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RESEARCH ARTICLE

STUDYON CHANGE IN THE TREND OF ANTIBIOTIC SUSCEPTIBILITY PATTERN OF KLEBSIELLA PNEUMONIAE ISOLATES FROM VARIOUS CLINICAL SAMPLES IN A TERTIARY CARE HOSPITAL

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Abstract

Background: Klebsiellapneumoniae colonizesskin,nasopharynx,gastro-intestinal tract,and oropharynx of hospitalized individuals.KlebsiellacausesPneumonia,Meningitis(neonates),Urinarytractinfections,Intra-abdominal infections,Skin and Soft tissue infections in both community and health-caresettings.It became a challenge to the ID(Infectious Disease) physicians to treat Klebsiella infections due to increasing resistance to various antibiotics which led to significant morbidity and mortality. This study was done to know the change in the trend of antibiotic susceptibility pattern of K. pneumoniae for a period of 2 years and to identify Extended Spectrum β-lactamase and AmpCβ-lactamase producing organisms.

Materials and Methods: This is a prospective study done in the Department of Microbiology,Siddhartha Medical College,Vijayawada for a period of 2 years(August 2019- July 2021).Blood,pus, andurine specimens received from both Out-patients and In-patients of Government General Hospital,Vijayawada during the study period weresubjected to culture according to CLSI guidelines.Antibioticsusceptibility testing was done by modified Kirby-Bauer disc diffusion method on Muller-Hinton agar.ESBL and AmpC β-lactamase producing organisms were identified using Cefotaxime(30µg), Ceftazidime + Clavulanic acid (30µg/10µg) and Cefoxitin(30µg) discs respectively.

Results: Out of the 3021 and 3558 samples received during period 1(August 2019 – July 2020) and period 2(August 2020 to July 2021),254 and 320 K.pneumoniae were isolated respectively.167(65%) isolates toPiperacillin-Tazobactam(PIT), 13(5.1%)isolates to Amikacin(AK)and 6(2.36%)isolates to Meropenem(MR) were resistant during period 1.240(75%)isolates to PIT,40(12.5%)isolatesto AK and 28(8.75%)isolates to MR were resistant during period 2.More than 50% resistance was observed toCefoxitin,Co-trimoxazole, and Ciprofloxacin during both periods 1 and 2.57 ESBL,8 AmpC β-lactamase producing organisms were identified during period 1 and 108 ESBL,25AmpCβ-lactamaseproducing organismsduring period 2.

Conclusion: Antibiotic resistance has increased during period 2 when compared withperiod 1.It isimportant to monitor and optimize antibiotic use through antibiotic stewardship programmes.The

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collaboration of Microbiologists and clinicians is also necessary fortheeffective management of infectious diseases.

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Introduction:-

Klebsiella pneumoniae belongs to the family Enterobacteriaceae. It is a Gram-negative encapsulated bacterium that grows in the mucosal surfaces of humans and soil, vegetation and water. In humans, K.pneumoniae colonizes the oropharynx and gastrointestinal tract, from where it can easily enter the circulation and other tissues, causes infections such as bacteremia, septicemia, surgical site infections, urinary tract infections, hospital-acquired pneumonia and ventilator-associated pneumonia.K.pneumoniae can form biofilms. It became a challenge to the ID (Infectious Disease) physicians to treat Klebsiella infections due to increasing resistance to various antibiotics which led to significant morbidity and mortality.One major drug resistance mechanism of K. pneumoniae is through the production of β-lactamases like Extended-Spectrum β-Lactamases (ESBLs) and/or AmpC β-lactamases or both.K. pneumoniae is often resistant to severalclasses of non-β-lactam antibiotics.Intensive and prolonged use of antibiotics is another reason for the emergence and spread of highly resistant nosocomial infections.

Methods:-

Blood, pus and urine specimens were received from both Out-patients and In-patients from different wards of Government General Hospital, Vijayawada for a period of 2 years from August 2019 - July 2021 which was divided into 2 periods. Period 1 is from August 2019 to July 2020. Period 2 is from August 2020 to July 2021. The samples were inoculated onfresh Nutrient agar, 5% sheep Blood agar and MacConkey's agar.The plates were incubated aerobically at 37^0 C for 24 hrs.The organisms were identified phenotypically by cultural characteristics, Gram's stain, Motility and standard biochemical tests as per CLSI guidelines.Antibiotic susceptibility testing of the isolated bacteria was done by Modified Kirby-Bauer Disc Diffusion method on Muller Hinton's agar with proper standardization using ATCC control strains.

Phenotypic screening of ESBL producing Klebsiella isolates was doneusing cefotaxime (30µg)disks and confirmation was done using ceftazidime (30µg) disk and clavulanate (10µg) on Mueller-Hinton agar. A difference of more than or equal to 5 mm between the zone diameters of Ceftazidime disks and Ceftazidime/ clavulanate disks was taken to be phenotypic confirmation of ESBL production.

AmpCβ-lactamase producing isolates were detected using 30µg cefoxitin disks on inoculatedMuller Hinton's agar. Isolates producing zone diameters less than 18 mm were confirmed as AmpC β-lactamase producers.

Results:-

Out of 3021 samples received during period 1, 1442 were pus samples, 594 were blood samples, 985 were urine samples. The no. of Klebsiella pneumoniae isolates from the pus, blood and urine samples were 139, 67 and 48 respectively during period 1, which accounts for a total of 254.

Out of 3558 samples received during period 2, 1778 were pus samples, 612 were blood samples, 1168 were urine samples. The no. of Klebsiella pneumoniae isolates from the pus, blood and urine samples were 175, 82 and 63 respectively during period 2,which accounts for a total of 320.

Out of the 254 Klebsiella pneumoniae isolates during period 1,167(65%) isolates were resistant to Piperacillin-Tazobactam(PIT),13(5.1%) isolates were resistant to Amikacin(AK) and 6(2.36%) isolateswere resistant to Meropenem(MR) respectively. The no. of isolates resistant to Amoxicillin + Clavulanic acid,Cefoperazone + Sulbactam, Cefotaxime, Cefoxitin, Ceftriaxone, Ciprofloxacin, Co-trimoxazole,Tetracycline were 195(76.7%), 165(65%), 87(34.25%), 186(73.2%), 205(80.7%), 145(57%), 221(87%) and 200(78.7%) respectively.

Out of the 320 Klebsiella pneumoniae isolates during period 2, 240(75%) isolates were resistant to PIT, 40(12.5%) isolates were resistant to AK and 28(8.75%) isolates were resistant to MR respectively. The no. of isolates resistant to Amoxicillin + Clavulanic acid, Cefoperazone + Sulbactam, Cefotaxime, Cefoxitin, Ceftriaxone, Ciprofloxacin, Co-trimoxazole, Tetracycline were 274(85.6%), 242(75.6%), 233(72.8%), 249(77.8%), 285(89.06%), 199(62.1%), 288(90%) and 293(91.5%) respectively.

Resistance to Nitrofurantoin was tested only for urine samples. 33(68.75%) urine samples out of 48 during period 1 and 45(71.4%) urine samples out of 63 during period 2 were resistant to Nitrofurantoinrespectively.

57 ESBL (22.4%),8 (3.14%) AmpC β-lactamaseproducing organisms were identified during period 1.108(33.75%) ESBL,25 (7.8%) AmpC β-lactamaseproducing organisms were identified during period 2.

Discussion:-

The present study shows the antibiotic resistance pattern of Klebsiella pneumoniae over a period of 2 years.

The above study shows 34.25% resistance to Cefotaxime during period 1, which increased to 72.8%during period 2 whichcorrelateswith 20% resistance to cefotaxime in the groupB of Hyun M et al. study, 73.2% in Guo et al. study and 79.2% in Effah et al study respectively.Cefoxitin resistance increased from 73.2% to 77.8% in the present study which is in line with the Zorgani et al. study with 71% resistance. Amikacin resistance increased from 5.1% during period 1 to 12.5% during period 2 which were almost similar to 4.9% resistance in group B and 7.1% in group A of Hyun M et al. studyrespectively. Piperacillin+ Tazobactam resistance increased from 65% to 75% in the present study showing similarity with 67% and 73.13% resistance during periods 2 and 3 of the Sharma et al. study. A.F.Saleem et al study showed decreased resistance to Piperacillin+Tazobactam(41.34%).Meropenem was the least resistant drug with 2.36% resistance during period1 and 8.75% during period 2 among all the drugs tested in the above study which correlates with 5.8% resistance in Guo et al. study.

In the present study, Cefaperazone+ Sulbactam resistance increased from 65% (period 1) to 75.6%(period 2) which is in line with the Sharma et al. study showing 60.19% resistance. The present study shows an increase in resistance from 80.7% to 89.06% for ceftriaxone which correlates with 78.5% and 81% resistance during periods 2 and 3 of the Sharma et al. study respectively.Ciprofloxacin resistance increased from 57% to 62.1% in the present study which has similarity with 59.8% resistance in Effah et al study and 76.8% in Zorgani et al study. Sharma et al. study showed less resistance to fluoroquinolones(31.12%). There is an increase in the resistance from 87% to 90% for Co-trimoxazole in the present study which is in line with 90.78% resistanceduring period 1 and 95% during period 2 of the Sharma et al. study. Zorgani et al. study showed 76.5% resistance to Co-trimoxazole. In the present study, resistance observed to Tetracycline was 78.7% during period 1 and 91.5% during period 2 which correlates with 89% resistance in Mitra et al study. Amoxicillin+ Clavulanic acid resistance increased from 76.7% to 85.6% in the present study which is in line with 73.79% resistance during period 1,84% during period 2 of the Sharma et al. study and 76.1% in Zorgani et al. study.

Nitrofurantoin resistance increased from 68.75%(period 1) to 71.4%(period 2) which correlates withZorgani et al. studyshowing 72.3% resistance.

In this study 22.4%(57 samples) ESBL producing organisms were identified during period 1 which correlates with group B(19.6%) of Miri Hyun et al. study. 8 (3.14%) AmpC β-lactamase producing organisms were identified during period 1 which correlates with Song W et al study which shows the isolation of 2.9% AmpC β-lactamase producing organisms.

During period 2, ESBL producing organisms identified in the present study were 108, that corresponds to 33.75% which is similar to 33.2% ESBL producing organisms in Antonella Agodi et al. study during 2013. 25 (7.8%) AmpC β-lactamase producing organisms were identified during period 2 that correlates with Abdulaziz et al study which shows the isolation of 7.9% AmpC β-lactamase producing organisms.

Table 1:- No. of samples received during the study period.

Year of study	No. of Pus samples received	No.ofBlood samples received	No. of Urine samples received	Total no. of samples received in a year
AUGUST 2019 – JULY 2020 (Period 1)	1442	594	985	3021
AUGUST 2020 – JULY 2021 (Period	1778	612	1168	3558

2)				

Figure 1:-

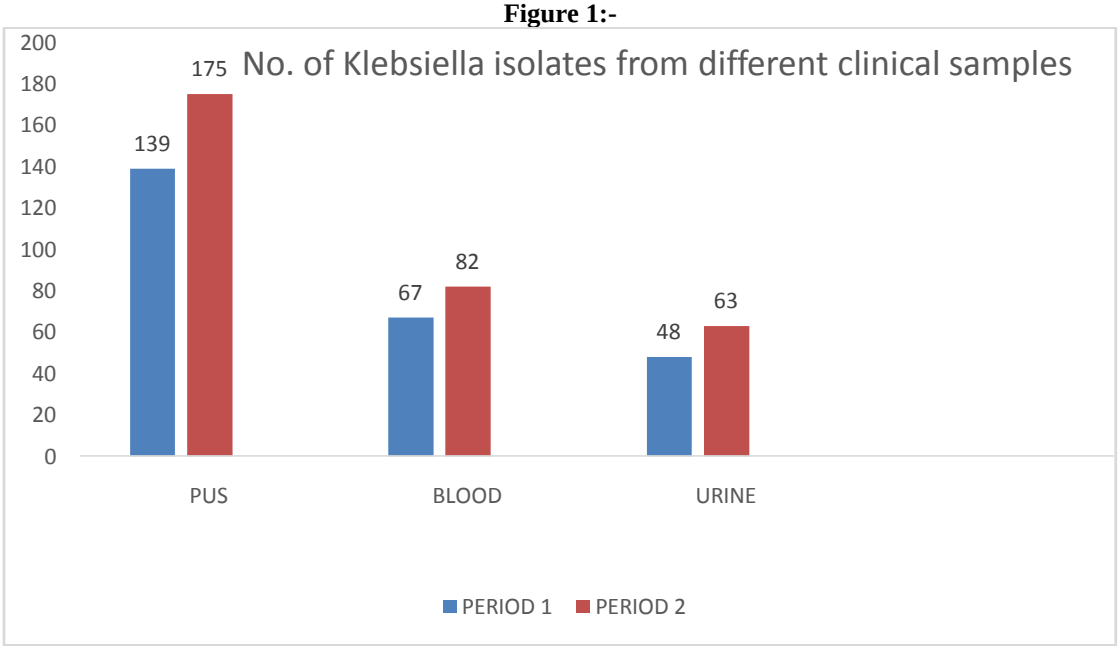
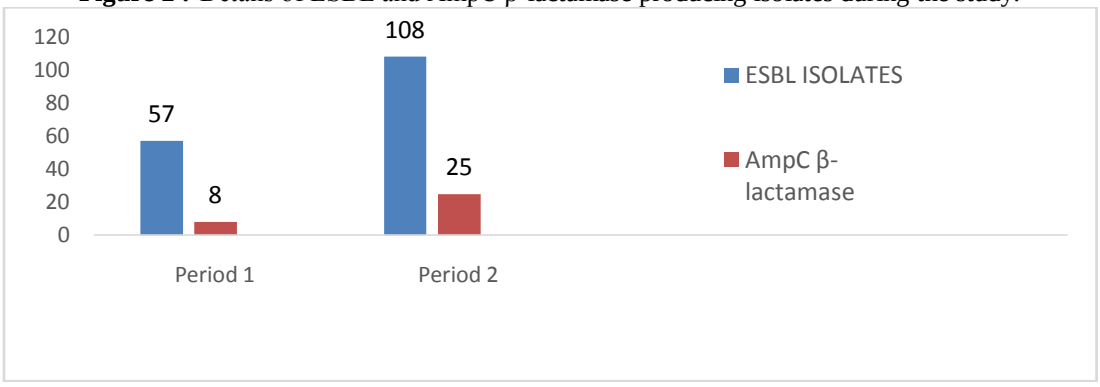


Table 2:- Antibiotic susceptibility pattern of K.pneumoniae isolates during the study period.

ANTIBIOTICS	PERIOD 1 (n=254)		PERIOD 2 (n=320)	
	SENSITIVE	RESISTANT	SENSITIVE	RESISTANT
Amikacin	241	13	280	40
Amoxicillin+clavulanic acid	59	195	46	274
Cefaperazone + Sulbactam	89	165	78	242
Cefotaxime	167	87	87	233
Cefoxitin	68	186	71	249
Ceftriaxone	49	205	35	285
Ciprofloxacin	109	145	121	199
Cotrimoxazole	33	221	32	288
Meropenem	248	6	292	28
Piperacillin + Tazobactam	87	167	80	240
Tetracycline	54	200	27	293

Figure 2 :-Details of ESBL and AmpC β-lactamase producing isolates during the study.



Conclusion:-

There is an increase in the antibiotic resistance during period 2 when compared with period 1. Intensive and prolonged use of antibiotics is likely the main underlying factor in the transmission of antibiotic-resistant nosocomial infections. so it is very important to monitor and optimize antibiotic use through antibiotic stewardship programmes. The collaboration of Microbiologists and clinicians is also necessary for the effective management of infectious diseases.

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References:-

1. Abdulaziz Zorgani1,4,*, Hiyam Daw2, Najib Sufya2, Abdullah Bashein3,4, Omar Elahmer4,5 and Chedly Chouchani6,7. Co-Occurrence of Plasmid-Mediated AmpC β-Lactamase Activity Among Klebsiella pneumoniae and Escherichia Coli
2. Clement Yaw Effah1, Tongwen Sun2, Shaohua Liu2 and Yongjun Wu1*. Klebsiella pneumoniae: an increasing threat to public health
3. Katrijn L. Rensing1* , H. M. Abdallah2, Alex Koek1, Gamal A. Elmowalid2, Christina M. J. E. Vandenbroucke-Grauls1, Nashwan al Naiemi3,4 and Karin van Dijk1. Prevalence of plasmid-mediated AmpC in Enterobacteriaceae isolated from humans and from retail meat in Zagazig, Egypt
4. Hera Nirwati1*, Kian Sinanjung2, Fahrina Fahrunissa3, Fernando Wijaya3, Sarastia Napitupulu3, Vania P. Hati3, Mohamad S. Hakim1, Andreanita Meliala4, Abu T. Aman1 and Titik Nuryastuti1. Biofilm formation and antibiotic resistance of Klebsiella pneumoniae isolated from clinical samples in a tertiary care hospital, Klaten, Indonesia
5. Antonella Agodi1*, Martina Barchitta1, Annalisa Quattrocchi1, Andrea Maugeri1, Eugenia Aldisio2, Anna Elisa Marchese2, Anna Rita Mattaliano2 and Athanassios Tsakris3. Antibiotic trends of Klebsiella pneumoniae and Acinetobacter baumannii resistance indicators in an intensive care unit of Southern Italy, 2008–2013.
6. Miri Hyun, Chang In Noh, SeongYeol Ryu, and Hyun Ah Kim. Changing trends in clinical characteristics and antibiotic susceptibility of Klebsiella pneumoniae bacteremia
7. Neetu Sharma, Anita K. Gupta, Geeta Walia1, Rupinder Bakhshi1. A retrospective study of the changing trends of antimicrobial resistance of Klebsiella pneumoniae isolated from urine samples over the last 3 years (2012-2014)
8. Ali Faisal Saleem a,*, Farah Naz Qamar a, Hira Shahzad b, Maqbool Qadir a, Anita K.M. Zaidi a. Trends in antibiotic susceptibility and incidence of late-onset Klebsiella pneumoniae neonatal sepsis over a six-year period in a neonatal intensive care unit in Karachi, Pakistan
9. Musa A. Garbati1*, Areedj I. Al Godhair2. THE GROWING RESISTANCE OF KLEBSIELLA PNEUMONIAE; THE NEED TO EXPAND OUR ANTIBIOGRAM: CASE REPORT AND REVIEW OF THE LITERATURE
10. Wu-Pu Lin1, Jann-Tay Wang1,2, Shan-Chwen Chang1,3, Feng-Yee Chang4,5, Chang-Phone Fung6, Yin-Ching Chuang7, Yao-Shen Chen8,9, Yih-Ru Shiau2, Mei-Chen Tan2, Hui-Ying Wang2, Jui-Fen Lai2, I-Wen Huang2 & Tsai-Ling Lauderdale2. The Antimicrobial Susceptibility of Klebsiella pneumoniae from Community Settings in Taiwan, a Trend Analysis
11. Broberg, C. A., Palacios, M. & Miller, V. L. Klebsiella: a long way to go towards understanding this enigmatic jet-setter. F1000prime reports 6, 64, doi: 10.12703/p6-64 (2014).
12. Li, X. M. et al. [Frequency of extended-spectrum beta-lactamase (ESBL) and AmpC beta-lactamase genes in Escherichia coli and Klebsiella pneumoniae over a three-year period in a University Hospital in Korea]. The Korean journal of laboratory medicine 30, 616–623, doi: 10.3343/kjlm.2010.30.6.616 (2010).
13. Liu, H. C. et al. Antimicrobial susceptibility of clinical Enterobacteriaceae isolates at the emergency department in a regional hospital: A threat of extended spectrum beta-lactamase-producers among nursing home residents. Journal of microbiology, immunology, and infection =Wei mianyugan ran za zhi, doi: 10.1016/j.jmii.2015.10.001 (2015).
14. Kumar AR, Kalpana S. Prevalence and antimicrobial susceptibility pattern of Klebsiella pneumonia causing urinary tract infection and issues related to the rational selection of antimicrobials. Sch J Appl Med Sci 2013;1:395-9.

15. Sikarwar AS, Batra HV. Prevalence of antimicrobial drug resistance of Klebsiella pneumoniae in India. Int J BiosciBiochem Bioinformatics 2011;1:211-5.
16. Park MJ, Kim TK, Song W, Kim JS, Kim HS, Lee J. An Increase in the clinical isolation of acquired AmpC β-lactamase-producing Klebsiella pneumoniaee in Korea from 2007 to 2010. Ann Lab Med 2013; 33(5): 353-5.
17. Guo X, Cao Z, Dai Z, Li Y, He X, Hu X, Tian F, Ren Y. Antimicrobial susceptibility and molecular epidemiology of multidrug-resistant Klebsiella pneumoniae in Central China. Jpn J Infect Dis. 2017;70(3):229–34.
18. Mitra S, Mukherjee S, Naha S, Chattopadhyay P, Dutta S, Basu S. Evaluation of co-transfer of plasmid-mediated fluoroquinolone resistance genes and bla NDM gene in Enterobacteriaceae causing neonatal septicaemia. Antimicro- bial Resist Infect Control. 2019;8(1):46.
19. Chew KL, Lin RT, Teo JW. Klebsiella pneumoniae in Singapore: hypervirulent infections and the carbapenemase threat. Front Cell Infect Microbiol. 2017;12(7):515.
20. Mansury D, Motamedifar M, Sarvari J, Shirazi B, Khaledi A. Antibiotic sus- ceptibility pattern and identification of extended spectrum β-lactamases (ESBLs) in clinical isolates of Klebsiella pneumoniae from Shiraz, Iran. Iran J Microbiol. 2016;8(1):55.
21. Song W, Kim JS, Kim HS, Yong D, Jeong SH, Park MJ, Lee KM. Increasing trend in the prevalence of plasmid-mediated AmpC beta-lactamases in Enterobacteriaceae lacking chromosomal ampC gene at a Korean university hospital from 2002 to 2004. Diagn Microbiol Infect Dis. 2006 Jul;55(3):219-24. doi: 10.1016/j.diagmicrobio.2006.01.012. Epub 2006 Mar 20. PMID: 16545935.
22. Zhao D, Zuo Y, Wang Z, Li J. Characterize carbapenem-resistant Klebsiella pneumoniae isolates for nosocomial pneumonia and their Gram-negative bacteria neighbors in the respiratory tract. Mol Biol Rep. 2019;46(1):609–16.
23. FatinIzzatiMohdkhari, Rina Karunakaran, RoshalinaRosli, Sun Tee Tay. Genotypic and Phenotypic Detection of AmpC β-lactamases in Enterobacter spp. Isolated from a Teaching Hospital in Malaysia
24. Lee JA, Kang CI, Joo EJ, et al. Epidemiology and clini- cal features of community-onset bacteremia caused by extended-spectrum □-lactamase-producing Klebsiella pneumoniae. Microb Drug Resist 2011;17:267-273.
25. Huh K, Kim J, Cho SY, et al. Continuous increase of the antimicrobial resistance among gram-negative pathogens causing bacteremia: a nationwide surveillance study by the Korean Network for Study on Infectious Diseases (KONSID). Diagn Microbiol Infect Dis 2013;76:477-482.
26. Manikandan C, Amsath A. Antibiotic susceptibility pattern of Klebsiella pneumoniae isolated from urine samples. Int J Curr Microbiol Appl Sci 2013;2:330-7.