Multivariate Analysis of Klebsiella pneumoniae Antimicrobial Resistance Phenotypes Isolated from Different Clinical Specimens at Mila Hospital, Algeria

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ABSTRACT

Aims There are few data regarding the prevalence and trends of *Klebsiella pneumoniae* antibiotic resistance in Algeria. The present study was conducted to investigate the spatial distribution of K. pneumoniae antibiotic resistance phenotypes in time and according to specimen source.
Materials & Methods This retrospective study was performed between January 2011 and December 2015 at Mila Hospital, Algeria. A total of 172 *K. pneumoniae* were isolated from consulting and hospitalized patients, and their antimicrobial susceptibility was tested. The Principal Component Analysis (PCA) was used to study correlations among antimicrobial resistance phenotypes observed, and Factorial Correspondence Analysis (FCA) was used to study the spatial distribution of antibiotic resistance phenotypes according to specimen source.
Findings The specimens were obtained from urine (n=89), vagina (n=39), pus (n=33), blood (n=9) and surgery (n=2). PCA showed two principals associations of resistance phenotypes gathered in two clusters. The first profile regroups amoxicillin-clavulanic acid, cefazolin and ampicillin. The second assembles cefotaxime, nalidixic acid and sulfamethoxazole-trimethoprim. In FCA, nalidixic acid was connected with urine specimens, registering maximum resistance (52.8%) compared to the other samples. Vagina specimens were associated to sulfamethoxazole-trimethoprim and colistin phenotypes registering maximum resistances with 89.7 and 76.9%, respectively. Pus manifested a near association to cefotaxime with a maximum resistance (48.5%).
Conclusion The model developed in FCA, highlights typical associations of antibiotic resistance phenotypes to specimen source and confirms the difference in resistance profile according the source of specimen in *K. pneumoniae* infections.

Keywords *Klebsiella pneumoniae*; Antibiotic Resistance; Clinical Specimens; Multivariate analysis; Algeria

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[1] Virulence profiles and antibiotic susceptibility patterns of Klebsiella pneumoniae strains isolated from different ... [2] Complete nucleotide sequence of klebsiella pneumoniae multidrug resistance ... [3] Prevalent phenotypes and antibiotic resistance in Escherichia coli and Klebsiella pneumoniae at ... [4] Comparative genomics of Klebsiella pneumoniae strains with different antibiotic ... [5] Antimicrobial susceptibility of urinary Klebsiella pneumoniae and the emergence of carbapenem-resistant ... [6] Molecular characterization of clinical multidrug-resistant ... [7] Isolation of human pathogenic bacteria causing urinary ... [8] Antimicrobial resistance of Klebsiella pneumoniae in a Saudi Arabian hospital: Results of a 6-year ... [9] Use of multivariate analysis to compare antimicrobial agents on the basis of in vitro activity ... [10] Antibiogram Committee of the French Society ... [11] TEM & SHV genes in extended spectrum ... [12] Resistance to β-lactam ... [13] Molecular epidemiology and resistance mechanisms ... [14] Norwegian Study Group on Aminoglycoside Resistance. Increased prevalence ... [15] Resistance determinants and mobile enetic elements of an NDM-1-encoding ... [16] In vivo emergence of colistin resistance in Klebsiella pneumoniae ... [17] Epidemiological study of Klebsiella spp. uropathogenic strains producing extended-spectrum ... [18] Resistance to fluoroquinolone among Klebsiella spp. strains producing ... [19] Aerobic vaginal pathogens and their sensitivity ... [20] Prevalence of Klebsiella pneumoniae strains producing carbapenemases ... [21] Antimicrobial sensitivity pattern of Klebsiella pneumoniae isolated from pus from tertiary care hospital and issues related to ... [22] 3rd Generation cephalosporin resistance in Klebsiella pneumoniae from pus ... [23] Molecular epidemiology and risk factors of bloodstream infections caused ... [24] Cefotaxime resistance and outcome of Klebsiella spp. bloodstream ... [25] A comparison of principle component analysis and factor ...

Introduction

Klebsiella pneumonia, a member of Enterobacteriaceae family, is a Gram-negative, nonmotile and facultative anaerobic bacillus. It inhabits different environments, e.g. soil, water, plant and the mammalian nasopharynx and gastrointestinal tract, as a commensal occupant. At present, *K. pneumoniae* is considered as one of the principal opportunistic pathogens involved in nosocomial and community infections, specifically among immune-compromised individuals, rising hospital settings associated to antibiotics use [1]. *K. pneumoniae* is characterized by a typical thick polysaccharide coat, which helps it to escape from host defenses. The close genetic association within the Enterobacteriaceae species makes the transmission of plasmids and insertion elements possible, which are frequently the support of horizontal genetic exchange of antibiotic resistance genes. In addition, some important diversity and recombination events were demonstrated in *K. pneumoniae* multidrug resistance plasmids [2].

Drug resistance dissemination among pathogenic bacteria is expanded by antibiotic resistance genes carried on bacterial plasmids. By acquisition of new antibiotic catalytic genes, mutations of antibiotic targets and membrane proteins, and differential expression of specific genes as those for efflux pumps, the clinical isolates of *K. pneumoniae* are equipped with the large amount of mechanisms of antibiotic resistance among Gram-negative bacteria. Commonly, resistance of *K. pneumoniae* with Extended-Spectrum Beta-Lactamases (ESBL) is linked to other antimicrobials, as well as aminoglycosides, fluoroquinolones, trimethoprim, and sulfamethoxazoles [3-5]. The horizontal transfer of antimicrobial resistance genes is largely conducted by mobile genetic elements such as integrons. ESBLs encoding genes, plasmid mediated quinolone resistance (PMQR) genes and exogenously acquired 16S rRNA methyltransferase (16S-RMTase) genes are usually implicated in multidrug resistance to frequently used antimicrobial agents. In recent years, *K. pneumoniae* carbapenemases (KPC) resistance determinants coding carbapenem-hydrolyzing β-lactamases (CHβLs) appear among *K. pneumoniae* isolates [6].

The alarming pattern of antimicrobial resistance observed in many parts of the world becomes a major public health problem because of the inappropriate use of antibiotics, causing treatment failure of infections, augments the medical charges and the mortality and morbidity levels [6, 7]. The geographical update and adaptation of epidemiological records are the basis of the empirical antibiotic therapy. The regional surveillance of antibiotic resistance patterns is fundamental to establish appropriate infection control actions in order to operate with adapted and rational strategy guide for antibiotic use. These measures improve the efficacy of evaluation procedures for the detection of new points to monitor the bacterial resistance [5, 8].

The multivariate analysis by principal component analysis (PCA) and factor analysis (FA) allows the synchronized analyses of correlations between several variables. The multivariate techniques reveal components or factors and determine associations among antimicrobial agents and their contributions in the building of each factor. The application of multivariate analysis in the methodology of data processing enlarges knowledge on the interrelationships among the different classes of antimicrobial agents [9]. Despite the importance of these mathematical tools, the use of multivariate analysis in the study of antibiotics and correlations between antimicrobial resistance phenotypes is still missed in the literature, especially for *K. pneumoniae* clinical isolates.

In Algeria, the data on the prevalence of *K. pneumoniae* antibiotic resistance is missing. At the present time, antimicrobial surveillance in Algeria was restricted to a small number of hospitals and presented the resistance pattern of little number of isolates. In addition, although *K. pneumoniae* antibiotic resistance pattern is well developed in many parts of the world, the multivariate analysis of its resistance phenotypes, especially according to specimen nature, is undertaken. The majority of the data treated solitary one or two types of clinical specimens especially from urinary and blood samples infected by *K. pneumoniae*. For these reasons, our goal was to evaluate the prevalence and modes of *K. pneumoniae* antimicrobial resistance at Mila hospital, Algeria, using Principal Component Analysis and Factorial Correspondence Analysis methods.

Materials and Methods

In this retrospective study that was performed between January 2011 and December 2015, a total of 172 *K. pneumoniae* samples (one per patient) were isolated in the Laboratory of Microbiology at Mila Hospital (Meghlaoui Brothers) from consulting and hospitalized patients. The specimens were obtained from urine (n=89), vagina (n=39), pus (n=33), blood (n=9) and from general surgical patients (n=2). The hospital is affiliated to the Ministry of Public Health and Population with 152 beds, situated in the small city of Mila in the North East of Algeria and covering predominantly rural population.

The susceptibility to antibiotics (AMP: ampicillin; AMC: amoxicillin-clavulanic acid; CZ: cefazolin;

CTX: cefotaxime; AN: amikacin; NA: nalidixic acid; SXT: trimethoprim-sulfamethoxazole and CS: colistin) was tested using the diffusion method on Mueller-Hinton agar, with respect to the Antibiogram Committee of the French Society for Microbiology guidelines [10].

The multivariate analyses were conducted with XLSTAT 2014 software. The Principal Component Analysis (PCA) was used to study correlations between the whole of observed antibiotic resistance phenotypes. The matrix of correlation was calculated according to Pearson coefficient. Factorial Correspondence Analysis (FCA) was used to study antibiotic resistance phenotypes distributions according to the nature of specimens.

Findings

The most resisted antibiotics in all isolates from different sources were AMP (94.8%) and AMC (88.4%) and the least resisted were CTX (31.4%) and AN (33.1%; Table 1).

Table 1) Antibiotic resistance (AMP: ampicillin; AMC: amoxicillin-clavulanic acid; CTX: cefotaxime; CZ: cefazolin; AN: amikacin; NA: nalidixic acid; SXT: trimethoprim-sulfamethoxazole; CS: colistin) of 172 *Klebsiella pneumoniae* isolates from different clinical specimens at Mila Hospital in Algeria (Data values are numbers of isolates resistant to the specified antibiotic and the numbers in parentheses are percentages of resistant isolates)

Source	AMP	AMC	CZ	CTX	AN	NA	SXT	CS
Urine (n=89)	86 (96.6)	85 (95.5)	74 (83.1)	31 (34.4)	16 (18.0)	47 (52.8)	51 (57.3)	33 (37.1)
Vagina (n=39)	35 (89.7)	32 (82.1)	23 (59.0)	7 (17.9)	20 (51.3)	15 (38.5)	35 (89.7)	30 (76.9)
Pus (n=33)	33 (100)	27 (81.8)	25 (75.8)	16 (48.5)	15 (45.5)	14 (42.4)	20 (60.6)	16 (48.5)
Blood (n=9)	7 (77. 8)	6 (66. 7)	9 (100)	0 (0)	5 (55. 6)	1 (11.1)	0 (0)	3 (33.3)
Surgery (n=2)	2 (100)	2 (100)	2 (100)	0 (0)	1 (50)	0 (0)	1 (50)	1 (50)
Total (n=172)	163 (94.8)	152 (88.4)	133 (77.3)	54 (31.4)	57 (33.1)	77 (44.8)	107 (62.2)	83 (48.3)

Table 2) Pearson product-moment correlations between 8 tested antibiotics (AMP: ampicillin; AMC: amoxicillin-clavulanic acid; CTX: cefotaxime; CZ: cefazolin; AN: amikacin; NA: nalidixic acid; SXT: trimethoprim-sulfamethoxazole; CS: colistin) for *K. pneumoniae* antibiotic resistance

Antibiotics	AMP	AMC	CTX	CZ	AN	NA	SXT
AMP	1						
AMC	0.881	1					
CTX	-0.593	-0.648	1				
CZ	0.902	0.946	-0.474	1			
AN	-0.728	-0.365	0.242	-0.403	1		
NA	-0.477	-0.738	0.633	-0.714	-0.239	1	
SXT	0.039	-0.311	0.411	-0.010	-0.263	0.239	1
CS	-0.095	0.262	0.361	0.244	0.422	-0.230	-0.418

P.value for all of correlation coefficients is <0.05

AMC showed the strongest correlation (r=0.979) with the first principal component (PC1), while AN produced the most important correlation (r=0.794) with the second principal component (PC2). The first and the second principal components contribute with 75.85% in the antibiotic resistance variation (Table 2).

Two principal clusters (named A and B) were observed in PCA model by gathering antibiotic resistance phenotypes manifesting similar spatial distribution (Figure 1).

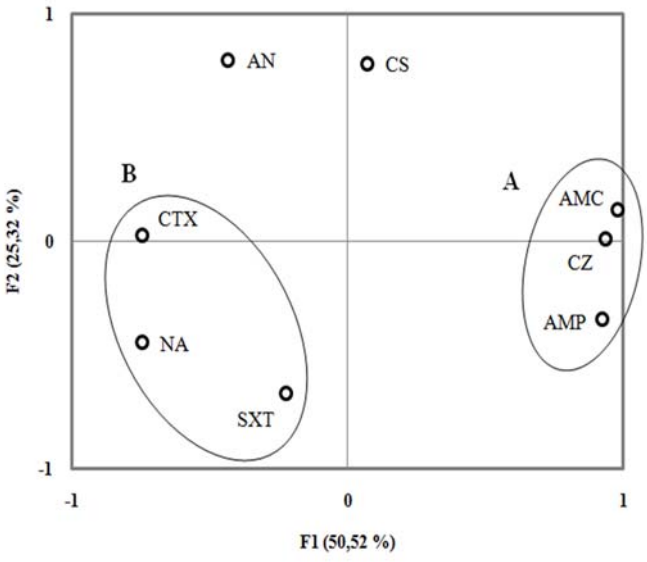

Figure 1) Principal Component Analysis (PCA) of *Klebsiella pneumoniae* antimicrobial resistance phenotypes (AMP: ampicillin; AMC: amoxicillin-clavulanic acid; CTX: cefotaxime; CZ: cefazolin; AN: amikacin; NA: nalidixic acid; SXT: trimethoprim-sulfamethoxazole; CS: colistin)

Cluster A situated at the East part of the graph, regroups an association of AMC, CZ and AMP. Cluster B at the South-West, gathers CTX, NA and SXT. While AN and CS showed an individual spatial behavior, distributed in the North of the model, intermediary between the two clusters. SXT and NA were correlated positively (r=0.239), and higher correlation was observed between CTX and NA (r=0.633). Also, it is remarked that CTX showed negative correlations with AMC (r=-0.648), AMP (r=-0.593) and CZ (r=-0.474). In addition, AN registered a positive correlation with CTX (r=0.242) and a negative correlation with NA (r=-0.239; Table 2).

Two principal clusters were observed by regrouping clinical specimens' resistance phenotypes to their associated antibiotic in FCA model according to the source of isolates. Cluster A in the East of the model gathers SXT and CS with vagina specimen. Cluster B in the West assembles AMP, AMC, CZ and NA with urine specimen. Pus specimen was distributed in the South of the graphic in proximity of cluster B and showed an association with CTX. While AN in the South East, showed a solitary spatial behavior. However, blood and surgery specimens were not represented in FCA for their low number of repetitions (Figure 2).

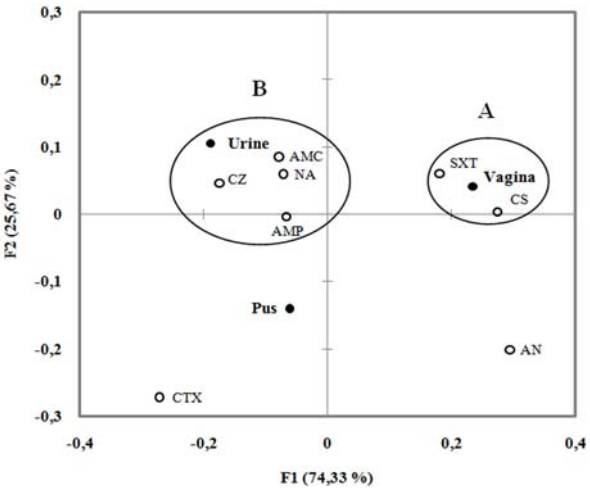

Figure 2) Factorial Correspondence Analysis (FCA) of *Klebsiella pneumoniae* antimicrobial resistance phenotypes according to the source of specimens (AMP: ampicillin; AMC: amoxicillin-clavulanic acid; CTX: cefotaxime; CZ: cefazolin; AN: amikacin; NA: nalidixic acid; SXT: trimethoprim-sulfamethoxazole; CS: colistin)

Urine specimens with their associated antibiotic resistance phenotypes (Cluster B) represented the most important gathering of the analysis. Cefotaxime (34.4%) as well amikacin (18.0%), showed far spatial distributions from cluster B with low percentages of resistance in urine. Typically, NA was associated in space with urine samples and registered the highest resistance (52.8%) in urine compared to the other specimens. Despite the resistance to SXT in urine was important (57.3%), it was associated in space with vagina samples in cluster A, registering the highest resistance level (89.7%) in vagina compared to the other specimens. Also, vagina specimens were associated to CS resistance phenotype in cluster A, registering the maximum rate of resistance to colistin (76.9%) compared to the other specimens. However, vagina samples registered low resistance level to cefotaxime (17.9%) situated very distant from cluster A. Concerning pus specimen, it showed remarkably important levels of resistance to the totality of antibiotics tested with 100% for ampicillin and 81.8% for AMC, followed by cefazolin (75.8%) and cefotaxime (48.5%). While resistance rate to SXT and amikacin were 60.6 and 45.5% respectively, NA registered 42.4% of resistance and colistin 48.5%. In addition, it is important to notify that pus showed the maximum rate of resistance to cefotaxime (48.5%) compared to the other specimens, manifesting a clear association with CTX resistance phenotype located in the South West of the model. Blood specimens registered the highest percentages of resistance to cefazolin (100%) and amikacin (55.6%) compared to the other specimens, low level of resistance to NA (11.1%), while all blood isolates were susceptible to cefotaxime and SXT.

Discussion

According to the results of antibiotics correlations with the two principal components, the first principal component (PC1) was considered representative of β-lactams family and the second principal component (PC2) was considered representative of aminoglycosides family. The present consideration of the two principal components with β-lactams and aminoglycosides families is in agreement with Shahid *et al.*, which have reported that in developing countries β-lactams and aminoglycosides are broadly prescribed in antibiotic therapy. Because of their large and excessive employ, the resistance developed to these antibiotics becomes an important concern particularly with the recent use of β-lactamases inhibitor/β-lactams antibiotics, broad-spectrum cephalosporins, monobactams, and carbapenems [3].

The principle we used here for the interpretation of antibiotic resistance phenotypes spatial distribution is supposed by the explanation of resistance expression pattern by the encoding genes positions on bacterial genome; nearer the encoding genes on genome, more likely their resistance profiles distributed in space and occurrence in time. Thus, the spatial distribution mode of antibiotic resistance phenotypes in PCA could be the result of encoded genes mapping.

Because the local gene mapping of antibiotic resistance determinants is not available until this time, we confront the results of modeling to the literature.

The gathering of β-lactams antibiotics in cluster A is in accordance with Jain & Mondal who have declared that bla_{SHV} genes alone can confer a resistance of *K. pneumoniae* to several antibiotics, e.g. ampicillin, amoxicillin-clavulanic acid and some cephalosporins at the same time [11]; this can explain the similar spatial behavior and high correlations registered for these antibiotics. Remarkably, cefotaxime situated in Cluster B, belonging to β-lactams family, subgroup of cephalosporins third generation, showed a far spatial distribution from the others β-lactams antibiotics located in Cluster A. The most likely explanation of cefotaxime resistance phenotype distance is probably its plasmid genetic localization compared to the chromosomal situation of penicillin's genes. Indeed, it was reported that bla_{SHV-1} gene that is universally found in *K. pneumonia*, had been previously recognized as chromosomal gene in Klebsiella spp., and was later integrated on plasmid, encouraging its dissemination in the species of Enterobacteriaceae family [11]. On the other hand, Kumar *et al.* have reported that bla_{SHV} genes coding for penicillin and some cephalosporins can be located in chromosome or plasmid [4]. However, bla_{CTX-M} genes in *K. pneumoniae* coding cefotaxime resistance phenotype were detected only in plasmids in many studies [12-14]. Moreover, Hudson *et al.* have reported that resistant to amoxicillin and ampicillin is naturally expressed by chromosomal class-A β-lactamases in the whole of *K. pneumoniae* isolates [15].

Moreover, in cluster B, it has been reported that resistance to non-β-lactams antibiotics is often associated to ESBL-producing Enterobacteriaceae. This status of multidrug resistance restrains strictly the choices of antibiotic therapy. The incorporation of integrons carrying additional antibiotic resistance to some ESBL genes explains this pattern well [12]. El Bouamria *et al.* have confirmed that genetic resistance determinants encoding ESBL enzymes are usually co-transferred on the same plasmid with fluoroquinolones, aminoglycosides, and SXT genes [5].

The positive correlation of amikacin with cefotaxime is in agreement with Yan *et al.* who have reported that in *K. pneumoniae* multidrug resistance; plasmid pKP048 includes bla_{DHA-1}, bla_{KPC-2}, *armA*, and *qnrB4* genes, encoding resistance to cephalosporins, carbapenems, aminoglycosides, and fluoroquinolones, respectively [2].

Concerning colistin resistance phenotype, it showed non-regular correlations with the whole of resistance phenotypes. It was remarked that gene mapping of colistin resistance determinants stills missing, however, we can suggest than the localization of its genetic determinants is too irregular. Cannatelli *et al.* have demonstrated a novel colistin genetic resistance mechanism based on the inactivation of the *mgrB* gene, encoding a transmembrane regulator in command of the negative control of signaling system PhoQ/PhoP [16].

The principle we proposed for the interpretation of antimicrobial resistance phenotypes spatial distribution according to specimen source in FCA, is based on the explanation of antibiotic resistance phenotypes and specimens associations by the high level of resistance. On the contrary, the distance between them could be explained by the low level of resistance. Thus, we can suggest that the assembly of antibiotic resistance phenotypes with the specimen is the result of the dominant resistance profile.

In contrast to the present results of resistance to antibiotics in urine specimens, Shahid *et al.* in India [3], have remarked lower susceptibility to amikacin (54.5%) followed by cefotaxime (31.8%) in *K. pneumoniae* isolates from urine samples. Moreover, Haldorsen *et al.* in Norway have reported more reduced susceptibility to amikacin with 0.2% for Klebsiella spp. from urine [14]. However, the present percentage of resistance to cefotaxime (34.4%) was higher than the resistance to the third generation cephalosporins (22.7%) remarked in urinary strains of Klebsiella spp. in Tunisia [17]. Although the present percentage of resistance to trimethoprim-sulfamethoxazole (57.3%) was high in urine, it is at a low level compared to the resistance rate (95.5%) reported by Shahid *et al.* in India [3]. In Morocco [5], antimicrobial non-susceptibility to trimethoprim-sulfamethoxazole (61%) displayed by urinary *K. pneumoniae* isolates is almost similar to the present study. In addition, the result of nalidixic acid resistance (52.8%) is remarkably higher than the resistance to quinolones observed in urinary Klebsiella spp. in Morocco (33%), Tunisia (19.2%) and India (11.5%) [7, 17, 18]. According to Kumar *et al.*, Klebsiella spp. is one of the most common pathogens causing urinary tract infections (UTI). Because of therapy failure with habitual drugs, the prescription of quinolones as alternative treatment could be the reason of the elevated quinolones resistance development in *K. pneumoniae* urinary isolates [7]. A number of mechanisms are responsible of acquired resistance to quinolones comprising a reduction in membrane permeability, an excess of efflux systems expression and mutations in topoisomerase and quinolone resistance determinants [5]. In the present context of antibiotic resistance in urine specimens,

amikacin, cefotaxime and colistin are proposed to be an alternative and better treatment of *K. pneumoniae* urinary infections in Mila.

In vagina specimens, the present resistance to SXT (89.7%) is extremely higher than the percentage (38.2%) observed for *K. pneumoniae* isolated from vagina in Pakistan [19]. While the low resistance to cefotaxime (17.9%) remarked is almost near to the value 20.9%, found by the same authors. Remarkably, colistin resistance (76.9%) in vagina samples is greatly higher than the result of Parisi *et al.* in Italy [20], who have detected only 2 (0.4%) strains resistant to colistin from vaginal swabs. It is important to notify that few studies developed *K. pneumoniae* colistin resistance pattern especially in vagina. According to Parisi *et al.*, horizontal genetic transmission and drug-selection pressure are the established cause of colistin resistance emergence [20]. Regarding the present resistance results, the best antibiotic therapy proposed for vaginal *K. pneumoniae* infections in the region of Mila is limited to cefotaxime and nalidixic acid.

The high resistance to cefotaxime observed in pus specimens is in accordance with Shahid *et al.* in India [3], who have observed very low susceptibility to cefotaxime (7.7%) in *K. pneumoniae* isolates from pus samples. Furthermore, Kumar in India [21] has observed higher resistance rates to cefotaxime (88.8%) in *K. pneumoniae* strains isolated from pus. Also, Hussain *et al.* in Pakistan [22] have remarked a high level of resistance to cefotaxime (81%) in *K. pneumoniae* isolated from pus samples. According to Kumar, among pus samples, *K. pneumoniae* accounted as the second most common isolated organism after *Staphylococcus aureus* [21]. In the present study, *K. pneumoniae* isolated from pus showed an alarming pattern of resistance to the whole of antibiotics tested, limiting empiric chemotherapy choices. Probably, we expect that horizontal genetic transfer from *Staphylococcus aureus* could explain the present *K. pneumoniae* antimicrobial resistance. Indeed, during the same period of study in our Hospital, we remarked an increase of abscess due to multidrug-resistant *S. aureus*. Thus, in the region of Mila new drugs should be used for antibiotic therapy, such as carbapenems, in abscess infections due to *K. pneumoniae*.

Regarding blood specimens, Mosqueda-Gómez *et al.* in Mexico, have registered lower resistance to amikacin (29%) and higher resistance to quinolones (29%) in bloodstream infections caused by *K. pneumoniae* [23]. Haldorsen *et al.* in Norway [14] have reported more reduced susceptibility to amikacin (0.4%) for Klebsiella spp. from blood. In Spain [24], 12% of cefotaxime resistance was demonstrated in Klebsiella spp. isolated from blood. Consequently, according to the present antimicrobial resistance pattern, several drugs can be recommended as cefotaxime, SXT, quinolones and colistin in blood *K. pneumoniae* infections.

The multivariate analyses are frequently used to elucidate the contribution of genetic determinants involved in the intricate disease phenotypes. The objective of the analysis is to refine a genetic signal observed among several interconnected phenotypes. The PCA and FA procedures support gene mapping studies by uncovering hidden genetic factors associated to phenotypes. These mathematical procedures support gene mapping studies by uncovering hidden genetic factors associated to phenotypes [25]. We note here that data on similar studies stills missing in the literature, especially regarding multivariate analysis of *Klebsiella pneumoniae* antimicrobial resistance phenotypes.

Among the restrictions of our study we can declare the nonexistence of data regarding antibiotic usage, no completion of confirmation test for ESBL production in our laboratory, not testing the susceptibility to carbapenems and the lack of information on the source of samples outside and inside the community hospital. Despite all, our study is the first report made to Mila Hospital in Algeria. The model developed in PCA showed dominant resistance profiles manifesting similar occurrence in time. By comparing these results to the literature, the most probably explanations of divergences between antibiotic resistance phenotypes spatial distribution and resistance gene mapping available in the literature, are the different geographic origins of *K. pneumoniae* strains, protocols used in antibiotic therapy carrying specific selection pressure and the nature of *K. pneumoniae* infections. Although this study is based on the correlations among antibiotic resistance phenotypes in our region and gene mapping available in the data, the perspective of genetic exploration of antibiotic resistance determinants is very pertinent. Finally, the data of this study establish the state and mode of antimicrobial resistance in our region provide a support for the development of a geographical strategy for antibiotic resistance control and can be suggested to adapt an update antibiotic therapy protocol in accordance with specimen nature in *K. pneumoniae* infections in this region of the country. Furthermore, the data help to limit the spread of antibiotic resistance, reduce hospital stay and the economic cost of therapy.

Conclusion

The model developed in FCA, highlights typical associations of antibiotic resistance phenotypes to specimen source and confirms the difference in resistance profile according the source of specimen in *K. pneumoniae* infections.

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