Epidemiology of Meningococcal Meningitis in Niger : a district-based comparative study

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CONTEXT and OBJECTIVES

Meningococcal Meningitis is a major public health problem in Sub-Saharan Africa, mainly in the region called the meningitis belt. Despite the obvious seasonality of epidemics, the factors driving them are still poorly understood. The timing of the future outbreaks has appeared unpredictable until today, limiting the efficacy of the current reactive vaccination strategy.

The aim of this study was to better understand the epidemiology and the spatio-temporal dynamics of meningitis outbreaks in order to identify parameters that would allow earlier outbreak detection and timely response. Based on surveillance data covering over two decades, we first explored the spatial structure of meningitis using cluster analysis methods. We then investigated a new definition of 'epidemic year' in order to compare epidemiological patterns in epidemic and non-epidemic situations.

DATA and METHODS

Data sources

- Epidemiological data, collected through the national enhanced surveillance system, correspond to weekly records of the number of suspected Meningococcal Meningitis cases reported by district (1986-2008, 38 districts). This enhanced system of surveillance was initiated and supported by the World Health Organization.

- Population data from three national censuses conducted over the study period were provided by the Nigerien National Institute of Statistics. Annual population size was evaluated assuming a linear population growth at a district level between two consecutive censuses.

Cluster analysis

We performed cluster analysis to highlight similarities and dissimilarities between districts, putting them into groups depending on selected characteristics. Using the weekly attack rate time series, we computed for each district the mean annual pattern of the disease. From this averaged time series we extracted 6 variables : the mean, the maximum, the standard deviation, the week of maximum attack rate, and the Skewness and Kurtosis indices (i.e. respectively the curve's symmetry and 'peakedness' coefficients).

A principal components analysis was first performed on these 6 variables to eliminate their redundancy. We selected the hierarchical ascendant method using Wards distance, which minimizes the intra-group heterogeneity. 3 groups of districts were defined.

Seasonal Patterns and Epidemic Year Definition

For each district, we computed the annual cumulative incidence rates. A given district was considered as experiencing an epidemic year when the yearly incidence rate was higher than the mean value over the 22 years (positive anomaly). Otherwise, it was considered as a non-epidemic year (negative anomaly).

We then compared (i) epidemic years between groups and (ii) epidemic vs. non-epidemic years in each group. To do so, we extracted the 6 previously defined variables from each individual annual incidence curve, and performed means tests for each variable.

We then approached the epidemic year definition to the current alert and epidemic thresholds. Six new variables were extracted from the individual annual incidence curves: the first week when alert threshold was exceeded, the number of weeks between then and the peak of incidence and the number of weeks above the alert threshold. The same 3 variables were defined considering the epidemic threshold. All 6 indices were compared through means tests.

RESULTS: Factorial analysis

The factorial analysis summarized 99% of the information contained in the 6 input variables into 3 resultant variables, which correspond to aggregates of the original ones and resume the district' epidemic pattern characteristics. Those three variables were then used as input for the cluster analysis.

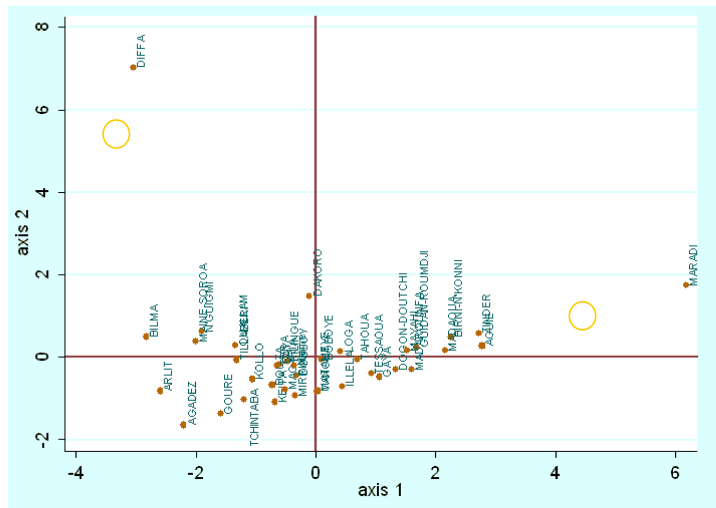

Figure 1: Districts' coordinates in the (axis 1 * axis 2) plan defined from the results of the principal components analysis.

Two districts were considered as outliers for showing apparently incoherent patterns, and were not included in the cluster analysis to prevent their large impact on the results:
- Diffa notified 172 cases in a single week during a low-incidence period.
- Maradi presents an unusually high incidence rate reaching in 1986 the weekly incidence of 400 cases/100 000 habitants

RESULTS: Cluster analysis

Groups of districts constituted geographically coherent areas. Group N1 is composed of 11 higher incidence districts which are located in the South-West, around the Nigerian boundary; group N3 assembles the 3 northern districts where disease incidence is very low. The remaining 22 districts constitute the group N2, where a few severe outbreaks are reported.

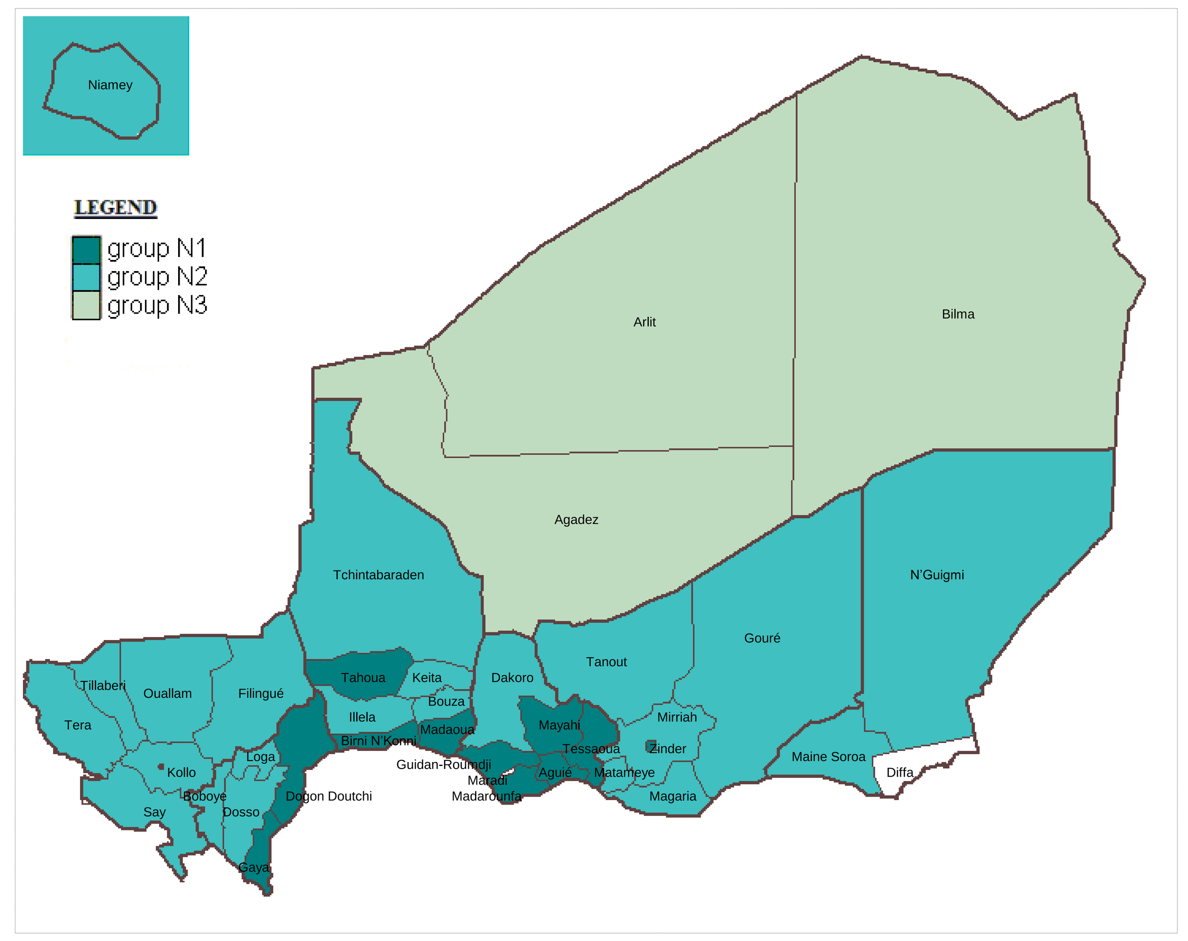

Figure 2: Mapping of the results from the clustering analysis.

RESULTS: Epidemic years Definition

25% of the years were considered as epidemic years using our definition. An example of epidemic year definition is given below for Dosso district.

In 96% of the epidemic years the alert threshold was exceeded against 31% in non-epidemic years (respectively 85% against 11% when considering the epidemic threshold).

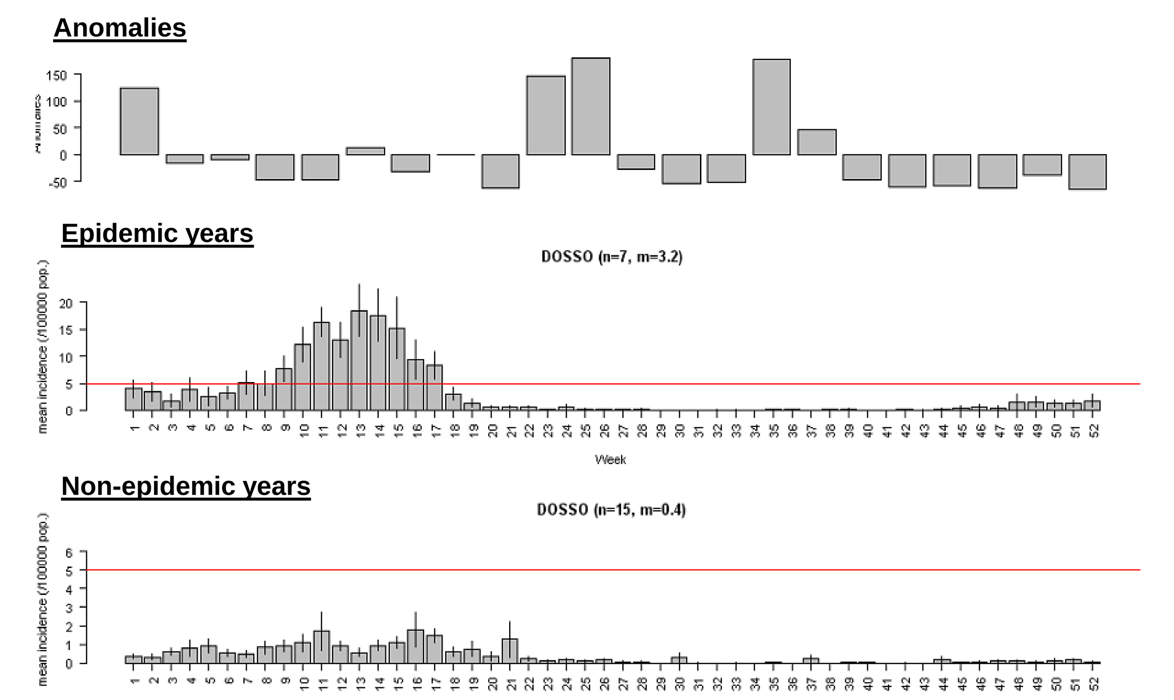

Figure 3: Example of epidemic year definition for the district of Dosso. Top graph: anomalies (/100000 pop.) represent the distance to the annual mean (m), from 1986 to 2007. All years presenting a positive anomaly were considered as epidemic years. Mean annual patterns are represented for epidemic years (middle graph) and non-epidemic years (bottom graph). The red line corresponds to the alert threshold; n= the number of years.

RESULTS

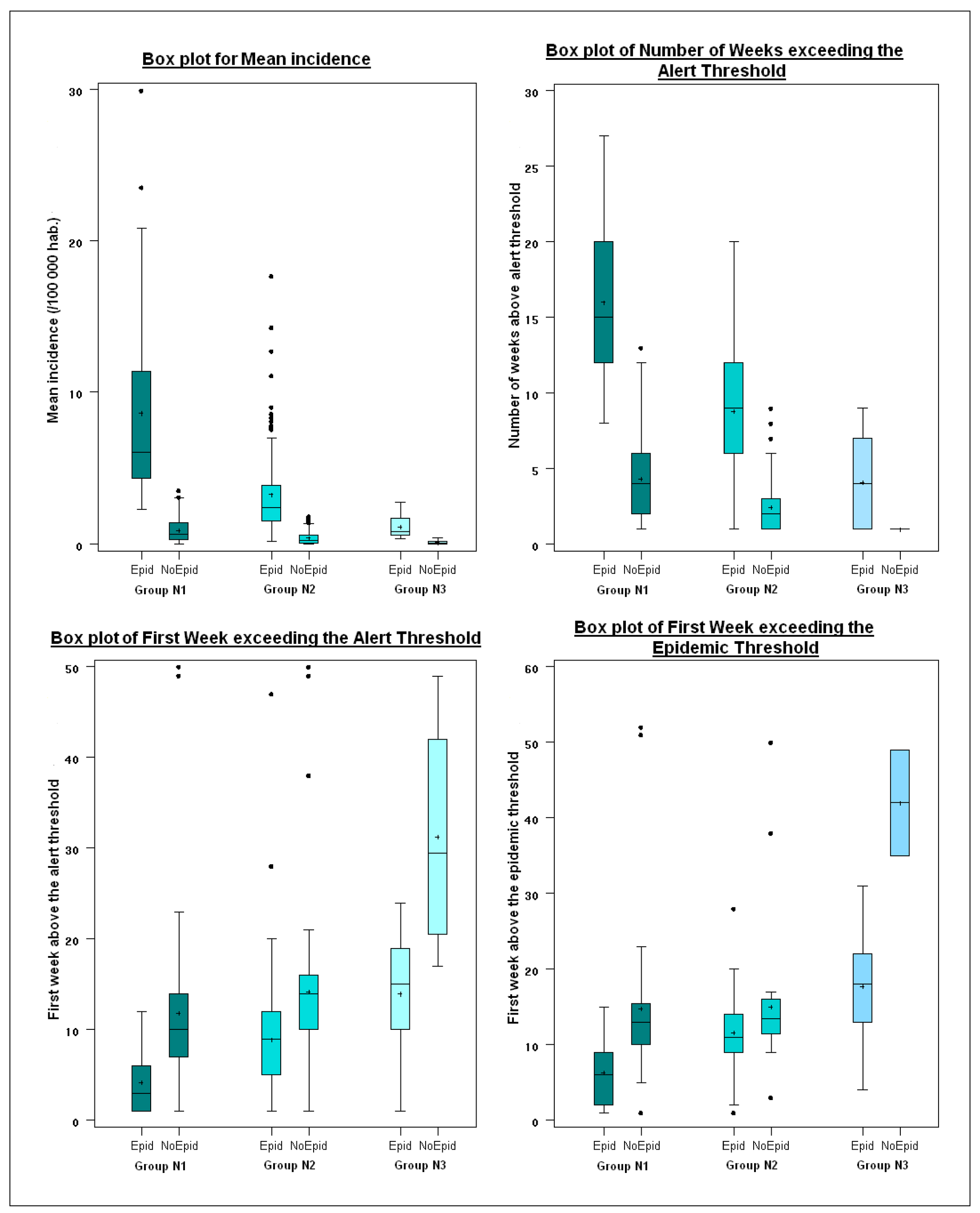

Figure 4: Box plots of indices extracted from the individual annual incidence curves in order to compare groups and epidemic (Epid) vs. non-epidemic years (NoEpid).

Group comparison in epidemic years

The mean and the maximum of weekly incidence are significantly different between groups, and decreases from group N1 to group N2 to group N3; as well as the number of weeks above the thresholds.

Group N1 presents significantly earlier outbreak onset (i.e. first week exceeding the thresholds) in comparison to groups N2 and N3.

Epidemic/non-epidemic year comparison

The mean and the maximum of weekly incidence are significantly higher in epidemic years than in non-epidemic years in each group, as well as the number of weeks above the thresholds.

The first week exceeding the alert threshold occurs significantly earlier in epidemic years as compared to non-epidemic years for every group, partly inducing a longer outbreak progression (i.e. higher number of weeks between crossing the thresholds and reaching the peak). No significant difference is observed considering the timing of crossing of epidemic threshold or reaching the maximum of incidence.

Globally, the highest the mean weekly incidence is, the longer the outbreaks are and the earlier the thresholds are exceeded. In epidemic years, high mean weekly incidence coincides with earliest peaks while it coincides with latest peaks in non-epidemic years. The week of maximum of incidence is more heterogeneous in non-epidemic years than in epidemic years, likely due to low incidence levels leading to unstable peak time.

DISCUSSION

❖ Based on epidemiological patterns, the cluster analysis identified **geographically coherent groups of districts** which present similar epidemiological patterns. The highest at-risk regions are located in the south of the country, whereas the lowest-risk region is mainly situated in the northern area. Overall, **high cumulative annual incidence concurs with an increase in incidence early in the year and with long outbreaks**.

❖We explored an **alternative way to define an epidemic at the district level**, and showed that the timing of the outbreak is specific to each group of districts and differ between epidemic and non-epidemic years. **The week when the alert and/or epidemic threshold is reached could help forecasting an epidemic situation at the district level.**
For instance in districts belonging to group N1, if the alert threshold is exceeded before week 9, the likelihood that the given district will indeed experience an epidemic year is 65%. In other words, if the decision to vaccinate a given district was informed by this criteria, vaccination would be justified in 65% of the situation, no vaccination would be justified in 96%, and no vaccination would have been implemented in 12% of the cases when it should have been (vaccination justified in case epidemic year is defined a posteriori).

❖A similar analysis has been run for Burkina Faso and Mali, and despite epidemiological differences in terms of timing, location and severity of the outbreaks, similar results were found concerning the epidemic definition and the differentiation between groups.

❖The most at-risk areas are located in high population density districts, leading the idea to further **explore the impact of population density** as well as **population migrations** on meningitis dynamics. Future research should incorporate and investigate a wide range of parameters in order to better understand the meningitis outbreak dynamics and thus improve control strategy through the implementation of timely vaccination campaigns.