Therapeutic Challenges of Multidrug Resistant *Acinetobacter baumannii* in Eastern Africa: Systematic Review

Alene Geteneh^{1*}, Assalif Demissew², Alemale Adimas³, Derbie Alemu⁴ and Lencho Girma⁵

¹ Department of Medical Laboratory Sciences, College of Health Sciences, Woldia University, Woldia, Ethiopia

² Department of Medical Laboratory Sciences, College of Medicine and Health Sciences, Ambo University, Ambo, Ethiopia.

³ Department of Medical Laboratory Sciences, College of Medicine and Health Sciences, Bahir Dar University, Bahir Dar, Ethiopia.

⁴ Department of Medical Laboratory Sciences, College of Health Sciences, Arbaminch College of health sciences, Arbaminch, Ethiopia.

⁵ Department of Medical Laboratory Sciences, College of Health Sciences, Mizan Aman College of health science, Mizan Aman, Ethiopia.

*Corresponding author: Alene Geteneh; aleneget@gmail.com

Abstract

Acinetobacter baumannii, an opportunistic gram negative bacterium, is known to emerge as a major health threat in Eastern Africa. Clinical isolates exhibit resistance to carbapenems and most or all available antibiotics. This review is intended to present concerns about resistance and therapeutic challenges of multi drug resistance *Acinetobacter baumannii* in Eastern Africa. Data was obtained from PubMed and Google scholar, and from free goggle access and web Medline for facts about *Acinetobacter baumannii* and its resistance pattern. Moreover, Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flow chart was used to guide the selection of study materials. Total of 98 articles identified, 13 fit the criteria and were included for the final analysis. In East Africa the overall prevalence of *Acinetobacter baumannii* was 4.95%, while the overall rate of multi drug resistance, carbapenem and pan resistance was 87.3%, 64.8% and 25.2% respectively. Colistin resurges as potential therapeutic options to overcome the lack of new antibiotic treatment of *Acinetobacter baumannii*. There needs a collaborative effort in researches targeted for *Acinetobacter baumannii* treatment and respond for call of “Research and Development of new antibiotics” to control its damning impact.

Key words: *Acinetobacter baumannii*, Eastern Africa, Multidrug resistance *Acinetobacter baumannii*

INTRODUCTION

Acinetobacter baumannii is an opportunistic bacterial pathogen primarily associated with hospital-acquired infections. Genus *Acinetobacter* is a strictly aerobic, non-fastidious, non-motile, oxidase-negative, non-lactose fermenter, catalase positive, gram-negative coccobacilli that is found as ubiquitous saprophytes (1-3). Unlike *Acinetobacter baumannii*, *A. lwoffii* and *A. haemolyticus* are non-glucose oxidizing species in this genus with less common role in disease causation (4). While, *A. baumannii* takes the lions share because of its increasing involvement in a number of severe infections and outbreaks occurring in clinical settings with an intrinsic or acquired resistance to multiple classes of antibiotics(5, 6).

Acinetobacter baumannii has come to light as a major threat to the global health, with a rapid expansion of resistance to carbapenems and most or all available antibiotics (7, 8).

The growth of resistance to at least one agent in three or more classes of antibiotics (aminoglycosides, carbapenems, cephalosporins, beta-lactams/beta-lactamase inhibitor, quinolones etc.) defined the development of multidrug-resistant *Acinetobacter baumannii* (MRAB) traits (9-12). This notable success is granted by its strange capacity to develop or acquire antibiotic resistance determinants and by its ability to adapt and survive for long periods in the hospital environment (13, 14).

Acinetobacter baumannii appears well apt for genetic exchange and are among a unique class of gram-negative bacteria that are described as “naturally transformable”(15, 16). Antibiotic resistance in *A. baumannii* is due to enzymatic degradation, modification of targets, and active efflux of drugs collectively with formation of biofilms (16, 17). Although outbreaks are typically clonal, horizontal-gene transfer has an important role in broadcasting of antibiotic resistance to *A. baumannii* and pass on *bla*_{NDM} gene to other *Enterobacteriaceae* (18-20).

Although, there is no organized data in developing countries who administered broad spectrum antibiotics empirically and had limited facility for isolation and susceptibility testing of bacteria for patient care, there could have high distribution of MRAB even resistant to carbapenems. *Acinetobacter baumannii*, being resistant for multiple antibiotics also results in high case-fatality rate 38% in Kenya(21) and 32% in South Africa(22)) due to an overwhelming systemic infection and lack of treatment options(23).

Updated realization is very essential for the prevention of MRAB infections and to cope up with therapeutic challenges, thus we had included 13 recent articles of East Africa (published from 2013-2017, from Uganda, Tanzania, Sudan and Ethiopia). The objectives of this review were to consolidate existing data about the resistance and therapeutic challenges of MRAB, and to show its burden in Eastern Africa.

METHODOLOGY

Here in this update we have searched for articles using mesh terms like *Acinetobacter baumannii*, multidrug resistant *Acinetobacter baumannii*, “ (*Acinetobacter baumannii*) AND multidrug resistant AND Uganda” (multidrug [All Fields] AND resistant [All Fields]) AND (“*Acinetobacter baumannii*” [MeSH Terms] OR (“*Acinetobacter*” [All Fields] AND “*baumannii*” [All Fields]) OR “*Acinetobacter baumannii*” [All Fields]) AND (“Uganda” [MeSH Terms] OR “Uganda” [All Fields]) AND (“2013/01/01” [PubDate]: “2017/12/31” [PubDate]) , (multidrug [All Fields] AND resistant [All Fields]) AND (“*Acinetobacter baumannii*” [MeSH Terms] OR (“*Acinetobacter*” [All Fields] AND “*baumannii*” [All Fields]) OR “*Acinetobacter baumannii*” [All Fields])) AND (“Ethiopia” [MeSH Terms] OR “Ethiopia” [All Fields]) AND (“2013/01/01” [PubDate]: “2017/12/31” [PubDate]) and similarly for other East African countries from PubMed, and Google scholar, free goggle access and web Medline for facts about *Acinetobacter*

baumannii and its resistance pattern. Moreover, PRISMA flow chart was used to guide the selection of study materials.

Selection criteria

Any sort of article who mentioned the prevalence of *Acinetobacter baumannii*, described patterns of resistance for commonly used antibiotics (resistance to multiple antibiotic including carbapenem and colistin) and being in an Eastern African region were included.

Inclusion (Eligibility) and exclusion criteria

In this review we have been looking for studies (both prospective and retrospective), not more than 5 years and study theme similar to the review questions were included, and studies done on non-clinical samples, review articles, articles without pdf access and papers describing isolates outside Eastern Africa were excluded.

Data extraction

Data extraction was done manually using Microsoft Excel 2010. Information extracted included article information (country, year of publication, number of participants enrolled, number of participants positive for *A. baumannii*), study design (sample size and types of specimens used), and antimicrobial resistance data.

Data analysis

Based on the review questions sought, we compile data on Microsoft excel 2010 and transported to STATA for use to calculate proportion, ratio and mean resistance to highlight the pattern of antibiotic resistance among isolates in eastern Africa context.

Figure 1: PRISMA Diagram of the article selection procedure for articles published from 2013 -2017

* Preferred Reporting Items for Systematic Reviews and Meta-Analysis

RESULTS

Of the 98 articles identified, 13 fit the criteria and were included for the final analysis (Fig.1). Majority of the articles were from Uganda (5) and Ethiopia (4). As shown in the table the overall prevalence of *A. baumannii* was 4.95 % [95% CI; 0.8 -9%], while the overall proportional rate of MDR, carbapenem and pan resistance was 87.3% [95%CI; 78.2-96.5%], 64.8% [95% CI; 27.7-100%] and 25.2% [95% CI; 7.3- 43%] respectively.

Table 1: Summary of selected articles in Eastern Africa for multi-drug resistance *Acinetobacter baumannii* (2013-2017)

	Study design	Country	Year of publication	Patients enrolled	Patients positive	No. of MDRAB	CRAB	Pan resistance	Reference

					for AB				
1.	Cross-sectional	Ethiopia	2013	322	7	4	0	0	(24)
2.	Cross-sectional	Uganda	2013	314	52	52	2	2	(25)
3.	Cross-sectional	Tanzania	2014	100	15	15	6	0	(26)
4.	Cross-sectional	Tanzania	2015	469	6	0	0	0	(27)
5.	Cross-sectional	Sudan	2015	2899	275	253	244	102	(28)
6.	Cross-sectional	Uganda	2016	869	29	18	9	0	(29)
7.	Cross-sectional	Ethiopia	2016	107	23	22	19	8	(30)
8.	Cross-sectional	Uganda	2017	111	11	7	7	1	(31)
9.	Cross-sectional	Uganda	2017	736	7	7	1	0	(32)
10.	Cross-sectional	Tanzania	2017	575	5	1	0	0	(33)
11.	Cohort	Uganda	2017	1786	11	10	0	0	(34)
12.	Cross-sectional	Ethiopia	2017	224	14	8	8	2	(23)
13.	Cross-sectional	Ethiopia	2017	712	2	2	0	0	(35)
	Total			9224	457	399	296	115	

The average number of patients included were 710 (ranging from a minimum of 100 to a maximum of 2899), of them nearly 5% of patients enrolled were positive for *Acinetobacter baumannii*. On other hand, the mean proportional rate of resistance for multiple antibiotics was so high, provide 87.3% (nearly 31 out of 36) (Table 2).

Table 2: Overall mean estimate of *Acinetobacter baumannii* in East Africa (2013-2017)

Review questions	Mean	Std. Err.	[95% Conf. Interval]
Patients enrolled	709.5385	222.022	225.7941 1193.283
Patients positive for AB	35.15385	20.3274	-9.135752 79.44344

No of MDRAB	30.69231	18.90983	-10.50868	71.8933
CRAB	22.76923	18.50023	-17.5393	63.07776
Pan resistance	8.846154	7.787108	-8.120497	25.8128

* AB: *Acinetobacter Baumannii*; MDRAB: Multidrug resistant AB

Considering Eastern Africa as one sample population at a snapshot of review period, we tried to see ups and downs in incidence, and resistance for multiple antibiotics, carbapenems and all available treatments options as well. Therefore, the overall positivity rate in patients screened for *Acinetobacter Baumannii* was shown to decrease from 2013 to 2017 (Figure 2).

The amalgamated prevalence and pan-resistance rate downs to nullity, while the resistance rate for multiple drugs was relatively stable during 2016 to 2017(Figure 2). There were variation in state of decrement in prevalence, proportional rate of MRAB, CRAB and pan-resistance according to an individual country data of Ethiopia and Uganda (Figure 3 and figure 4).

Figure 2: Overall prevalence of AB, MDRAB, CRAB and pan resistance with year of publication

* AB: *Acinetobacter Baumannii*; MDRAB: Multidrug resistant AB; CRAB: Carbapenem resistance

All of the isolates in the revision were only from clinical specimens such as blood, urine, wound swabs, sputum, tracheal swabs and CSF etc., to show its detectability with culture (all the articles use culture for isolation).

Figure 3: Prevalence and proportional rate of resistance in isolates in Ethiopia, 2013-2017

Figure 4: *Acinetobacter baumannii* isolates incidence rate and proportional rate of resistance in Uganda, 2013- 2017

DISCUSSION

Multidrug-resistant *Acinetobacter baumannii* infections posed a serious health trouble all over the world (36, 37). Even though, the overall prevalence (4.95%) was not considerably high, our review assured that resistance to multiple antibiotics was also a great concern for Eastern Africa (87.3%). Similarly carbapenem-resistant *Acinetobacter baumannii* (CRAB) were found the most important group of actors in the ongoing antibiotic resistance crisis, i.e. proportionally 64.8% were resistant to carbapenems. This incidence is nearly comparable with a study finding in Egypt (70%) (38).

World health organization (WHO) has prioritized *Acinetobacter baumannii* as a “critical” pathogen for Research and Development of new antibiotics; and old antibiotics such as

fosfomycin and polymyxins was got considerations as potential treatment options to prevail over the lack of new antibiotics (13, 39-41). This was true for East African countries, because proportionally 87.3% of the isolates want to be treated with carbapenems, but the pragmatic concern is 64.8% of them were resistant for these drugs putting its user-friendliness into consideration.

Our findings were higher as compared to study of India, which was 42.3% and 6.7% carbapenem and pan resistance respectively (42). Similarly, extensively drug resistant(resistance to at least one agent in all but two or fewer antimicrobial classes (12)(XDR)) phenotypes exhibited via carbapenem resistance were nearly equivalent to Pakistan (65.6%), but higher prevalence of MDR (96.7%)(43), relative to this review (87.3%). This difference might due to variability in socio-demography, specimen used and drug resistance pattern was checked from the already isolated strains, not from direct patient samples of Pakistan and India.

Generally, there has been a relative decrement from 2013-2017 in prevalence, resistance to multiple antibiotics, resistance to carbapenem and pan resistance as shown in figure 2. But, the progress of those MRAB strains to XDR phenotypes is the other worrying issue. In our case scenario, 74.2% MDRA isolates were XDR phenotypes, exhibited by carbapenem resistance (13) making the deal particularly challengeable for clinicians. The growing incidence of XDRAB infections, therefore quests for salvage therapy with colistin, amikacin, or tigecycline.

The specific country based data has also shown the proportional decrement in prevalence of *A. baumannii* in Uganda from 2013, 2016 and 2017(16.56%, 3.34% and 1.1% respectively), while in Ethiopia fluctuated incidence have occurred (2.17%, 21.5% and 1.7%) with respected years of publications. Similarly the proportional rate of resistance to carbapenem and pan drugs seems to decline in both Ethiopia and Uganda with time, as shown in figures 3 and 4.

Overall , the possible justification for reduction in prevalence and resistance in Eastern Africa may be due to research limitation to figure out the real burden in study areas, or the articles included with low number of study subjects may not represent the actual situation in the area, or use of strategies that may restrict broad spectrum antibiotics administration, the raise in awareness about multidrug resistance, delivery of guidelines to an international level, presentation of strategies in health care facilities and involvement of communities, and implementation of comprehensive control plans.

On the other hand, the average figure (4.95%) seems to represent a small prevalence, but the high multidrug-resistance pattern poses difficult therapeutic challenges. For example, the mortality rate due to this super-bug was much higher in South Africa (44.6%) (44), Kenya (38%) (21), although the articles which we analyzed did not specify *A. baumannii* related deaths. Those patients infected with carbapenem resistant strains have a 35.2% proportional chance of cure with these honored drugs and seeks for easily inaccessible drug colistin and resistant to 25.2% of those who had the chance in the poor nations of Eastern Africa.

The surgical site infections due *A. baumannii* in Ethiopia shown that 34.8% of the isolates were pan-resistant, unable to treat with locally available treatment options leading for unnoticed death (30). Similarly, 16.3% of isolates from the operation theatre and delivery rooms were responsible for untreatable infections to patients attending hospitals of Ethiopia (45). Whereas, in Uganda 55% of hospital environment isolates were resistant for carbapenem looking for the unavailable and 25.2% proportionally resistant drug, colistin (29).

Inappropriate empiric treatment administration results in resistance to multiple antibiotics and this has been associated with 2 to 4 fold increased risk of mortality (10). The high (87.3%) MDR proportion with other comorbidities and short handiness to better treatment options may let for a

considerable death in Eastern Africa that we may not noticed. *A. baumannii* infections was known to be nosocomial, but recently there were reports of high prevalence community acquired infections, exemplified by the high prevalence of *A. baumannii* among head and body lice of Ethiopia (46), and community acquired blood stream infections of Tanzania (27).

CONCLUSION AND RECOMMENDATIONS

A considerably rising rates of MDR as well as XDR *A. baumannii* has distributed throughout the study countries, assuring its major threat to the health of eastern Africa. Old antibiotics such as colistin resurge as potential therapeutic options to overcome the lack of new antibiotics, but the simultaneous emergence of colistin-resistant strains initiate necessity of new advances for control. Which in turn, quest researchers to respond to the call for “Research and Development of new antibiotics” to this super-bug.

Declarations

The authors declare that there is no conflict of interest regarding the publication of this paper.

REFERENCES

1. Gokmen TG, Akcimen B, Kayar B, Marzi M, Koksai F. The outbreak of *Acinetobacter baumannii* producing OXA-23 and OXA-51 type carbapenemases in a state hospital. *Journal of Experimental and Clinical Medicine*. 2016;33(3):157-61.
2. Hall GS. *Bailey & Scott's Diagnostic Microbiology*, 13th Edn. American Society for Clinical Pathology; 2015.
3. Murray PR, Rosenthal KS, Pfaller MA. *Medical microbiology*: Elsevier Health Sciences; 2015.
4. Longo F, Vuotto C, Donelli G. Biofilm formation in *Acinetobacter baumannii*. *New Microbiologica*. 2014;37(2):119-27.
5. Shoja S, Moosavian M, Rostami S, Farahani A, Peymani A, Ahmadi K, et al. Dissemination of carbapenem-resistant *Acinetobacter baumannii* in patients with burn injuries. *Journal of the Chinese Medical Association*. 2017;80(4):245-52.
6. Potron A, Poirel L, Nordmann P. Emerging broad-spectrum resistance in *Pseudomonas aeruginosa* and *Acinetobacter baumannii*: mechanisms and epidemiology. *International journal of antimicrobial agents*. 2015;45(6):568-85.
7. Zarrilli R, Pournaras S, Giannouli M, Tsakris A. Global evolution of multidrug-resistant *Acinetobacter baumannii* clonal lineages. *International journal of antimicrobial agents*. 2013;41(1):11-9.
8. Antunes L, Visca P, Towner K. *Acinetobacter baumannii*: evolution of a global pathogen. *Pathogens and disease*. 2014;71(3):292-301.

9. Logan LK, Gandra S, Trett A, Weinstein RA, Laxminarayan R. *Acinetobacter baumannii* Resistance Trends in Children in the United States, 1999–2012. *Journal of the Pediatric Infectious Diseases Society*. 2018.
10. Zilberberg M, Nathanson B, Sulham K, Fan W, Shorr A. D24 GRAM NEGATIVE PNEUMONIAS: FROM BENCH TO BEDSIDE: Multidrug Resistance In *Acinetobacter Baumannii* Pneumonia And Sepsis Increases The Risk Of Receiving Inappropriate Empiric Treatment. *American Journal of Respiratory and Critical Care Medicine*. 2016;193:1.
11. Kalin G, Alp E, Akin A, Coskun R, Doganay M. Comparison of colistin and colistin/sulbactam for the treatment of multidrug resistant *Acinetobacter baumannii* ventilator-associated pneumonia. *Infection*. 2014;42(1):37-42.
12. Magiorakos AP SA, Carey RB, Carmeli Y, Falagas ME, Giske CG, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. *Clinical microbiology and infection*. 2012;18(3):268-81.
13. Rossolini GM, Arena F, Pecile P, Pollini S. Update on the antibiotic resistance crisis. *Current opinion in pharmacology*. 2014;18:56-60.
14. Dent L, Marshall D. Multi-Drug Resistant *Acinetobacter baumannii*. 2016.
15. Wilharm G, Piesker J, Laue M, Skiebe E. DNA Uptake by the Nosocomial Pathogen *Acinetobacter baumannii* Occurs during Movement along Wet Surfaces. *Journal of bacteriology*. 2013;195(18):4146-53.
16. Yoon E-J, Chabane YN, Goussard S, Sniesrud E, Courvalin P, Dé E, et al. Contribution of resistance-nodulation-cell division efflux systems to antibiotic resistance and biofilm formation in *Acinetobacter baumannii*. *MBio*. 2015;6(2):e00309-15.

17. Blair JM, Webber MA, Baylay AJ, Ogbolu DO, Piddock LJ. Molecular mechanisms of antibiotic resistance. *Nature Reviews Microbiology*. 2015;13(1):42.
18. Adler A, Glick R, Lifshitz Z, Carmeli Y. Does *Acinetobacter baumannii* Serve as a Source for bla NDM Dissemination into Enterobacteriaceae in Hospitalized Patients? *Microbial Drug Resistance*. 2018;24(2):150-3.
19. Leylabadlo HE, Asgharzadeh M, Aghazadeh M. Dissemination of carbapenemases producing Gram negative bacteria in the Middle East. *Iranian journal of microbiology*. 2015;7(5):226.
20. Azizi O, Shakibaie MR, Badmasti F, Modarresi F, Ramazanzadeh R, Mansouri S, et al. Class 1 integrons in non-clonal multidrug-resistant *Acinetobacter baumannii* from Iran, description of the new blaIMP-55 allele in In1243. *Journal of medical microbiology*. 2016;65(9):928-36.
21. Talbert AW, Mwaniki M, Mwarumba S, Newton CR, Berkley JA. Invasive bacterial infections in neonates and young infants born outside hospital admitted to a rural hospital in Kenya. *The Pediatric infectious disease journal*. 2010;29(10):945.
22. Thomas R, Wadula J, Seetharam S, Velaphi S. Prevalence, antimicrobial susceptibility profiles and case fatality rates of *Acinetobacter Baumannii* sepsis in a neonatal unit. *The Journal of Infection in Developing Countries*. 2018;12(04):211-9.
23. Pritsch M, Zeynudin A, Messerer M, Baumer S, Liegl G, Schubert S, et al. First report on bla NDM-1-producing *Acinetobacter baumannii* in three clinical isolates from Ethiopia. *BMC infectious diseases*. 2017;17(1):180.
24. Godebo G, Kibru G, Tassew H. Multidrug-resistant bacterial isolates in infected wounds at Jimma University Specialized Hospital, Ethiopia. *Annals of clinical microbiology and antimicrobials*. 2013;12(1):17.

25. Seni J, Najjuka CF, Kateete DP, Makobore P, Joloba ML, Kajumbula H, et al. Antimicrobial resistance in hospitalized surgical patients: a silently emerging public health concern in Uganda. *BMC research notes*. 2013;6(1):298.
26. Manyahi J, Matee MI, Majigo M, Moyo S, Mshana SE, Lyamuya EF. Predominance of multi-drug resistant bacterial pathogens causing surgical site infections in Muhimbili National Hospital, Tanzania. *BMC research notes*. 2014;7(1):500.
27. Onken A, Said AK, Jørstad M, Jenum PA, Blomberg B. Prevalence and antimicrobial resistance of microbes causing bloodstream infections in Unguja, Zanzibar. *PloS one*. 2015;10(12):e0145632.
28. Omer MI, Gumaa SA, Hassan AA, Idris KH, Ali OA, Osman MM, et al. Prevalence and Resistance Profile of *Acinetobacter baumannii* Clinical Isolates from a Private Hospital in Khartoum, Sudan. *American Journal of Microbiological Research*. 2015;3(2):76-9.
29. Kateete DP, Nakanjako R, Namugenyi J, Erume J, Joloba ML, Najjuka CF. Carbapenem resistant *Pseudomonas aeruginosa* and *Acinetobacter baumannii* at Mulago Hospital in Kampala, Uganda (2007–2009). *SpringerPlus*. 2016;5(1):1308.
30. Dessie W, Mulugeta G, Fentaw S, Mihret A, Hassen M, Abebe E. Pattern of bacterial pathogens and their susceptibility isolated from surgical site infections at selected referral hospitals, Addis Ababa, Ethiopia. *International journal of microbiology*. 2016;2016.
31. Agaba P, Tumukunde J, Tindimwebwa J, Kwizera A. Nosocomial bacterial infections and their antimicrobial susceptibility patterns among patients in Ugandan intensive care units: a cross sectional study. *BMC research notes*. 2017;10(1):349.

32. Kateete DP, Nakanjako R, Okee M, Joloba ML, Najjuka CF. Genotypic diversity among multidrug resistant *Pseudomonas aeruginosa* and *Acinetobacter* species at Mulago Hospital in Kampala, Uganda. *BMC research notes*. 2017;10(1):284.
33. Kumburu HH, Sonda T, Mmbaga BT, Alifrangis M, Lund O, Kibiki G, et al. Patterns of infections, aetiological agents and antimicrobial resistance at a tertiary care hospital in northern Tanzania. *Tropical Medicine & International Health*. 2017;22(4):454-64.
34. Bebell LM, Ngonzi J, Bazira J, Fajardo Y, Boatn AA, Siedner MJ, et al. Antimicrobial-resistant infections among postpartum women at a Ugandan referral hospital. *PloS one*. 2017;12(4):e0175456.
35. Bitew A, Molalign T, Chanie M. Species distribution and antibiotic susceptibility profile of bacterial uropathogens among patients complaining urinary tract infections. *BMC infectious diseases*. 2017;17(1):654.
36. Falagas ME, Vardakas KZ, Kapaskelis A, Triarides NA, Roussos NS. Tetracyclines for multidrug-resistant *Acinetobacter baumannii* infections. *International journal of antimicrobial agents*. 2015;45(5):455-60.
37. Thandar M, Lood R, Winer BY, Deutsch DR, Euler CW, Fischetti VA. Novel engineered peptides of a phage lysin as effective antimicrobials against multidrug resistant *Acinetobacter baumannii*. *Antimicrobial agents and chemotherapy*. 2016:AAC. 02972-15.
38. Al-Agamy MH, Khalaf NG, Tawfick MM, Shibl AM, El Kholy A. Molecular characterization of carbapenem-insensitive *Acinetobacter baumannii* in Egypt. *International Journal of Infectious Diseases*. 2014;22:49-54.
39. Stein RA. Mugs of the bugs: The most wanted ones. *International Journal of Clinical Practice*. 2017.

40. Ventola CL. The antibiotic resistance crisis: part 1: causes and threats. *Pharmacy and Therapeutics*. 2015;40(4):277.
41. Medina E, Pieper DH. Tackling Threats and Future Problems of Multidrug-Resistant Bacteria. *How to Overcome the Antibiotic Crisis: Facts, Challenges, Technologies and Future Perspectives*. 2016;398:3-33.
42. Basireddy S, Ali S, Singh M, Kabra V. Pan resistant *Acinetobacter baumannii* in a tertiary care hospital. *Journal of The Academy of Clinical Microbiologists*. 2015;17(1):58.
43. Hasan B, Perveen K, Olsen B, Zahra R. Emergence of carbapenem-resistant *Acinetobacter baumannii* in hospitals in Pakistan. *Journal of medical microbiology*. 2014;63(1):50-5.
44. Bahemia I, Muganza A, Moore R, Sahid F, Menezes C. Microbiology and antibiotic resistance in severe burns patients: A 5 year review in an adult burns unit. *Burns: journal of the International Society for Burn Injuries*. 2015;41(7):1536-42.
45. Solomon FB, Wadilo F, Tufa EG, Mitiku M. Extended spectrum and metallo beta-lactamase producing airborne *Pseudomonas aeruginosa* and *Acinetobacter baumannii* in restricted settings of a referral hospital: a neglected condition. *Antimicrobial Resistance & Infection Control*. 2017;6(1):106.
46. Kempf M, Abdissa A, Diatta G, Trape J-F, Angelakis E, Mediannikov O, et al. Detection of *Acinetobacter baumannii* in human head and body lice from Ethiopia and identification of new genotypes. *International Journal of Infectious Diseases*. 2012;16(9):e680-e3.

PRISMA Flow Diagram

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit www.prisma-statement.org.