



Emergence of carbapenem resistant hypervirulent *K.pneumoniae* – a global threat?

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Background

- There has been increasing reports of hypervirulent (hv) *K.pneumoniae* (Kp) from various parts of the world.
- Hypervirulent *K.pneumoniae* are also referred to as hypermucoviscous since the colonies are highly mucoid and are detected by the string test¹.
- Most studies till date reported these strains to be community acquired and susceptible to most antimicrobials.
- However, two recent reports from China describe carbapenem resistant hvKp².
- *rmpA*, *rmpA2* are molecular markers.
- The hvKP commonly belong to K1/ K2 capsular types which can be detected by PCR for *magA* and *K2wzy* genes respectively.

Objectives:

- To study the prevalence of hypervirulent strains among the susceptible, ESBL and carbapenem resistant (CR) *K.pneumoniae* isolates from bacteremia
- To study the incidence of community acquired and hospital acquired infections in the three groups

Materials and Methods

- The first 76 non-repetitive *K.pneumoniae* blood cultures obtained during 2015 were included in the study.
- Isolates were classified into three groups based on antimicrobial susceptibility testing performed by disk diffusion and interpreted according to CLSI 2015 guidelines.

Materials and Methods (cont.)

- First group included isolates that were susceptible to amoxicillin/clavulanic acid and cephalosporins.
- Second group comprised of ESBL producers and third group comprised of carbapenem resistant isolates.
- For screening of hvKp strains, string test was performed and the isolates positive for string test were grouped as hvKp in this study.
- The three most important genes associated with hypervirulence, *rmpA*, *rmpA2* and *magA* were screened for by PCR. PCR for K2 capsular type was also performed.
- Clinical details of patients were obtained from electronic medical records.
- Multiplex PCR was performed for the detection of carbapenamase genes and the minimum inhibitory concentration (MIC) for meropenem was determined by E-test for the carbapenem resistant isolates.

Results

- 56 patients were male (74%) and the age range of patients was from 3days to 83years. The median age was 48years.
- Meropenem MIC ranged from 0.38µg/ml to >32µg/ml among the carbapenem resistant isolates
- Overall rate of string test positivity was found to be 30%.
- Seven isolates co-expressed *rmpA* and *rmpA2*, while *rmpA* was singly expressed in 2 isolates and *rmpA2* in 10 isolates.

Table1: Results of hvKp characterization

Total n=76	String test positive	String test negative	<i>rmpA</i>	<i>rmpA2</i>	<i>magA</i>	<i>K2wzy</i>	Community acquired	Health care associated
Susceptible (n=28)	10	18	6	7	4	2	7	21
ESBL (n=18)	2	16	2	2	0	1	3	15
Carbapenem resistant (n=30)	11	19	1	8	0	5	0	30

Table2: Prevalence of carbapenamase genes and hvKp among the carbapenem resistant isolates

Carbapenamase gene	No. of isolates (n=30)	String test positive	<i>rmpA</i>	<i>rmpA2</i>
<i>bla_{NDM}</i>	5	3	0	2
<i>bla_{OXA48-like}</i>	2	1	0	0
<i>bla_{NDM}</i> and <i>bla_{OXA48-like}</i>	19	7	1	4
<i>bla_{NDM}</i> and <i>bla_{VIM}</i>	1	0	0	1
Negative	2	0	0	1

Discussion

- Though 30% (23) of the isolates were string test positive, 83% (19) among them carried *rmpA*, *rmpA2* or both the genes.
- Only four isolates were of the K1 capsular type and 8 isolates were of the K2 type, unlike most studies which mainly comprise of K1 and K2 types.
- Though most hvKP infections are community acquired¹, this study showed a higher rate of hospital acquired infections (78%) which is worrisome.
- The prevalence of hvKp was similar in the group which comprised of susceptible isolates and the group of carbapenem resistant isolates. However, relatively lower number of hvKp was seen among the ESBL producers.

Discussion (cont.)

- *bla_{NDM}* and *bla_{OXA48-like}* were co-expressed in 63% of the carbapenem resistant isolates.
- *rmpA2* was present more often *rmpA* gene among the study isolates

Conclusion

- String is not very specific and molecular markers are more reliable in identifying the hv strains.
- In this study 22% of hvKp infections were community acquired which reflects on presence and spread of these strains within the hospital posing a threat to treatment and management of infections.
- There has been an increase in incidence of hvKp among CR isolates. The hypervirulent strains are no longer restricted to susceptible phenotypes.
- There is a need to establish an international definition for the hypervirulent *K.pneumoniae*.

References

1. Shon AS, Bajwa RP, Russo TA. Hypervirulent (hypermucoviscous) *Klebsiella pneumoniae*: a new and dangerous breed. *Virulence*. 2013 Feb 15;4(2):107-18.
2. Zhang Y, Zeng J, Liu W, Zhao F, Hu Z, Zhao C, Wang Q, Wang X, Chen H, Li H, Zhang F, Li S, Cao B, Wang H. Emergence of a hypervirulent carbapenem-resistant *Klebsiella pneumoniae* isolate from clinical infections in China. *J Infect*. 2015 Nov;71(5):553-60

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