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Establishment and molecular epidemiology of a new invasive *Neisseria meningitidis* clonal complex, ST-9316.

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Background

Invasive meningococcal disease (IMD) caused by *Neisseria meningitidis* remains a public health problem, with mortality rates as high as 10%. In 2010 new sequence type ST-9316 was reported in Poland which has subsequently become widespread in the country, with incidence reaching 33% of all reported cases in 2021. This sequence type is mostly associated with serogroup B and W but isolates of serogroup C and Y were also observed. Further analysis of the epidemiological and molecular features of ST-9316 is required, translating to public health benefits in Poland and other countries.

Aim/Methods

This investigation aimed to establish a new *Neisseria meningitidis* clonal complex ST-9316 based on previously unpublished genome dataset, as well as to provide insights into some aspects of its molecular epidemiology. Whole genome sequencing was used to obtain genomic data from isolates collected in Poland

between 2010-2022 (n=184). Bioinformatic tools such as PIRATE, Genome Comparator, RAXML and ClonalFrameML were used to align and compare all complete genomes of ST-9316 and close locus variants uploaded to PubMLST from all countries (N=177) and produce phylogenetic trees and recombination analysis. Further work was focused on specific metabolic features shared by ST-9316, such as the absence of functional hmbR gene. MenDeVAR tool was used to predict the reactivity of Bexsero® and Trumenba® vaccines against ST-9316 isolates

Results

RAXML and ClonalFrameML recombination analysis allowed to formally establish a new *Neisseria meningitidis* clonal complex ST-9316. PubMLST analysis highlighted metabolic differences between ST-9316 and other common clonal complexes in Poland (including ST-11), most notably an altered iron metabolism due to loss of functional hmbR gene responsible for haemoglobin binding. Analysis suggested a capsule switching event which resulted in emergence of W serogroup ST-9316 from the original B serogroup. This was linked to an increase in incidence of W-IMD in children under the age of 4, with nearly all cases attributed to ST-9316.

Conclusions

Molecular epidemiology plays an important part in surveillance of meningococcal disease in both high and low-income countries. Understanding *N. meningitidis* virulence factors and trait acquisition results in better predictions of the dangers associated with newly emerging clonal complexes such as ST-9316.