

Analysis of *Acinetobacter baumannii* hospital infections in patients treated at the intensive care unit of the University Hospital, Wroclaw, Poland: a 6-year, single-center, retrospective study

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Background: *Acinetobacter baumannii* (AB) is one of the most frequently isolated strains of bacteria in intensive care unit (ICU) patients, which provides huge therapeutic problems due to its multidrug resistance (MDR).

Patients and methods: The overall purpose of the study was analysis of health care-associated infections in terms of the incidence of AB strain infections and the changing susceptibility of this strain within a 6-year observation (2011–2016). The study was carried out in an ICU of the University Hospital in Wroclaw (Poland).

Results: Among 589 isolated strains responsible for 540 health care-associated infections (21.2%) in 2549 ICU patients, AB was the pathogen in 183 (31%) cases. The incidence of AB infection amounted to 6.4/1000 patient-days. An increase was noted in the total number of hospital infections caused by AB strain from 16.5% and 3.39/1000 patient-days in 2011 to 41% and 9.64/1000 in 2016 ($p=0.0003$ and $p=0.000$, respectively). AB infections most frequently concerned ventilator-associated pneumonia (73.8%). AB was susceptible to colistin, amikacin, imipenem, meropenem, and ciprofloxacin in 100%, 10.7%, 12.3%, 11.5%, and 2.4% respectively, and it was characterized by MDR in 98.36% of the strains.

Conclusion: The study revealed a 3-fold increase in the incidence of AB strain infections, significant increase in the resistance to carbapenems in the observed period, and a very high MDR. The solution to this problem would be the implementation of a repair program aiming at inhibition of AB strain transmission, measures to prevent infections, and restricted use of antibiotics.

Keywords: *Acinetobacter baumannii*, hospital infections, multiresistance

Introduction

Acinetobacter genus belongs to the Moraxellaceae family and includes 41 genospecies.¹ In the clinical aspect, the most important one is *Acinetobacter baumannii* (AB), an-aerobic, pleomorphic, gram-negative coccus–bacillus. Due to its extraordinary ability to exogenous colonization of human body (throat, gastrointestinal tract, skin) and a high tolerance of difficult conditions (survivability in the environment up to 1 month), it has a great potential for spreading among hospitalized patients.² Despite the regional difference in the incidence and resistance, the role

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of *Acinetobacter* spp. has increased significantly in human infections over the last two decades.^{3,4} Additionally, its multidrug resistance (MDR) and tendency for epidemic spreading have been observed.^{5,6} AB strain infections are the most common cases among intensive care unit (ICU) patients with respiratory, urinary, blood, and surgical site infections.⁵ Severe infections of MDR AB are associated with high mortality rate up to 70% in the case of ventilation-associated pneumonia (VAP) and 43% in the case of blood infection.⁷⁻⁹ Detailed analyses of risk factors for AB infection, methods of prevention of transmission and suppression of the epidemic outbreaks, as well as therapeutic proposals due to AB MDR have been the subject of numerous publications, indicating the importance of the problem.^{10,11} The purpose of this study was to analyze health care-associated infections (HAIs) in terms of the incidence of AB strain infections and the changing susceptibility of this strain within a 6-year observation.

Patients and methods

Setting

The study covered 2549 patients treated in the 20-bed ICU of the University Hospital in Wroclaw from 01.01.2011 to 31.12.2016. This retrospective study was approved by the Bioethics Committee of Wroclaw Medical University. The patients' written consent to review their medical records was not required by the Ethics Committee of Wroclaw Medical University since microbiological monitoring is a routine practice in our hospital and a statement covering patients' data confidentiality was fully respected during manuscript preparation.

Data collection

The analysis was conducted with the use of data on pathogens of hospital infections. Data on clinical form of the infection and microbiological data concerning HAIs pathogen susceptibility were obtained from individual hospital infection registration cards and the electronic hospital databases. The study also included data collected for epidemiological purposes concerning patient-days of hospitalization.

The supervision process of hospital infections was carried out routinely by departmental infection control team (physician, microbiologist, and two nurses) and the Hospital Committee for Infection Control. Hospital infections were diagnosed based on the definitions adopted by the Centers for Disease Control and Prevention/International Nosocomial Control Consortium in patients hospitalized >48 hours.^{12,13}

Microbiological diagnostics methods and definitions

Microbiological diagnostics of infections were carried out in the Microbiological Laboratory of the University Hospital in Wroclaw. For the diagnosis of VAP, the protective and quantitative methods of mini-bronchoalveolar lavage or bronchoalveolar lavage were used. The significant value for the diagnosis of VAP was $>10^4$ colony-forming units (CFU)/mL. Urinary tract infection (UTI) was diagnosed in the case of presence in the urine one pathogen $\geq 10^3$ CFU/mL or no more than two pathogens $<10^5$ CFU/mL and pyuria. The significant value for the diagnosis of central line associated bloodstream infection (CLA-BSI) was >15 CFU in semi-quantitative method or $>10^3$ CFU/mL in quantitative method from the tip of vascular catheter and positive blood culture.¹³ Identification of gram-positive and gram-negative bacteria was carried out with the use of specific biochemical tests and by applying automatic method (gram-negative and gram-positive card) in the Vitek 2 automatic system, according to Good Laboratory Practice principles. Susceptibility of microorganisms was determined as well as interpretation of the results was done with the use of disk diffusion method on Muller Hinton (BioRad, Berkley, CA, USA) substrate, automatic method (AST-N332 card) in the Vitek 2 system and by using strips with antibiotic concentration gradient E-test (bioMerieux, Paris, France) for minimum inhibitory concentration assessment. All techniques were conducted in accordance with the applicable recommendations of the European Committee on Antimicrobial Susceptibility Testing.¹⁴ MDR of the AB strain was defined as resistance of the strain to at least three groups of antibiotics.⁴

Calculation of incidence of the hospital infections with AB etiology

Incidence of AB hospital infections in the given period of time was calculated by dividing the number of AB infections by the number of patient-days in the given period of time and multiplying it by 1000.

Statistical analysis

Statistical analyses were performed using SPSS 13.0 for Windows NT software package (SPSS Inc., Chicago, IL, USA). Descriptive statistics were computed for all study variables. Discrete variables are expressed as counts (percentage). Data were analyzed using chi-square, chi-square with Yates correction, and Fisher's exact tests, as appropriate. $p < 0.05$ was considered as statistically significant.

Ethical approval

Approval for this study was given by the Ethics Committee of the Wroclaw Medical University (Wroclaw, Poland). Institutional Ethics Committee consent included approval for publication of the data.

Results

Among 2549 patients treated in the ICU during 28,532 patient-days of hospitalization, hospital infections (n=540) were diagnosed in 21.2% cases. In patients with VAP, CLA-BSI, and UTI, 314 (12.3%), 85 (3.3%), 190 (7.45%) strains (bacterial and fungal) had been identified, respectively. Among the total number of 589 cultured strains responsible for HAIs, gram-negative microorganisms (n=430) were dominant and they constituted 73%, while gram-positive bacteria and fungi constituted 20.5% and 6.4%, respectively. AB strains (n=183) were responsible for 31% of HAIs and these were the most frequently isolated pathogens among gram-negative bacilli (42.6%). AB was the pathogen found to be most frequently responsible for VAP (53.3%) and UTI (32.2%), whereas it was identified in 14.4% cases for CLA-BSI.

In the study period, an increase in the total number of AB hospital infections from 16.5% to 41% ($p=0.0003$) was observed. The details concerning these data are presented in Figure 1. The incidence of AB infections in 2016 was higher than in 2011 (26.6% vs. 54%; $p=0.0005$). Detailed analysis of HAIs pathogens and the incidence of AB infections in the context of gram-negative bacterial infections are presented in Table 1.

On evaluation of the number of infections with AB/1000 patient-days, a significant increase in the incidence AB infections from 3.39/1000 to 9.64/1000 ($p=0.0000$) was also observed. Detailed analysis of the incidence of AB infections is presented in Table 2.

As for AB infections, VAP (135 [73.8%]) was the most frequent, while the incidence of UTI (40 [21.9%]) and CLA-BSI (8 [4.37%]) was substantially lower. The share of AB strain in the individual clinical forms of hospital infections (VAP, UTI, CLA-BSI) is presented in Figure 2.

While comparing the susceptibility of AB data from 2011 to 2016, a statistically significant increase in the resistance was found in the case of imipenem ($p=0.0016$) and meropenem ($p=0.0016$). Juxtaposition of the sus-

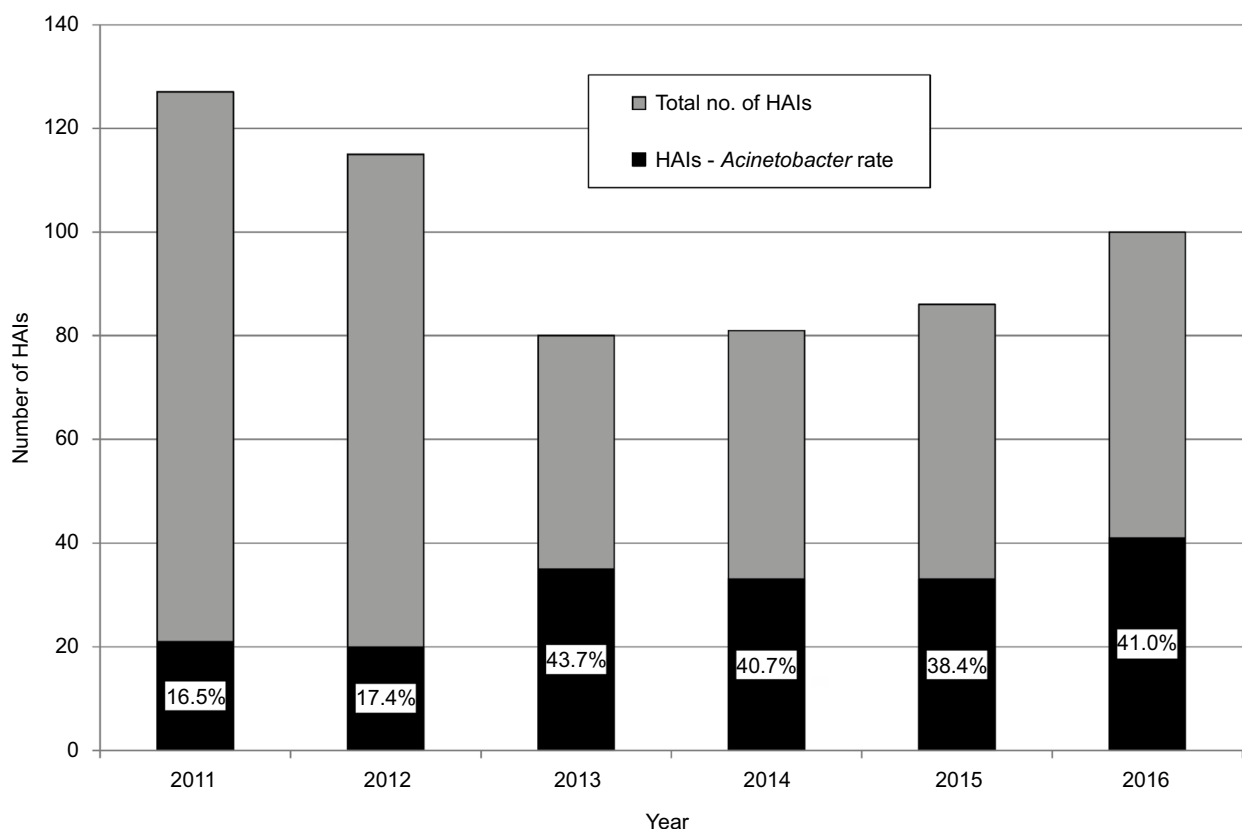


Figure 1 Percentage of *Acinetobacter baumannii* infections (HAIs – *Acinetobacter*) among the total number of HAIs.
Abbreviation: HAIs, health care-associated infections.

Table 1 Etiological analysis of health care-associated infections and the percentage of *Acinetobacter baumannii* infections among gram-negative bacterial infections

	Year						p-value
	2011	2012	2013	2014	2015	2016	
G(-), n (%)	79 (62.2)	82 (71.3)	57 (71.25)	68 (83.9)	68 (79.1)	76 (76)	0.0266
<i>Acinetobacter baumannii</i> , n (%)	21 (26.6)	20 (24.4)	35 (61.4)	33 (48.5)	33 (48.5)	41 (54)	0.0005 0.0000*
G(+), n (%)	39 (30.7)	31 (27)	10 (12.5)	9 (11.1)	13 (15.1)	19 (19.0)	0.0246
Fungi, n (%)	9 (7.1)	2 (1.75)	13 (16.25)	4 (4.9)	5 (5.8)	5 (5.0)	0.7107

Notes: Data are presented as number and percentage value. p-value was calculated for the years 2011 vs. 2016. *p-value for the years 2011 vs. 2013.

Table 2 Incidence of *Acinetobacter baumannii* HAIs per 1000 patient-days

	Year						Sum or mean	p-value
	2011	2012	2013	2014	2015	2016		
No. of HAIs	21	20	35	33	33	41	183	
No. of patient-days	6162	5327	4445	4234	4143	4251	28,562	
No. of HAIs/1000 patient-days	3.39	3.75	7.87	7.79	7.96	9.64	6.4	0.0000 0.0017*

Notes: p was calculated for the correlation of data 2011 vs. 2016. *p-value for 2011 vs. 2013.

Abbreviation: HAIs, health care-associated infections.

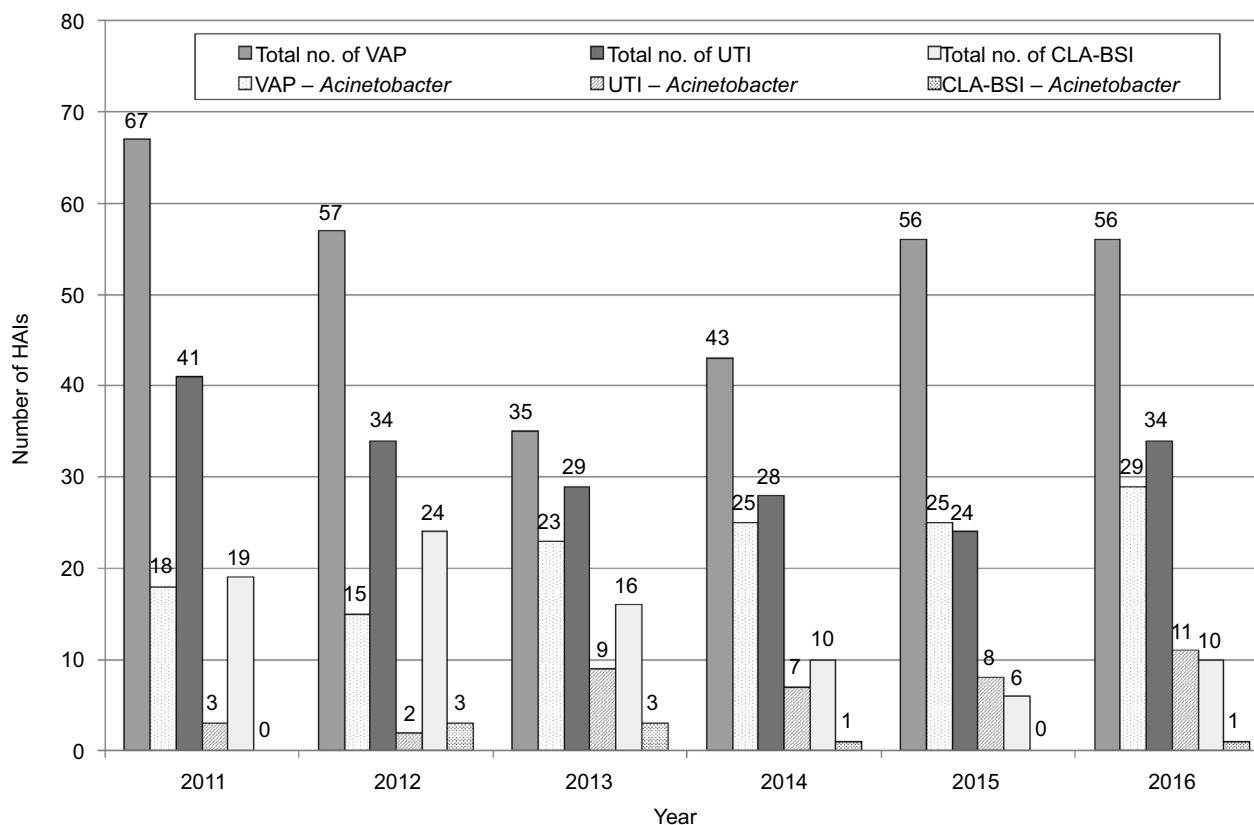


Figure 2 Analysis of the share of *Acinetobacter baumannii* strain in hospital infections.

Note: The number of *A. baumannii* infections among the total number of VAP, UTI, and CLA-BSI.

Abbreviations: CLA-BSI, central line associated bloodstream infection; UTI, urinary tract infection; VAP, ventilator associated pneumonia.

ceptibility of AB strain in regard to selected antibiotics and chemotherapeutics (colistin, amikacin, gentamicin, imipenem, meropenem, ciprofloxacin) is presented in Table 3.

In the period 2013–2015, all the AB strains were MDR, whereas in 2011, 2012, and 2014, the rate of MDR was 20/21, 19/20, and 40/41 strains, respectively. Globally, MDR was found in 98.36% of AB strains.

Table 3 Percentage of the susceptibility of *Acinetobacter baumannii* strain to selected antibiotics

Strains/antibiotics	Year						p-value
	2011	2012	2013	2014	2015	2016	
No. of strains	21	20	35	33	33	41	
Colistin (n/%)	21/100	20/100	35/100	33/100	33/100	41/100	
Amikacin	4/19	3/15	2/6	1/3	3/9	5/12	0.3563
Gentamicin	5/24	3/15	2/6	0/0	4/12	5/12	0.1352
Imipenem	9/43	3/15	2/6	0/0	1/3	3/7	0.0016
Meropenem	9/43	2/10	2/6	0/0	1/3	3/7	0.0016
Ciprofloxacin	1/5	1/5	0/0	0/0	0/0	2/5	0.737
Trimetoprim/sulfametoksazol	1/5	1/5	0/0	1/3	0/0	3/7	0.5829

Notes: Data are presented as the number of susceptible strains and % of susceptibility. p-value was calculated for the correlation of data 2011 vs. 2016.

Discussion

This study showed that starting from 2013, the AB strain has constituted a serious epidemiological problem in the local hospital. Compared to the data published from the same center, AB constituted 17% in 1995 and 9% in 2000, while in the years 2007–2010, its role in the pathogenesis of HAIs (25%) has been considered as significant.¹⁵ The average incidence of AB infections in our study (31%) was slightly lower than in the ICU of other Polish university hospital (38.3%)¹⁶ and higher than it was reported in another Polish ICU (18.6%).¹⁷ In the European Prevalence of Infection in Intensive Care study, it was determined that the most common pathogens of infections in the ICUs were Enterobacteriaceae (34.4%), while AB was responsible for 9% of all infections.¹⁸ Also, in the Sepsis Occurrence in Acutely Ill Patients study and the Extended Study on Prevalence of Infection in Intensive Care (European Prevalence of Infection in Intensive Care II), the incidence of AB infections was lower (3.6% and 8.8%, respectively) than in our study.^{19,20} Moreover, there are published reports of a large variation in the incidence of AB infections in various geographic regions (3.7% in North America, up to 19.2% in Asia, 17.1% in Eastern Europe).²⁰ The incidence of AB infections in the ICU patients in countries such as Italy (66.7%) and Spain (63.9%) was higher compared to that in our study.^{6,21} Our data indicate that, in the stage of the greatest increase in the incidence of infections, a lower incidence of infections/1000 patient-days has occurred, compared to the studies from Taiwan and Italy. This incidence averaged 12.15/1000 in the preintervention period in the study from Taiwan²² and 147/10,000 in the study from Italy, which may indicate the diagnosed epidemiological outbreak.²³ The incidence of HAIs with AB etiology in our study was higher compared to another Polish study, where AB caused pneumonia in 23.09%, UTI in 6% and blood infections in 5.06% of the patients.¹⁷ In another Polish study, AB

was slightly less frequently responsible than in our study for pneumonia (41.6%) and for UTI (25%), while it was responsible more often for CLA-BSI (25%).¹⁶ The incidence of VAP with AB etiology in the period 2011–2012 was found to be similar to that reported in a Brazilian study (29.2%).²⁴ The incidence of AB VAP and UTI from 2016 was higher in our study than in a Greek study (VAP [28%] and UTI [6.4%]).²⁵

Our study showed a very high percentage of MDR of the AB strain (98.36%), which is significantly higher than the percentage of *Acinetobacter* MDR reported in Poland (2015), based on data from the European Antimicrobial Resistance Surveillance Network, which amounted to 54.6%.²⁶ Similarly, the MDR of AB strain in our study was higher than in the 5-year study from Greece (2010–2014), where the percentage of AB MDR amounted to 92.89%.²⁷ Additionally, the percentage of AB MDR strain infections in our study was higher than in 2014 in France (1.5%), Germany (2.1%), Sweden (2.8%), Spain (56.4%), Greece (86.9%), Italy (86.9%), and the USA (43.7%–69.1%).^{26,28} Analysis of the European Antimicrobial Resistance Surveillance Network data from Poland (2012–2015) shows an increase in the resistance of AB to fluoroquinolones (from 78% to 88.1%), to aminoglycosides (from 63.4% to 70.2%), and to carbapenems (from 38.3% to 65.6%).²⁶ Tendency for increase in the resistance is consistent with the results of our studies, but the percentage of strains resistant to the groups of drugs listed in our study is higher. Interestingly, in our study from 2016, the susceptibility of AB strain to fluoroquinolones was significantly lower than in Germany (94%), Spain (33.9%), and the USA (28%) and similar to the susceptibility reported in Greece (4.7%) and Italy (7.8%).^{26,29} Apparently, a similar pattern was found in relation to the susceptibility to aminoglycosides, as the percentage of susceptible strains in our study was lower than that reported in Germany (95.9%), Spain (40%), and the USA (39%) and similar to the relevant percentage reported

in Greece (12.4%) and Italy (10.9%).²⁶ Susceptibility to carbapenems in our study was similar to the susceptibility reported in Greece (6.8%), whereas it is significantly lower than that reported in Germany (94.5%), Spain (34.6%), and the USA (44%).^{26,29} Reports coordinated by the International Nosocomial Control Consortium and covering 50 developing countries have shown higher resistance of AB strain to imipenem or meropenem (85.6%–90.2%)³⁰ when compared to our results. Although most of the published data demonstrate disturbing results of AB strain resistance to colistin either in ICUs (3.4%) or in surgical wards (5.3%),^{6,27} such a phenomenon was not found in our study throughout the period of observation.

Limitations

However, the study has numerous limitations. First, it is a one-center study, so both the incidence and susceptibility of AB strain in Poland can be different. Second, in the context of methodological assumption, the analysis was carried out on the basis of hospital infections only, which could be the reason for such a high percentage of AB MDR strains. Third, the results may have been affected by heterogeneity of the patient group in the individual years, severity of the disease, and the methods used for the prevention of infections and spreading of MDR strains. Fourth, a small number of studies showed an epidemiologically significant incidence of infection with *Acinetobacter* spp. in relation to the patient-days of hospitalization, which did not allow us to carry out a broader comparative analysis. Finally, despite the fact that we have used well-recognized standards of microbiological diagnostics, the new methods of microbiological diagnostics, such as matrix-assisted laser desorption ionization time of flight mass spectrometry or polymerase chain reaction, are not routinely used in our center; so, molecular analysis technologies are not taken under consideration in this study. Data from this study demonstrate the urgent need to implement the repair program through searching for the infection sources and transmission mechanisms, hand hygiene control, environmental decontamination, prevention of transmission, and restrictive use of antibiotics in our center.

Conclusion

The study showed a triple increase in the incidence of AB strain infections, significant increase in the resistance to carbapenems in the observed period, and a very high MDR. The solution to this problem would consist of implementation of a repair program aiming at inhibition of AB strain transmission, measures to prevent infections, and restricted use of antibiotics.

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Author contributions

WD conceived the study protocol. WD and AL coordinated the study. AL, AS, SR, and AC participated in data collection. WD, AL, AS, SR, and AC carried out the literature search. WD and AL drafted this manuscript. All authors contributed toward data analysis, drafting and critically revising the paper and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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