

Patterns and trends of *Klebsiella pneumoniae* resistance to Carbapenems

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The growing prevalence of drug-resistant infections has led to increased morbidity, mortality, and healthcare costs worldwide. Bacterial resistance to antimicrobials has been increasing in Europe over the last few years. According to WHO, new antimicrobials or strategies are urgently needed to treat this kind of infections. Addressing this issue, it is needed not only coordinated policy action but also a deep understanding of the epidemiological patterns and trends underlying antimicrobial resistance (AMR), particularly across different European countries. In the present study, and considering the WHO alert reports, the particular case of carbapenem-resistant Gram--negative bacterial infections was evaluated. Agglomerative hierarchical cluster analysis was employed to explore patterns and relationships among various countries in the context of AMR, particularly in the case of the pair *Klebsiella pneumoniae*|Carbapenems. These data are time series of different lengths; therefore, to perform the cluster analysis, the Autoregressive Integrated Moving Average (ARIMA) models are the ones that best represent the behaviour of resistant isolate percentage values over time, in the case of the pair *Klebsiella pneumoniae*|Carbapenems, across several countries. To measure the similarity among different countries in the context of AMR, in the case of the pair *Klebsiella pneumoniae*|Carbapenems, the generalized Affinity coefficient between ARIMA models was applied. R software was used, and, for that reason, the associated distance of the generalized Affinity coefficient is also applied.

The resulting hierarchy reveals four main branches and four large clusters of countries at the cut-off, as shown in Figure 1.

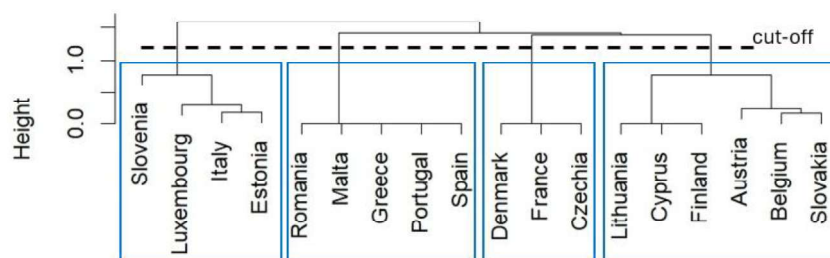


Figure 1 – Dendrogram based on the square root of $2(1 - \text{Affinity})$ distance and average linkage aggregation criterion between countries in *Klebsiella pneumoniae*|Carbapenems resistance context.

From the analysis of the dendrogram, it can be observed that the generalized affinity coefficient separates the estimated ARIMA models that best fit the resistance behaviour of *Klebsiella pneumoniae* to carbapenems across several European countries into four distinct groups. The behaviour of resistance values over the years within each group generally shows fluctuations, with each group displaying a distinct pattern of variation and a different growth trend. In the case of Group II, which includes Portugal, the growth trend is more pronounced, indicating a group where there appears to be a greater need for controlling the incidence of this type of resistance and for closer attention to policies aimed at preventing its spread.

Keywords: *Klebsiella pneumoniae*, hierarchical cluster analysis, generalized Affinity coefficient, ARIMA models