

Evaluation of mumps IgG assay to retrospectively identify asymptomatic cases among vaccinated individuals for public health use

Background

Mumps infections in vaccinated persons are not uncommon but because the live attenuated mumps vaccine and wild-type mumps infection both induce IgG antibodies, it is difficult to identify asymptomatic infections based on antibody responses. This is of great importance for transmission studies since asymptomatic individuals might also be able to spread the disease, hence laboratory data might be able to identify missing links in transmission studies. The existing ELISA was validated using oral fluids to address a public health question rather than individual diagnostic. The study aims to elucidate if an ELISA (Microimmune) designed for mumps IgG detection in unvaccinated individuals is capable of identifying vaccinated individuals with an asymptomatic mumps infection and to assess the attack rate (AR) among vaccinated individuals in two epidemiological studies.

Methods

1) ELISA validation of commercial assay using control samples

The commercial available Microimmune assay was performed according to the manufacturers instructions, using OF pre-diluted 1:4.

Different cutoff values of the optical density (OD) were evaluated in the following groups to improve the ability to identify mumps virus infections (MVI)

- in the vaccinated group:
- MMR vaccinated (+MMR) and MVI-PCR positive
 - non-vaccinated (-MMR) and MVI-PCR positive
 - MMR vaccinated but never exposed to mumps (oral fluid collected prior to mumps circulated in the Netherlands)

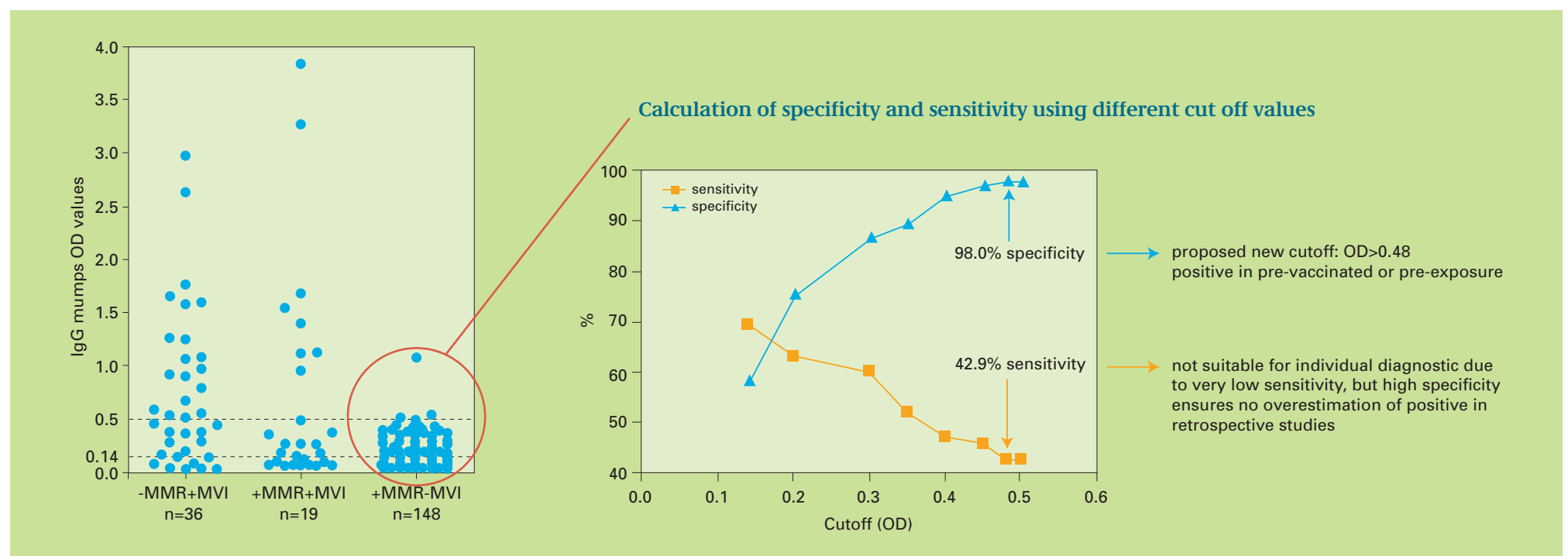
2) Application of newly defined cutoffs in epidemiological studies

The new cutoff values were applied to two ongoing studies and the lab-based attack rate (AR) was calculated.

- School study on 8 schools (n=1171) in the Dutch bible belt area to assess vaccine effectiveness during mumps outbreak.
- Family transmission study to assess mumps transmission from vaccinated individual to family members.

Results

1) ELISA validation of commercial assay using control samples



2) Performance of newly defined cutoffs in epidemiological studies

Dutch School study:

Oral fluids collected in the Netherlands during 2007-2008 were tested and the AR among the vaccinated, asymptomatic individuals was calculated.

	+MMR	-MMR
laboratory AR (%)	11.3	48.9
clinical AR (%)	1.6	52.7

→ Nearly 10% of MVI among vaccinated missed by purely epidemiological approach
 → VE(disease) = <95% vs VE(infection) = ~77%

Transmission study:

Oral fluids from household members and case collected

	+MMR	-MMR
laboratory AR (%)	8.9	0
clinical AR (%)	0	0

→ Nearly 9% of MVI among vaccinated household contacts identified using laboratory data
 → Evidence for household transmission

Conclusion

General

- Specific validation of a laboratory assay in public health investigations is absolutely essential!
- Depending on the study question sensitivity (individual diagnostic) or specificity (retrospective estimation) have to be priorities.
 Here, high specificity is important not high sensitivity to ensure no overestimation of asymptomatic cases.

For this study

- Transmission patterns during outbreaks can be retrospectively studied, taking asymptomatic cases into account.
- Virulence of different genotypes might be assessed by comparing AR/VE among vaccinated individuals.