Self-reported beta-lactam allergy: inpatients in government funded and privately funded hospitals Cape Town, South Africa

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March 31, 2022

Abstract

Background Up to a quarter of inpatients in high-income countries self-report beta-lactam allergy (BLA), which if incorrect, can increase use of alternative antibiotics that impact on bacterial resistance.. The epidemiology of BLA in low- and middle-income African countries is unknown. **Methods** Point-prevalence surveys were conducted at seven hospitals (adult, pediatric, government and private-funded, district- and tertiary-level) in Cape Town, South Africa between April 2019 and June 2021. Ward prescription records and interviews were conducted to identify BLA patients. De-labeling was attempted at the tertiary allergy clinic at Groote Schuur hospital. **Findings** A total of 1486 hospital inpatients were surveyed (1166 adults; 308 children). Only 48 (3.2%) patients self-reported a BLA with a higher rate amongst private- versus government-funded hospitals [6.3% vs 2.8%, p=0.014]. Using the PEN-FAST tool, only 10.4% (5/48) of self reported BLA patients were classified as high risk for true penicillin hypersensitivity. Antibiotics were prescribed to 70.8% (34/48) of self reported BLA patients, with 64.7% (22/34) receiving a beta-lactam. Despite three attempts to contact patients for de-labelling at the allergy clinic, only 3/36 underwent in vivo testing, with no positive results and one patient proceeded toa negative oral challenge. **Interpretation** Unlike high-income countries, self-reported BLA is low amongst inpatients in South Africa. The majority of self-reported BLA were low risk for type 1 hypersensitivity, but out-patient de-labeling efforts were largely unsuccessful. **Funding** None

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Dunge[2], T. Msimanga [2], A. Singh[2], O. Monnaruri [2], B. Molale[2], T. Butler [3], K. Browde[5], C. Muller [6], J. Van Der Walt[1], , R. Whitelaw [8], D. Cronwright[8], N. Parker [2], S. Sinha[2], U. Binase [2], I. Francis[8], D. Boakye [8], , S. Dlamini[7], M. Mendelson [7], J. Peter[1,6]

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Background

Up to a quarter of inpatients in high-income countries self-report beta-lactam allergy (BLA), which if incorrect, can increase use of alternative antibiotics that impact on bacterial resistance.. The epidemiology of BLA in low- and middle-income African countries is unknown.

Methods

Point-prevalence surveys were conducted at seven hospitals (adult, pediatric, government and private-funded, district- and tertiary-level) in Cape Town, South Africa between April 2019 and June 2021. Ward prescription records and interviews were conducted to identify BLA patients. De-labeling was attempted at the tertiary allergy clinic at Groote Schuur hospital.

Findings

A total of 1486 hospital inpatients were surveyed (1166 adults; 308 children). Only 48 (3.2%) patients self-reported a BLA with a higher rate amongst private- versus government-funded hospitals [6.3% vs 2.8%, p=0.014]. Using the PEN-FAST tool, only 10.4% (5/48) of self reported BLA patients were classified as high risk for true penicillin hypersensitivity. Antibiotics were prescribed to 70.8% (34/48) of self reported BLA patients, with 64.7% (22/34) receiving a beta-lactam. Despite three attempts to contact patients for de-labelling at the allergy clinic, only 3/36 underwent in vivo testing, with no positive results and one patient proceeded toa negative oral challenge.

Interpretation

Unlike high-income countries, self-reported BLA is low amongst inpatients in South Africa. The majority of self-reported BLA were low risk for type 1 hypersensitivity, but out-patient de-labeling efforts were largely unsuccessful.

Funding

None

Introduction

Beta-lactams are the commonest antibiotic class reported to cause allergy, yet globally, there is a large burden of patients mis-labeled as having a Beta-lactam allergy (BLA) (1). In high income countries (HICs) 6-25% of the population are labeled as having a BLA, but only 1-10% of the population have a true BLA. In keeping with this low prevalence rate, the prevalence of life-threating anaphylaxis to beta-lactams is estimated to be 0.02-0.04%, a rate unchanged in the last sixty years (1-3). While the epidemiology of BLA in HICs is well described, there is no published epidemiological data available on BLA in Africa or other low- and middle -income countries (LMIC)(4).

Being labeled with a BLA is harmful to patients, including the risk of antibiotic failure (1), increased duration of hospital stay (5), higher rates of post operative sepsis (6, 7), and adverse reactions to prescribed alternative antibiotics(1). In addition to increased patient risk there is an additional financial cost to the health care system with the increased cost of broad-spectrum antibiotics, longer duration of hospital admission, and higher rates of readmission (8, 9). Globally BLA drives antibiotic resistance (ABR) due to the increased use of broader-spectrum antibiotics than the penicillins. This results in increased risks of infection with vancomycin resistant enterococci (VRE) (5), methicillin resistant *Staphylococcus aureus* (MRSA) (10), and *Clostridiodes difficile* (1, 11). In 2019, 4.95 million people worldwide died with an antibiotic resistant bacterial infection, and 1.3 million of those were as a direct result of bacteria being resistant to antibiotics(12). The burden of ABR is highest in low-income countries (LIC) (4, 13, 14). Western-sub-Saharan Africa has the highest all-age death rate attributable to ABR (27.3 deaths per 100 000 [CI 20.9-35.3])(14). The high mortality due to ABR in sub-Saharan Africa makes de-labeling BLA a public health and antibiotic stewardship priority.

The success of programmatic antibiotic allergy testing incorporated into antibiotic stewardship programs has been increasingly reported with the use of clinical decision tools that can be used by allergists and non-allergists (15). Direct de-labeling of inpatients is safe and effective, with rates of negative testing being comparable to the outpatient setting(16). The need to establish the true prevalence and incidence of BLA in LMICs is paramount to improve our management of beta-lactam allergy in settings with the highest burden of infectious diseases (4).

Methods

We conducted a multicenter point prevalence survey of hospitalised patients. Between 4th of April 2019 and 14th of June 2021, a total of 1486 hospital inpatients were surveyed at five government-funded hospitals and two privately-funded hospitals in Cape Town South Africa. The government-funded hospitals included Groote Schuur Hospital (GSH, tertiary level), Red Cross Memorial Children's Hospital (RXH, paediatric tertiary level), and three secondary level Hospitals - Victoria Wynberg Hospital (VWH), New Somerset Hospital (NSH), and Mitchells Plain Hospital. The two privately-funded hospitals were Christiaan Barnard Memorial Hospital (CBH) and University of Cape Town Academic Hospital (UCTPAH) **(Figure 1, Table 1, see Appendix for descriptions of hospitals)** .

This study was approved by the Human Ethics Research Counsel of the University of Cape Town (UCT) (HREC: 417/2019) and the Netcare Research Operations Committee. The delay in conducting the final surveys was due to the COVID-19 pandemic, as six of the surveys were performed in between the second and third COVID-19 waves in South Africa.

Point prevalence surveys were conducted after-hours to ensure that all inpatient prescription chart were available for review. All hospital inpatients on the day of the survey had basic demographic information (date of birth and gender) captured via electronic case record form (eCRF) but detailed medical information was only captured for patients who reported a BLA or non-beta-lactam (BL) antibiotic allergy. Medical information included documentation of antibiotic allergies in the patients notes and prescription charts, description of the allergic event, and review of information on the antibiotic prescription chart. Classification of patients with a self-reported BLA was completed by an allergist after completion of all surveys using the PEN-FAST tool. The PEN-FAST BLA phenotype clinical decision tool (developed by Trubiano et al(15)) has a high negative predictive value of 96.3% (95% CI 94.1-97.8%) (15, 17). The major criteria for the PEN-FAST tool are: the allergy event occurring within the preceding five years (2 points); anaphylaxis,

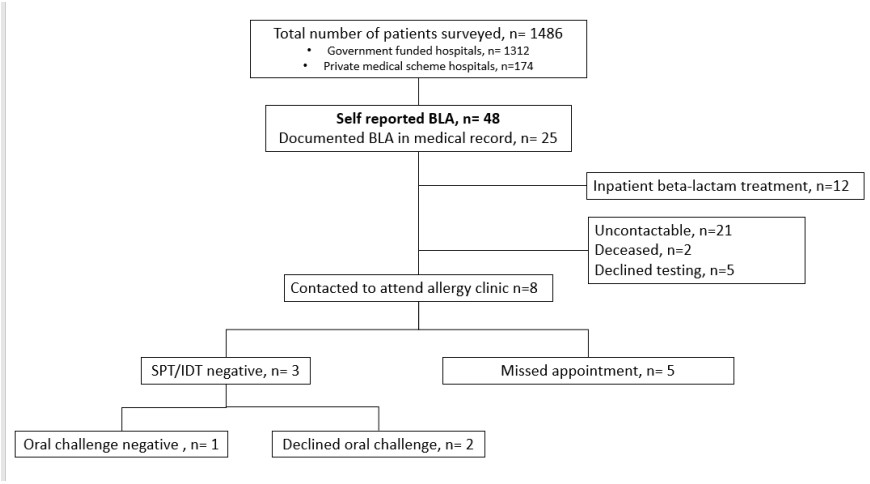
angioedema or severe cutaneous delayed reactions (2 points). A single minor criterion of whether the allergic reaction required treatment scores 1 point. The PEN-FAST tool has a validated area under the curve of 0.805 (for a cut-off of 3 points chosen to classify as low risk of penicillin allergy) (15). The novel PEN-FAST BLA clinical decision mobile app was used by investigators to classify patients as low risk (1-5%), moderate risk (20%), or high risk (50%) of a positive penicillin allergy test.

Descriptive statistics were performed using counts and proportions for categorical data, and medians and interquartile ranges for continuous variables. All statistical analyses were conducted using STATA version 14 (STATA Corp., College Station, TX, USA).

Results

A total of 1486 hospital inpatients (1166 adults [?]18 years and 320 children < 18 years) were surveyed in seven hospitals in Cape Town, South Africa during the study period **(Figure 1, Table 1, Table 2)** . Of these, 52.8% were female with a median age of 40 years (IQR 25;60). Overall, 48 (3.2%) patients self-reported a BLA with a significantly higher rate of self-reported BLA in the privately-funded hospitals as compared to the government-funded hospitals (2.8% vs 6.3% respectively, p=0.014). None of the facilities had 100% bed capacity at the time of the surveys (GSH=721/893 80.7%; RXH= 189/300 63%; VWH 107/206 51.9%; NSH 200/330 60.6%, MPDH 95/200 47.5%, CBH 129/248 52%, UCTPAH 45/124 36.3%), six of the seven surveys occurred between March 2021 and July 2021. The decreased bed occupancy in these facilities was likely due to the COVID-19 pandemic and decreased utilization of nonurgent clinical services.

Figure 1: Consort diagram



Abbreviations: BLA Beta-lactam allergy, IDT Intradermal testing, SPT skin prick testing

Table 1: Summary of all patients surveyed stratified by hospital funding-base

	All, n=1486	Government funded hospitals, n=1312	Privately funded hospitals
Bed capacity	2301	1929	372
Bed occupancy (%)	64	68	47*
Female	785 (52.8)	703 (53.6)	81 (47)
Age, IQR in yrs	40 (25; 60)	39 (24; 57)	16 (1; 58)
Unable to speak to patient/parent, (%)	303 (20.4)	264 (20.1)	40 (23)
BLA reported, (%)	48 (3.2)	37 (2.8)	11 (6.3)

*The low bed occupancy in these hospitals was the result of COVID19 restrictions at the time of the survey

Abbreviations: BLA: Beta lactam allergy, IQR: interquartile range

Table 2: Summary of all patients surveyed stratified by hospital funding-base and age group

Age	All, n=1486	Reported BLA	Government funded hospitals, n=1312	GSH, n=721	VWH, n=107	RXH
< 1 year	147 (9.9)	0	124 (9.5)	0	8 (7.5)	81 (4
1- 5 years	89 (6)	0	84 (6.4)	7 (1)	7 (6.5)	63 (3
6-11 years	43 (2.9)	0	39 (3)	5 (0.7)	0	34 (1
12-18 years	29 (2)	0	26 (2)	12 (1.7)	0	11 (5
> 18 years	1166 (78.5)	48 (3.2)	1027 (78.3)	685 (95)	92 (86)	0
Unknown	12 (0.8)	0	12 (0.9)	12 (1.7)	0	0

Abbreviations: BLA: Beta-lactam allergy; CBH: Christiaan Barnard Memorial Hospital; GSH: Groote Schuur Hospital; IQR: Interquartile range; MPDH: Mitchell's Plain District Hospital; NSH: New Somerset Hospital; UCTPAH: University of Cape Town Academic Hospital; VWH: Victoria Wynberg Hospital

Of the 48 self-reported BLA patients, 60.4% were female, and the median age was 59 years (IQR 37;68). There were no reported BLA under the age of 18 years (**Table 3** , **Supplement Table 2**). There were 12 patients (0.8%) that reported non-BL antibiotic allergies. The majority (n=35 [71%]) of participants reported that the allergic event had taken place more than ten years previously. Most (64.6% [n=31]) could recall the details of the allergic event, but 12.5% (n=6) of patients reported a BLA based on family history alone. In total 64.6% (n=31) patients were classified as low risk, 22.9% (n=11) as moderate risk, while only 10.4% (n=5) patients were classified as high risk for positive penicillin testing. Eight patients reported anaphylaxis and ten reported angioedema (six of whom had laryngeal angioedema). The most common reported symptoms were a mild/self-limiting skin rash in 25% (n=12) of patients. In total, 30 patients (62.5%) required treatment for the BLA but only 10 (20.8%) required adrenaline.

Table 3: Summary of self-reported beta-lactam antibiotic allergy stratified by hospital funding-base and age group

	All, n=48	Government funded hospitals, n=37	Privately funded hospitals, n=11
Female, (%)	29 (60.4)	22 (59.4)	8 (72.7)
Age, years (IQR)	59 (38; 68)	59 (38; 68)	58 (52; 63)
PENFAST, %			
Low risk	31 (64.6)	24 (64.9)	7 (63.6)
Moderate risk	11 (22.9)	8 (21.6)	3 (27.3)
High risk	5 (10.4)	4 (10.8)	1 (9)
Unknown	1 (2)	1 (2.7)	0
Questions from PENFAST			
Penicillin allergy reported	48 (100)	37 (100)	11 (100)
Five years or less since reaction	9 (18.8)	5 (13.5)	4 (36.3)
Anaphylaxis or angioedema	10 (20.8)	7 (18.9)	3 (27.2)
Severe cutaneous adverse reaction	7 (14.6)	6 (16.2)	1 (9)
Required treatment	30 (62.5)	24 (64.9)	6 (54.5)
Reaction >10 years	35 (72.9)	28 (75.7)	7 (63.6)

	All, n=48	Government funded hospitals, n=37	Privately funded hospitals, n=11
Patient can recall event	31 (64.6)	22 (59.5)	9 (81.8)
Family history only	6 (12.5)	4 (10.8)	2 (18.2)
Required adrenaline	10 (20.8)	8 (21.6)	2 (18.2)
Hospital admission and re-admission details			
Duration of admission, days (IQR)	6 (4; 15)	6 (4;15)	Unknown
Duration of admission not known	12 (24.5)	1 (2.6)	11 (100)
Number of re-admissions in following 6 months	0 (0;2)	0 (0;2)	Unknown

Abbreviations: IQR: interquartile range

A BLA was documented on 52.1% (n=25) of the inpatient prescription charts, with significantly higher rates of documentation in the privately-funded facilities (n=9, 81.8%) as compared to the government-funded facilities (n=16, 43.2%) (p=0.02) (**Table 4** ,**Supplement Table 3**). A total of 34 (71%) of the reported BLA patients were prescribed antibiotics, of which 22 (64.7%) still received a beta-lactam containing antibiotic: Beta-lactam / beta-lactamase inhibitor combination (amoxicillin-clavulanate or Piperacillin-tazobactam) n= 6; Aminopenicillin n=5; Cephalosporins n=9; Carbapenem n=2.

The 11 patients (32.4%) that were prescribed a beta-lactam / aminopenicillin, either alone or in combination with clavulanate, completed treatment with no subsequent allergic reaction. Seven of these patients who received a beta-lactam / aminopenicillin had no documentation of the reported BLA in the prescription charts or patient notes. Ten of these 11 patients were classified as low risk by PEN-FAST scoring; however one patient's risk was high with previous anaphylaxis and laryngeal angioedema. The remaining 14 (41.2%) patients were prescribed: Lincosamides n=5; Aminoglycosides n=3; Fluoroquinolones/ quinolones n=2; Macrolides n=2; and Nitroimidazole n=1.

Over a quarter of the patients were prescribed more than one antibiotic. As per antibiotic stewardship requirements 15 (44.1%) patients had the indication for the antibiotic documented on the antibiotic chart. The difference between the government funded and privately funded hospitals was not significant (p=0.1): n=10 [37%] in the government funded hospitals and n=5 [71.4%] in the privately funded hospitals. The most common indication for antibiotic therapy was pneumonia (n=4), followed by bloodstream infection (n=2), and finally gynecological/obstetric, urinary tract infection, and abdominal infection (n=1 respectively). In five patients the indication for an antibiotic was documented as "not defined".

Table 4: summary of antibiotic use in self-reported beta-lactam antibiotic allergy patients divided by government funded vs privately funded hospitals

	All, n=48	Government funded hospitals, n=37	Privately funded hospitals, n=11
BLA documented on antibiotic script, %	25 (52.1)	16 (43.2)	9 (81.8)
On antibiotic, %	34 (71)	27 (73)	7 (63.6)
Indication for antibiotics on script (% of patients on antibiotics)	15 (44.1)	10 (37)	5 (71.4)

	All, n=48	Government funded hospitals, n=37	Privately funded hospitals, n=11
Not defined	5 (33.3)	2 (20)	3 (60)
Pneumonia	4 (26.6)	3 (30)	1 (20)
Blood stream	2 (13.3)	2 (20)	0
Gynecological / obstetric	1 (6.7)	1 (10)	0
Abdominal infection	1 (6.7)	0	1 (20)
Urinary tract infection	1 (6.7)	1 (10)	0
Type of antibiotics, %			
Beta-lactam antibiotics	22 (64.7)		
Beta-lactam / beta-lactamase inhibitor (amoxicillin-clavulanate or Piperacillin-tazobactam)	6 (17.6)	4 (14.8)	2 (18.2)
Aminopenicillin	5 (14.7)	4 (14.8)	1 (14.2)
Carbapenam	2 (5.9)	1 (3.7)	1 (14.2)
Cephalosporin	9 (26.5)	8 (29.6)	1 (14.2)
Non beta-lactam antibiotics	14 (41.2		
Fluroquinalone / Quinalone	2 (5.9)	2 (7.4)	0
Glycopeptide	1 (2.9)	0	1 (14.2)
Lincosamide	5 (14.7)	2 (7.4)	3 (42.9)
Macrolide	2 (5.9)	2 (7.4)	0
Nitroimidazole	1 (2.9)	1 (3.7)	0
Aminoglycoside	3 (6.3)	2 (7.4)	(14.2)
Antibiotic Unknown, %	5 (14.7)	5 (18.5)	0
More than one antibiotic, %	9 (26.5)	5 (18.5)	4 (57.1)

Abbreviations: BLA: Beta lactam allergy

The median duration of admission for the government funded hospital patients was six days (IQR 4;15) with longer admission durations at GSH and MPDH as compared to NSH and VWH (**Table 3, Supplement Table 2**). There were 37 re-admissions to government-funded hospitals in the six months following hospitalization. Overall, 34 of these admissions occurred in seven patients (four patients had four readmissions, and three patients had three readmissions). The data for admission, length of stay, and readmission rates were not available for the privately-funded hospitals. A total of eight patients were contactable after discharge with 21 patients lost to follow up (not including two deaths and five patients that declined further investigation) (**Table 5**). However, only 3/8 patients returned to the GSH Allergy Clinic for evaluation, 5 patients missed clinic follow up and were subsequently not contactable. All three patients had negative epidermal testing but, two of these patients declined an oral challenge. Ultimately only one patient proceeded to direct oral challenge, which was negative.

Table 5: BLA de-labeling efforts at the tertiary Groote Schuur hospital allergy clinic

	All, n=48	Government funded, n=37	Privately fund
Uncontactable, %	21 (43.8)	16 (43.2)	5 (45.4)
Contacted but now living in a different province, %	5 (10.4)	5 (13.5)	0
Contacted and declined testing, %	5 (10.4)	3 (8.1)	2 (18.2)

	All, n=48	Government funded, n=37	Privately fund
Deceased, %	2 (4.2)	1 (2.7)	1 (9)
BL antibiotic given in ward, %	12 (25)	9 (24.3)	3 (27.2)
Intradermal testing and SPT negative, declined oral challenge, %	2 (4.2)	2 (2.7)	0
Intradermal testing and SPT negative, declined oral challenge, %	1 (2.1)	1 (2.7)	0

Abbreviations: BL: Beta lactam, SPT: skin prick testing

Discussion

Spurious BLA labels are dangerous to patients and pose a public health emergency in terms of health care costs and driving ABR. In what we believe to be the first publication on the epidemiology of reported BLA in Africa, we found that the prevalence of reported BLA in hospitalised patients was only 3.3%, a rate considerably lower than HIC rates. The self reported BLA rates were lower in government-funded hospitals than in the privately-funded hospitals. Sadly, very few participants in our study with a BLA label returned for allergy de-labeling.

The lowest rate of self-reported BLA from a HIC inpatient settings is 9.9% of 1738 patients enrolled over a one-year period in Montreal, Canada (9). Our study reports a rate less than half of this low-end rate. Furthermore, more than 80% of our small number of self-reported cases of BLA were considered low risk for true BLA, meaning that the prevalence of confirmed beta-lactam hypersensitivity may in fact be even lower in our South African population. There are several possible contributing factors that may explain both a lower rate of BLA label as well as a possible lower rate of true beta-lactam hypersensitivity in our population. Antibiotic prescribing patterns differ across the world, and involve a complex interplay of social, patient, provider, and economic factors(18). The majority of BLA labels are the result of viral or drug-related exanthems in childhood (2). But difficulties in accessing healthcare in South Africa (particularly in rural areas) resulting in less antibiotics being given(18), may limit the childhood exposure to BLA allergens and so contribute to less identification of true BLA in our setting.

Drug-related (and viral) exanthems, considered to be the predominant driver of incorrect BLA labels, are predominantly T-cell mediated, the majority of which are HLA-restricted. A recent genome-wide association study (GWAS) linked HLAB55:01 with penicillin allergy label. Interestingly, this allele has relatively low frequencies in Black African populations. This contrasts with another recent GWAS amongst confirmed cases of immediate hypersensitivity to beta-lactams, that identify HLA-DRB1*10:01 as a risk allele. HLA-DRB1*10:01 is carried twice as frequently in those of African ancestry (19). Other genetic studies in European populations with confirmed beta-lactam hypersensitivity have linked polymorphisms in cytokine genes (TNFA, IL-13, IL-4, IL4R)(20), which are also likely to be population-specific. Thus, it is possible that genetically African populations may have similar or higher risk for true immediate beta-lactam hypersensitivity, but less likelihood of mild delayed reactions, the major drivers of incorrect BLA labeling in childhood. Finally, skin colour may impact the detection of maculopapular exanthems in those with Fitzpatrick skin type IV, V and VI (Lehloenya North American clinics accepted for publication), as erythema and fine rashes are harder to detect in pigmented skin. Taken together, there may be several genetic, and biological factors that explain self reported BLA prevalence in in African populations.

BLA labels were significantly more common in patients attending private compared to (government funded) hospitals. South Africa is the most inequitable country in Africa with a GINI coefficient of 0.63 in 2015, an inequality reflected in its public versus private healthcare. Race and socioeconomic status are a major factor(21-23). The population utilizing privately funded health care sector in South Africa more closely resembles that of a HIC in that the predominant racial group is white (European ancestry)(22) with a higher income. The population that accesses government-funded health care has a high percentage of black African, Indian, or mixed race patients. Thus, the difference in BLA rates between government and private hospital inpatients may reflect both differences in access to healthcare in childhood with different levels of antibiotic

exposure, as well as genetic and skin pigment biological factors related to populations of origin. Further qualitative and basic science research is required to understand these differences.

Using the PEN-FAST tool, most patients with BLA label in our study were considered low risk for true type 1 hypersensitivity to beta-lactams. However, despite several attempts to contact and assist patients to attend our tertiary allergy clinic at GSH, only 1 patient could complete direct oral challenge for de-labeling. Multiple factors play into this failure, including: patient-perceived lack of importance of carrying a BLA label, fear of the testing and procedures or the time involved, changes in contact details and a mobile patient population, or even lack of resources to return for clinic visits (18, 22, 24). This inability to have patients return and attend allergy clinics or elective procedures has been highlighted, even in HICs, and undoubtedly aggravated across the world by the COVID-19 pandemic (25). In paediatric patients recommendations now exclude the use of SPT as a possible barrier to care and with concerns regarding increased false positive test rates(26). This data supports that the only viable option for BLA de-labeling in LMICs will be direct de-labelling or challenges in low-risk patients by non-allergists at the bedside. The development, validation and implementation of risk-stratification tools will be critical to this effort. A comprehensive framework for incorporation of BLA de-labeling in LMIC/LIC has been recently outlined (4).

The inclusion of several hospitals across different levels of the health system, and inclusion of private and government-funded hospitals, improved the generalizability of this data. However, the fact that the study was only performed in one city of SA is a limitation. The COVID-19 pandemic meant that there was a several month gap between the initial survey at GSH in April 2019 and the other surveys in the study, as well as limiting bed occupancy at the time of surveys in several hospitals, which may have impacted results. The lack of reported BLA in patients under 18 years is likely due to the low bed occupancy rates the high percentage of paediatric patients under the age of one year in the cohort, likely limits the generalisability of paediatric data.

In conclusion, this study provides the first data on the epidemiology of BLA in Africa and demonstrates that the overall prevalence of BLA is much lower than that reported in HICs. Furthermore, there is disparity of our results across health sectors, which highlights several of the complex social and biological determinants of both true and incorrectly labeled BLA. The inability to confirm BLA in the majority of cases through skin testing and direct oral challenge in the allergy clinic highlights the challenges of incorporating BLA de-labeling strategies in antibiotic stewardship programs in LMICs, and demands a different solution than HICs, by shifting the site of testing to the bedside. Epidemiology data from other LMIC is required to confirm our findings and help LMIC policy makers decide on the importance of targeting BLA de-labeling in local antibiotic stewardship efforts. Affordable strategies for direct de-labeling or inpatient challenge are supported by this data.

Conflict of Interest

None

Funding

None

Contributions

J. Peter, M. Mendelson, and S. Dlamini devised proposal and protocol. C. Day organized hospital surveys, and analysed data. C Day and J. Peter wrote and edited the manuscript. M. Deetlefs conducted all allergy testing. M. Boyd assisted with data cleaning and A.O'Brien assisted with communication with the survey team. All authors conducted the point prevalence surveys and reviewed the manuscript.

Conducted one survey : J. Peter, M. Mendelson, S. Dlamini, A. Geragotellis, Z. Parker , W. Amanjee, C. Joseph , Z. Zhao, S. Moosa, M. Bunting, Y. Pulani, P. Mukhari, M. de Paiva, G. Deyi, R. Peigou Wonkam, N. Mancotywa, A. Dunge, , T. Msimanga, A. Singh, O. Monnaruri, B. Molale, T. Butler, K. Browde, C.

Muller, M. Evreva, J. Van Der Walt, R. Whitelaw, D. Cronwright, N. Parker, S. Sinha, U. Binase, I. Francis, D. Boakye, S. Wasserman.

Conducted two surveys : A. Budge, T. Tarwa, O. Jim, T. Maharaj, S.Pandy, A. Panieri, S. Verhage, M. van der Merwe, M. Deetlefs.

Conducted three surveys: N. Embling, S. Patel, K. Moody, T. Ramabele.

Conducted four surveys: A. O'Brien, J Smith.

Conducted six surveys: C. Day

Dedication:

In memory of Tokoloho (Tuks) Ramabele.

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