworth Sleepiness Scale were administered to drivers recruited from six randomly selected motor parks. Weight, height, and blood pressure were also measured. Data were analysed using IBM SPSS statistics version 20. A total of 214 commercial drivers with mean age of 45.9 ± 10.0 years participated in the study. Obesity was observed in 29.9% participants while 79 (36.9%) were hypertensive. More than one third (36.4%) reported to have been involved in a road traffic accident. Almost half (105, 49.1%) of participants were found to have some OSA risk while 98 (45.8%) had a risk of EDS. Both OSA ($p=0.007$) and EDS ($p=0.010$) were significantly associated with road traffic accidents. Self-reported hypertension was significantly associated with both OSA and EDS ($p<0.001$). A higher proportion of drivers with OSA risk reported EDS ($p<0.001$). The most significant predictors of road traffic accidents was EDS risk (OR 1.931, 95% CI 1.013–3.541, $p=0.033$) and self-reported hypertension (OR 2.963, 95% CI 1.113–7.880, $p=0.030$). There was a high risk of both OSA and EDS among intercity commercial drivers in Benin City, Nigeria. Urgent measures aimed at reducing the risk of OSA and EDS among drivers should be taken to reduce the rates of road traffic accidents on Nigerian roads.

Introduction

Road traffic accidents (RTAs) are a daily occurrence in Nigeria, accounting for the deaths of 12 persons per day, with about 80% of these deaths occurring on the highways and involving intercity passengers and drivers.¹ The majority of people in developing and low-income countries like Nigeria depend heavily on road transportation for commuting between cities and towns. This

reliance on commercial drivers makes operators of commercial vehicles an important component in the development of any society.² Undiagnosed obstructive sleep apnoea (OSA) resulting in excessive daytime sleepiness (EDS) among vehicle drivers, is one of the most serious medical disorders liable to result in major road accidents.³

Studies have revealed that people at risk of OSA may also get sleepy during the day because they do not feel sufficiently restored after a night of interrupted sleep, which is quite common among long-distance drivers. The combined risk factors of OSA and EDS

Variable	Frequency (n= 214)	Percent
Age group (years)*		
25–34	25	11.7
35–44	84	39.3
45–54	56	26.1
55 and above	49	22.9
Level of education		
None	6	2.8
Primary	91	42.5
Secondary	101	47.2
Tertiary	16	7.5
Marital status		
Single	5	2.3
Cohabiting	21	9.8
Married	187	87.4
Separated	1	0.5
BMI		
≥ 30	64	29.9
< 30	150	70.1
Hypertension		
Yes	79	36.9
No	135	63.1

*Mean age 45.9 ± 10.0 years.

Table 1: Socio-demographic characteristics of respondents

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have been documented and have been found by researchers to raise the risk of RTAs among drivers driving long distances without sufficient sleep.^{4,5}

The most common symptoms of sleep apnoea include snoring, sleepiness, and spousal reports of apnoea episodes during sleep. Risk factors for OSA include being overweight, male, related to someone who has OSA, over the age of 65 years, being black or Hispanic and tobacco smoking.⁶

In many countries, research studies have documented an association between RTAs and undiagnosed OSA and EDS among drivers;^{4,5} however in Nigeria there is a paucity of data with regards to the relationship between OSA, EDS and RTAs in long-distance drivers. Complaints of sleep disorders

Variable	Road traffic accidents		p value
	Yes Freq. (%)	No Freq. (%)	
Obstructive sleep apnoea risk			
Risk present	48 (45.7)	57 (54.3)	0.007
Risk absent	30 (27.5)	79 (72.5)	
Excessive daytime sleepiness			
Risk present	45 (45.9)	53 (54.1)	0.010
Risk absent	33 (28.5)	83 (71.5)	

Table 2: Association between obstructive sleep apnoea risk, excessive day time sleepiness and road traffic accidents among respondents

Variables	Obstructive sleep apnoea		p value	Excessive daytime sleepiness		p value
	Risk n (%)	No risk n (%)		Yes n (%)	No n (%)	
Age group			0.122			0.045
25–34	8 (32.0)	17 (68.0)		6 (24.0)	19 (76.0)	
35–44	38 (45.2)	46 (54.8)		46 (54.8)	38 (45.2)	
45–54	30 (53.6)	26 (46.4)		23 (41.1)	33 (58.9)	
55 and above	29 (59.2)	20 (40.8)		23 (46.9)	26 (53.1)	
BMI			<0.001			0.596
Underweight	0 (0.0)	1 (100.0)		0 (0.0)	1 (100.0)	
Normal	20 (27.4)	53 (72.6)		30 (41.1)	43 (58.9)	
Overweight	31 (40.8)	45 (59.2)		38 (50.0)	38 (50.0)	
Obese	54 (84.4)	10 (15.6)		30 (46.9)	34 (53.1)	
Snoring			<0.001			0.001
Yes	86 (87.8)	12 (12.2)		57 (58.2)	41 (41.8)	
No	19 (16.4)	97 (83.6)		41 (35.3)	75 (64.7)	
Self-reported hypertension			<0.001			<0.001
Yes	39 (83.0)	8 (17.0)		32 (68.1)	15 (31.9)	
No	66 (39.5)	101 (60.5)		66 (39.5)	101 (60.5)	
Alcohol			0.077			0.342
Yes	84 (52.2)	77 (47.8)		77 (47.8)	84 (52.2)	
No	21 (39.6)	32 (60.4)		21 (39.6)	32 (60.4)	
Cigarette smoking			0.317			0.874
Yes	24 (45.3)	29 (54.7)		25 (47.2)	28 (52.8)	
No	81 (50.3)	80 (49.7)		73 (45.3)	88 (54.7)	
Kola nut*			0.103			0.679
Yes	63 (53.4)	55 (46.6)		56 (47.5)	62 (52.8)	
No	42 (43.8)	54 (56.2)		42 (43.8)	54 (56.2)	
OSA risk			-			<0.001
Yes	-	-		61 (58.1)	44 (41.9)	
No	-	-		37 (33.9)	72 (66.1)	

Table 3: Bivariate analysis of variables associated with obstructive sleep apnoea and excessive daytime sleepiness

among long-distance road drivers in Nigeria are largely undocumented. This non-availability of relevant data constrains the implementation of medical interventions for this causative factor of RTAs among long-distance drivers, a significant percentage of whom may be falling asleep while driving.

The objective of this study was to determine the prevalence of predictors of OSA and EDS among intercity, commercial long-distance drivers in Benin City, Nigeria. This will serve not only to provide a baseline for further studies in this area but also as a tool for the development of strategies and interventions aimed at reducing RTAs and prolonging the lives of drivers and passengers.

Materials and methods

Participants. This descriptive cross-sectional study was carried out in Benin City, Edo State, Nigeria. The city has a projected population of 1 085 676 and is made up of three Local Government Areas namely: Oredo, Egor, and Ikpoba-Okha.⁷ The city is strategically located in the heart of Nigeria, with proximity to the west, east and north of the country, making it a major transportation link to many parts of the country. This makes commercial driving a major occupation and there are numerous commercial road transportation operators in the city.

Ethical approval to conduct this study was obtained from the University of Benin Teaching Hospital Ethics and Research Committee. Permission was also sought from the management of the transport companies involved. Written informed consent was obtained from each respondent before conducting interviews. Confidentiality and privacy of the respondents was ensured during the interviews.

The participants were intercity commercial drivers involved in long-distance transportation in Benin City. Only drivers in registered transport companies were included in the study. The sample size for the study was calculated using the formula for studying proportions.⁸ Using an estimated EDS prevalence of 14.4% among drivers obtained from a previous study in Lagos, Nigeria,⁹ and after correcting for non-response at a rate of 10%, the minimum sample size required for the study was 210. A cluster sampling technique was used to recruit drivers for this study. A list of the 35 registered transport companies operating in Benin City at the time of this study was obtained from the State Ministry of Transport; three companies were selected using a simple random sampling method from each of the three Local Government Areas that make up Benin City. Thus a total of nine transport companies were used for the study. All the drivers in the selected clusters who met the inclusion criteria were investigated.

Data collection. Data were collected using the validated Berlin Questionnaire¹⁰ and the Epworth Sleepiness Scale validated for OSA risk profile.^{11,12} The Berlin Questionnaire was used to identify subjects who were at high risk and low risk for OSA by identifying snoring behaviour, daytime sleepiness, obesity, and hypertension. The questionnaire was divided into three sections. A section was considered positive if there were two affirmative answers in either section 1 or 2, or one affirmative

Factor	Odds ratio	p value	95% CI
Obesity	1.211	0.600	0.592–2.476
OSA risk	0.432	0.019	0.214–0.874
EDS risk	1.931	0.033	1.013–3.541
Self-reported hypertension	2.963	0.030	1.113–7.880

Table 4: Logistic regression model for the predictors of road traffic accidents among respondents

response in section 3. Individuals who had positive scores in two of the three sections were considered to be at risk for OSA.

An eight-question questionnaire was used to determine the level of the respondent's daytime sleepiness. The Epworth Sleepiness Scale is based on the assessment of the likelihood of the respondent falling asleep in certain situations commonly encountered in daily life. This was scored on a scale of increasing probability from 0 to three for the eight different situations that most people engage in during their daily lives, though not necessarily every day. The scores for the eight questions were added together to obtain a single number. A number in the 0–9 range was considered to be normal while a number in the 10–24 range indicated that expert medical advice should be sought because a score of 10 or higher indicates the patient is likely to have a sleep disorder such as OSA.

Anthropometric measurements. Bathroom weighing scales (Hana™) were used to measure the weights of the respondents. The weighing scales were zeroed and standardised daily. A standardised stadiometer was used to measure height. When measuring the height, the participants were asked to stand erect with their feet together; heels, buttocks, shoulders, and occiput touching the meter rule behind, with eyes looking straight ahead. Body mass index (BMI) was derived from weights and heights and was then used to classify participants into: underweight (BMI < 18.5), normal weight (BMI 18.5–24.9), overweight (BMI 25.0–29.9), and obese (BMI ≥ 30), according to WHO guidelines.¹³ Blood pressure (BP) was measured using a mercury Accosson's sphygmomanometer and was taken with the cuff covering about three-quarters of the left arm and over the brachial artery with the respondent in a sitting position. The BP measurement was done before and after the interviews and the average was recorded as the respondents' BP. An average systolic blood pressure of 140 mmHg and above and a diastolic pressure of 90 mmHg and above was regarded as hypertension as defined by the Joint National Committee on Hypertension (JNC) 7 classification.¹⁴

Data analysis. Data analysis was carried out using SPSS version 20.0 software (IBM Corp, Armonk, NY, USA). Qualitative data were summarised as proportions while continuous variables that were normal in distribution were expressed as means and standard deviation. The chi-square statistical test was used to test association between socio-demographic and OSA risk, EDS risk, and occurrence of RTAs. Variables that showed significant

association were fitted into the logistic regression model to determine statistically significant predictors of RTAs. The level of significance was set at a *p* value of less than 0.05.

Results

A total of 214 commercial drivers participated in this study. As shown in Table 1, their mean age was 45.9 (± 10.0) years with a higher proportion (84, 39.3%) in the age group of 35–44 years. The majority of the drivers (89.7%) had either primary- or secondary-level education while 187 (87.4%) were married. Obesity was observed in 29.9% of the respondents while 79 (36.9%) were hypertensive. However, only 47 (22.0%) gave a history of self-reported hypertension.

More than one third (36.4%) of the respondents reported that they had been involved in an RTA while being the driver. Almost half (105, 49.1%) of respondents were found to be at risk of OSA while 98 (45.8%) were at risk of EDS. A higher proportion of obese respondents (54, 84.4%) had a risk of OSA compared with 51 (34.0%) of the non-obese respondents. This association was statistically significant ($p < 0.001$). Table 2 shows that a statistically significant association was found between OSA risk and EDS risk and the reported incidence of RTAs among the respondents ($p = 0.007$ and 0.010 respectively).

A further bivariate analysis of variables associated with OSA and EDS is shown in Table 3. There was no statistically significant association between age and OSA, but the older age groups reported more EDS and this was statistically significant ($p = 0.045$). The risk of OSA was found to increase with increasing BMI of the respondents ($p < 0.001$), however, no statistically significant association was found between BMI and EDS ($p = 0.596$). Self-reported hypertension was significantly associated with both OSA and EDS ($p < 0.001$). A higher proportion of respondents with OSA risk reported EDS and this was statistically significant ($p < 0.001$). However, alcohol intake, cigarette smoking, and chewing of kola nut (a stimulant substance) were not statistically associated with both OSA and EDS.

Table 4 shows the logistic regression model for the predictors of RTAs among the respondents. The most significant predictors of RTAs among the respondents were EDS risk ($p = 0.033$) and being hypertensive ($p = 0.030$).

Discussion

This study showed a high risk of both OSA and EDS among intercity commercial drivers in Benin City, Nigeria, thus revealing a potentially huge public health challenge in Nigeria. The high prevalence of OSA in this study is comparable with previous studies in Lagos⁹ and Ile-Ife,¹⁵ all in south-west Nigeria, but the prevalence of EDS was far higher in this study than in both previous studies. A similar finding of high OSA and EDS has also been reported among drivers in Malaysia.¹⁶

The majority of the commercial drivers were aged between 35 and 54 years, and this represents the economically productive age group in Nigeria. Apart from increasing age being a risk factor for OSA, the fact that the drivers in this study were all males, with a greater proportion either overweight or obese, and with a history of hypertension, may have accounted for the high prevalence of OSA. This in turn probably explains the

high prevalence of EDS, since OSA was found to be significantly associated with EDS. Over one third of the drivers had been involved in RTAs in this study, with the rate of RTA associated with OSA, EDS, and self-reported hypertension. The high prevalence of RTAs among the drivers was concerning. Although, we did not explore whether the RTAs were associated with fatalities, most RTAs in Nigeria are associated with injuries and fatalities, probably compounded by the lack of emergency ambulance services. Thus many drivers and passengers may be losing their lives from RTAs in Nigeria as a result of EDS among commercial drivers. A study of occupational drivers in Iraq revealed a high prevalence (40%) of poor sleep quality and one quarter of the drivers were reported to have records of RTAs.¹⁷ Excessive sleepiness and likely sleep apnoea increase the risk of RTAs for occupational drivers. This is similar to our study in which OSA, EDS, and self-reported hypertension increased the likelihood of RTAs among the commercial drivers. It was observed that objective measurement of blood pressure revealed more drivers to be hypertensive than those who had self-reported as hypertensive. The reason for this may be either the drivers were truly not aware of their hypertensive status or they deliberately did not want to admit and report that they were hypertensive. Again this can jeopardise and compromise their health status.

In Nigeria, the majority of commercial drivers do not have enough rest and do not get a good night's sleep. Also, many of them use stimulant substances of various forms and types to keep awake while driving. This leads to poor sleep quality and excessive daytime tiredness, and poses a significant risk of cardiovascular conditions such as stroke, heart attack, heart failure, and cardiac rhythm disturbances – especially intermittent atrial fibrillation. Inadequate sleep is also associated with low work performance, poor personal relationships, and ultimately poor quality of life. The management of transport companies operating in Nigeria do not carry out medical examinations on their drivers before they are allowed to drive on the roads. In addition, there is poor regulation of the activities of drivers by government authorities leading to poor health outcomes and poor productivity on the part of the drivers and increased RTAs, resulting in avoidable morbidities and mortalities in both drivers and their passengers. Apart from the increase in the rate of RTAs, a large proportion of commercial drivers with OSA risk and EDS have remained undiagnosed, which poses a risk of increasing numbers of fatalities on Nigerian highways. This has serious implications for both the drivers, passengers, local communities, and the country at large.

In this study, we observed that almost one third of the respondents were obese. The sedentary lifestyle of the drivers coupled with an unhealthy diet and little or no physical exercise may have accounted for this finding. A similar finding of overweight and obesity among drivers was reported in the Lagos study.⁹ Also, another study documented a strong correlation between BMI and the degree of OSA, and obese drivers are highly prone to be sleepy during the day.¹⁸ Although being obese did not significantly predict RTAs in the regression model in this study, increasing BMI was significantly associated with OSA in the bivariate analysis. This finding underscores the need for commercial drivers to embark on weight reduction activities that will keep their BMI within an acceptable range and limit

complications that may arise from overweight and obesity.

In conclusion, this study showed that there was high risk of both OSA and EDS among intercity commercial drivers in Benin City, Nigeria. The burden of RTAs resulting from this finding is of serious public health concern. Therefore, urgent measures aimed at reducing the risk of OSA and EDS among drivers should be taken by government agencies to reduce the rates of RTAs on Nigerian roads. Transport companies should be made to carry out pre-employment screening of drivers for OSA and EDS risk before they are employed to drive.

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Author declaration

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Co-existing allergic rhinitis among asthmatics attending the Paediatric Pulmonology Clinic: implications for control

A A Gobir, S S Mohammed, and W B R Johnson

Abstract

Asthma is the most common chronic airway disorder and the prevalence has been increasing in the last two decades. Asthma causes significant morbidity among children due to its effects on daily and sporting activities, as well as school attendance. The focus of asthma management is to achieve good control of symptoms to enable better quality of life among those affected. Identifying and treating co-morbid conditions such as allergic rhinitis (AR) is important in the level of asthma control that is achieved. In Africa, there is a dearth of literature on the subject of AR among children with asthma. Furthermore, there is no study on the severity of AR and its effect on level of asthma control. This study was therefore designed to determine the prevalence of AR in children with asthma seen at the University of Ilorin Teaching Hospital Ilorin, Nigeria. In addition, the study assessed the level of asthma control and the association with AR severity.

A cross-sectional study was conducted among all patients with asthma aged between six and 17 years at the Paediatric Pulmonology Clinic between March and July 2016. Using standard tools, prevalence of AR, severity of the disorder, and level of asthma control were assessed. A total of 66 asthmatics were recruited, of which 30 (45.5%) had AR. Among those with AR, 12 (40.0%) had uncontrolled asthma compared with four (11.1%) of the 36 without AR ($p=0.018$). Those with mild AR had better levels of asthma control compared with those with moderate-severe AR ($p=0.010$). The data from this study show the high prevalence of AR among asthmatic children. In addition, asthmatic children with AR are more likely to have poor levels of asthma control. Hence, routine assessment of all asthmatic children for AR is recommended.

deaths are not so high. Asthma causes significant limitation in terms of daily activities, school attendance, and participation in recreational and sporting activities.¹ This is the reason why the concept of control is important and central to the Global Initiative for Asthma (GINA) 2014 guidelines.⁵

Identifying and treating co-morbidities is an important step in achieving control and better quality of life in asthmatic patients. Of particular interest are allergic rhinitis (AR) and allergic rhinosinusitis in line with the 'one linked airway disease concept' that suggest a shared pathophysiology for asthma and allergic rhinitis.⁶⁻⁸ There have been publications in the last decade that have proposed actively searching for other allergic/inflammatory conditions that are considered of same pathogenesis as asthma. However, there is a dearth of literature in Africa in general, and Nigeria in particular, on the occurrence of AR among children with asthma. Furthermore, to the best of our knowledge, there have been no studies in the country on the implications of AR for control of asthma symptoms in the paediatric population. The Paediatric Pulmonology Unit of the University of Ilorin Teaching Hospital (UITH) conducted a study on AR among children being managed for bronchial asthma at the unit. The implications for control were also studied among the population seen. It is hoped that the findings will influence routine practice in asthma care among children.

Materials and method

This was a cross-sectional study among children aged 6–17 years with previously diagnosed asthma attending the pulmonology clinic. None of the patients had had previous assessment or therapy for AR. The International Study of Asthma and Allergies in Childhood (ISAAC) rhinitis questionnaire was used as the study instrument to assess all asthmatics for AR. The severity of AR was classified according to Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines into mild and moderate-severe.⁹ Asthma symptom control was assessed using the Global Initiative for Asthma (GINA) 2014 guidelines. The Oyediji Scheme for social classification was used with Classes 4 and 5 merged as 'lower class', Class 3 was 'middle class', and Classes 1 and 2 combined as 'upper class'.¹⁰ An automated micro-peak flow meter (Piko-1®) (nSpire Health Inc., Longmont, USA) was also used in the study.

The study was nested in a larger study on asthma. Ethical approval was obtained from the UITH ethical review committee. The study adhered strictly to the Helsinki Declaration for the conduct of such studies. Only those who consented to the study had the questionnaire administered. The study was carried out between

Introduction

Asthma is the most common chronic airway disorder worldwide. There are indications that the prevalence of asthma is increasing in both developed and developing countries, although at different speeds.¹ Prevalence data vary between and within countries due to many factors. Asthma prevalence among Nigerian children is said to be between 5.1 and 14.3%.²⁻⁴ Asthma is a cause of significant morbidity among children although asthma-related

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	Number	Percentages (%)
Age group (years)		
6–9	29	44.0
10–13	21	31.8
14–17	16	24.2
Total	66	100.0
Sex		
Male	37	56.0
Female	29	44.0
Total	66	100.0
Social class		
Upper	21	31.8
Middle	27	40.9
Lower	18	27.3
Total	66	100.0

Table 1: Socio-demographic characteristics of the study population

Symptoms	Number (%)*
Watery nose	30 (100.0)
Excessive sneezing	22 (73.3)
Nasal obstruction	18 (60.0)
Itchy nose	15 (50.0)
Watery, itchy eyes	13 (36.7)
*Many subjects had multiple symptoms.	

Table 2: Symptoms of allergic rhinitis in those subjects with AR

Parameters	Mean±SD		t	p value
	Asthma	Asthmatic and AR		
Weight (kg)	37.4±11.8	33.7±11.5	1.299	0.199
Height (cm)	143.5±14.6	138.4±15.8	1.352	0.181
BMI (kg/m ²)	17.7±3.1	17.0±2.6	1.003	0.320
Abbreviations: t, independent samples t test value; SD, standard deviation; BMI, body mass index.				

Table 3: Distribution of some selected anthropometric parameters of the study participants

Parameters	Mean±SD		t	p value
	Asthma	Asthmatic + AR		
PEFR (l/min)	222.5±86.7	214.3±90.8	0.375	0.709
FEV ₁ (l)	1.9±1.3	1.6±1.0	0.910	0.367
Abbreviations: PEFR, peak expiratory flow rate; FEV ₁ , forced expiratory volume in 1 second; t, independent samples t test value.				

Table 4: Distribution of the FEV₁ and PEFR of the study participants

questionnaire with a focus on five main symptoms: watery nose, excessive sneezing, nasal obstruction, itchy nose, and watery red

itchy eyes. A micro-peak flow meter was used for the measurement of peak expiratory flow rate (PEFR), while forced expiratory volume in one second (FEV₁) was automatically generated by the equipment. GINA guidelines were used for the classification of control of symptoms into 'well-controlled', 'partially controlled' or 'uncontrolled'.⁵ It took an average of 20 minutes to complete the recruitment and study procedure for each patient. Data were analysed using SPSS version 20.0.

After obtaining informed consent, data were obtained on the age, sex, and so-

cial class of each subject. Anthropometric measurements were taken routinely but the body mass index (BMI) was only calculated for the purpose of this study. Each subject was taken through the

itchy eyes. A micro-peak flow meter was used for the measurement of peak expiratory flow rate (PEFR), while forced expiratory volume in one second (FEV₁) was automatically generated by the equipment. GINA guidelines were used for the classification of control of symptoms into 'well-controlled', 'partially controlled' or 'uncontrolled'.⁵ It took an average of 20 minutes to complete the recruitment and study procedure for each patient. Data were analysed using SPSS version 20.0.

Results

A total of 66 asthmatic children were recruited; ages ranged between six and 17 years: 29 (44.0%) were aged 6–9 years; 21 (31.8%) were aged 10–13 years, and 16 (24.2%) were between 14 and 17 years. There were 37 (56.0%) males and 29 (44.0%) females; M:F of 1.3:1. Twenty-one (31.8%) were in the upper social class; 27 (40.9%) in the middle class, while 18 (27.3%) were of the lower social classes. The socio-demographic characteristics of the study population are presented in Table 1.

Of the 66 subjects, 30 (45.5%) had co-existing AR. Table 2 shows symptoms found among the 30 patients with AR.

The mean±SD weight, height, and BMI of asthmatic subjects with AR were 33.7±11.5 kg, 138.4±15.8 cm and 17.0±2.6 kg/m² respectively, while the corresponding values in their peers without AR were 37.4±11.8 kg, 143.5±14.6 cm and 17.7±3.1 kg/m² respectively. The anthropometric parameters were not significantly different between the two groups (Table 3).

The mean±SD PEFR and FEV₁ of the subjects with AR were also compared with those without AR. No significant differences were found in the lung function parameters between the two groups (Table 4).

The relationship between the co-existence of AR and the level of asthma control is shown in Table 5. Among the 30 subjects with AR, 12 (40.0%) had uncontrolled asthma compared with four (11.1%) of the 36 who had asthma alone (p value 0.018).

The effect of AR severity on the level of asthma control among the subjects with AR was studied. Of the 11 subjects with moderate-severe AR, 9 (81.8%) had uncontrolled asthma compared with three (15.8%) out of the 19 subjects with mild AR (p=0.01). This is shown in Table 6.

Discussion

About 50% of the asthmatic children in our study had AR that had been previously untreated. An even higher prevalence of AR in asthmatic children has been reported in studies from Peru (66.4%), Netherlands (76.2%), Japan (77.7%), and France (58.7%).^{11–14} This shows that AR is a frequent co-morbidity in asthmatic children. This has also been documented by earlier workers, especially in respect to allergic asthma.^{7–9} In order of descending frequency of occurrence, the following symptoms have been found among study subjects: watery nose, excessive sneezing, nasal obstruction, itchy nose, and watery red itchy eyes. Many patients had multiple symptoms. No significant age, sex, or social class differences were found among those who had AR co-existing with asthma. The anthropometric measurements, including BMI, were also similar between those with AR and those without AR.

AR was mild in most of the asthmatics studied. Fewer patients had moderate-severe AR. This finding is consistent with those of earlier workers who documented mild AR to be more common than the other more severe forms. Asthma symptoms were well controlled in the majority of patients.

However, those with co-existing AR were significantly more likely to have poor control of asthma symptoms. Although many of the earlier reports on co-existence of AR with asthma did not examine the implications of AR on asthma control in children, a Netherlands study found a significant effect of AR on the degree of asthma control, similar to the finding of this study. Furthermore, there was significant association between severity of AR and level of asthma control. Those with moderate-severe AR were more likely to have poor asthma control. This study has thus gone a step further than the Netherlands study by exploring the severity of AR in the study subjects and the relationship between AR severity and level of asthma control. Since there are no comparative data on the co-existence of AR among asthmatic children in Africa, it is noteworthy that a similar study among adult asthmatics reported by Desalu et al¹⁵ in Ilorin (north-central Nigeria), where our study was also conducted, observed that as high as 63.9% of asthmatic adults had co-existing AR. However, the impact of AR on asthma control in the adult subjects studied was not examined. A retrospective study of patients aged 12–60 years with asthma co-existing with AR, reported a significantly lower risk of subsequent asthma-related events in those who were treated for AR compared with those who were not.¹⁶ It may thus be inferred that treatment of AR may improve the observed significant effect of AR on asthma control. There is however no documented randomised controlled trial on the effects of AR treatment on asthma control in children with asthma co-existing with AR and this is a possible direction for future research.

Although this study is hospital-based and the sample size is not large, it provides preliminary data to support the active search for AR in asthmatic children as a significant co-morbidity.

In conclusion, AR co-exists with asthma in a significant proportion of asthmatic patients, and the presence of AR is associated with poorer levels of asthma control. Recognition of AR in children with asthma and its appropriate treatment is likely to improve asthma control.

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Author declaration

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Level of asthma control	Asthma without AR n = 36 (%)	Asthma with AR n = 30 (%)	χ^2	p value
Well controlled	23	11	8.006	0.018
Partly controlled	9	7		
Uncontrolled	4	12		

Table 5: Relationship between co-existence of AR and level of asthma control

Level of asthma control	AR severity		χ_y^2	p value
	Mild n = 19 (%)	Moderate-severe n = 11 (%)		
Well controlled	10	1	9.245	0.010
Partly controlled	6	1		
Uncontrolled	3	9		

χ_y^2 : Yates corrected chi square.

Table 6 Relationship between AR severity and level of asthma control among asthmatic subjects with co-existing AR

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