Lipopolysaccharide (LPS) Specific Avidity of IgA and IgG antibodies in children given the Vivotif Vaccine and Typhoid patients in Bangladesh

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Typhoid vaccine

Two licensed vaccines are commercially available

1. **Parenteral Vi polysaccharide vaccine**

- ❖ Given single dose subcutaneously
- ❖ Recommended for use in person aged over 2 years

2. **Ty21a Live Oral Vaccine (Vivotif)**

- ❖ Requires 3 doses orally
- ❖ Not approved for use in children aged below 5 years

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Vaccine

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Evaluation of immune responses to an oral typhoid vaccine, Ty21a, in children from 2 to 5 years of age in Bangladesh

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ABSTRACT

Young children are very susceptible to typhoid fever, emphasizing the need for vaccination in under five age groups. The parenteral Vi polysaccharide vaccine is not immunogenic in children under 2 years and the oral Ty21a vaccine (Vivotif) available in capsular formulation is only recommended for those over 5 years.

We studied immune responses to a liquid formulation of Ty21a in children 2–5 years of age. Since children in developing countries are in general hypo responsive to oral vaccines, the study was designed to determine if anti-helminthic treatment prior to vaccination, improves responses.

In a pilot study in 20 children aged 4–5 years, the immune responses in plasma and in antibody in lymphocyte secretions (ALS) to the enteric coated capsule formulation of Ty21a was found to be comparable

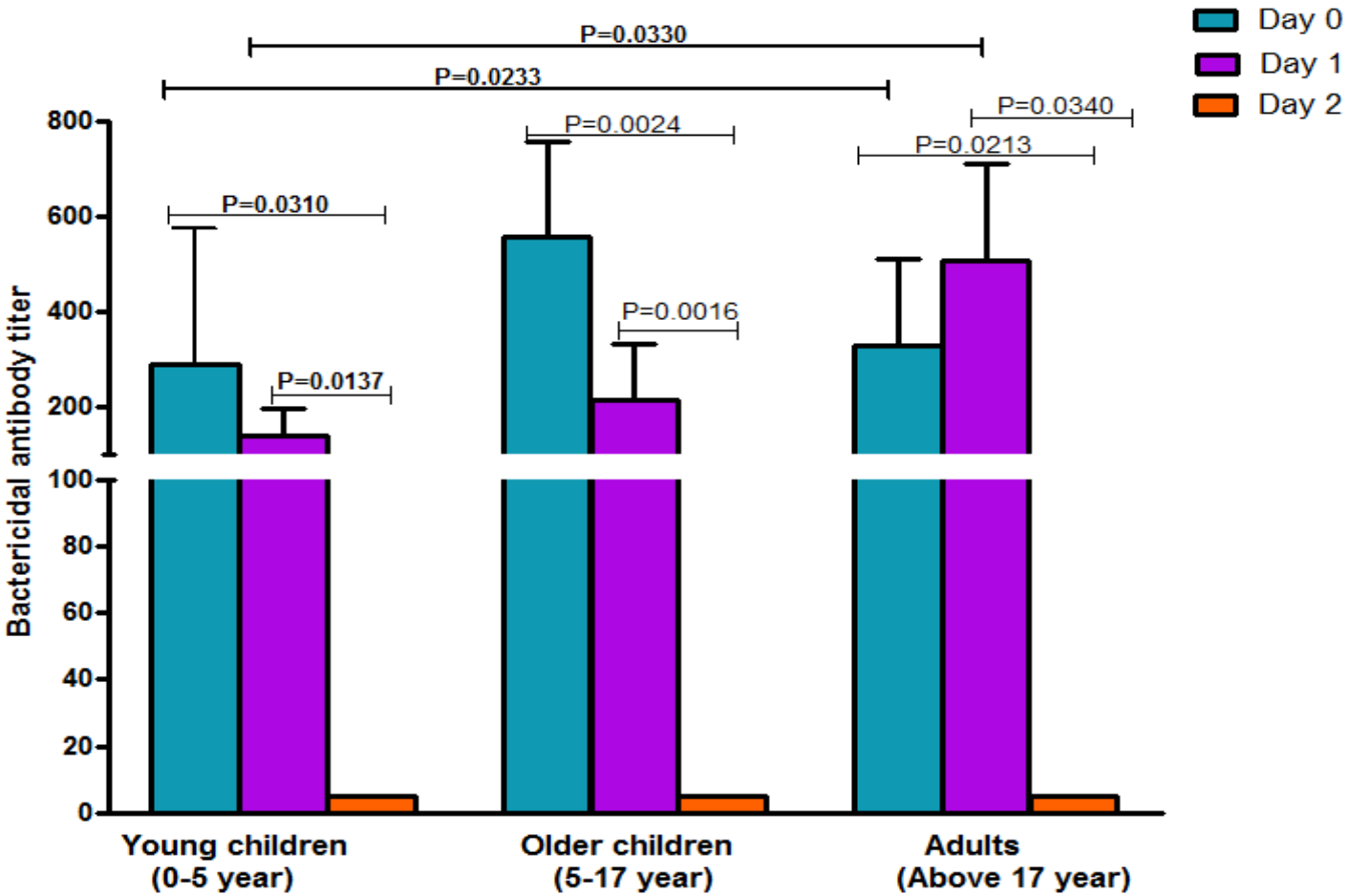
In order to better understand the immune response to the available and new vaccines we are evaluating the following methods:

- Bactericidal assay
- Opsonophagocytosis assay
- T cell responses
- **Antibody Avidity**

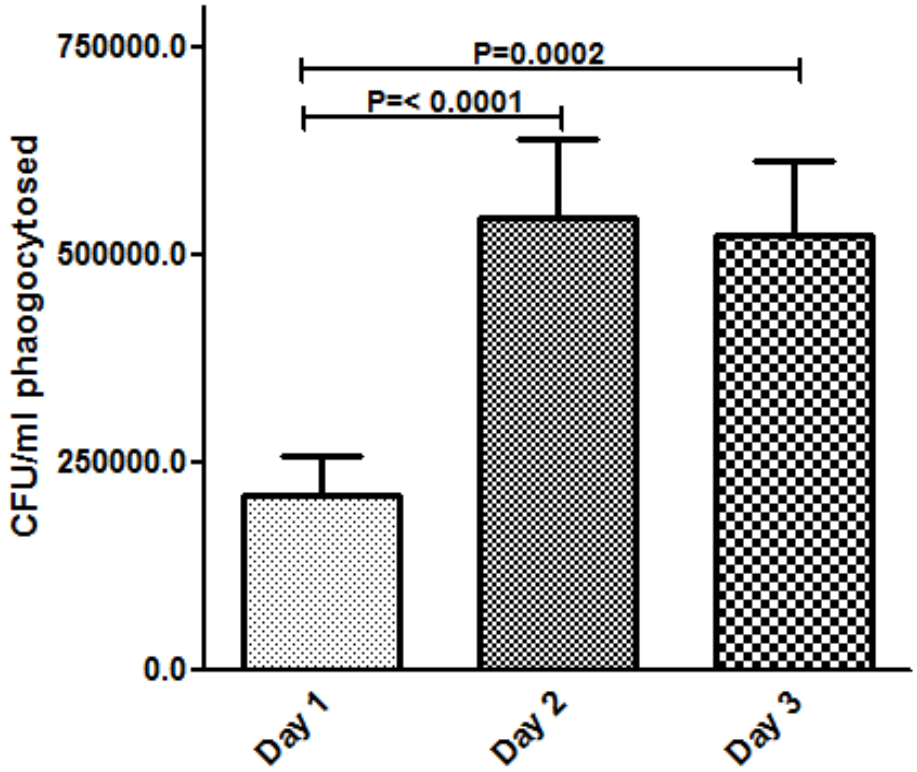
In patients with confirmed typhoid fever

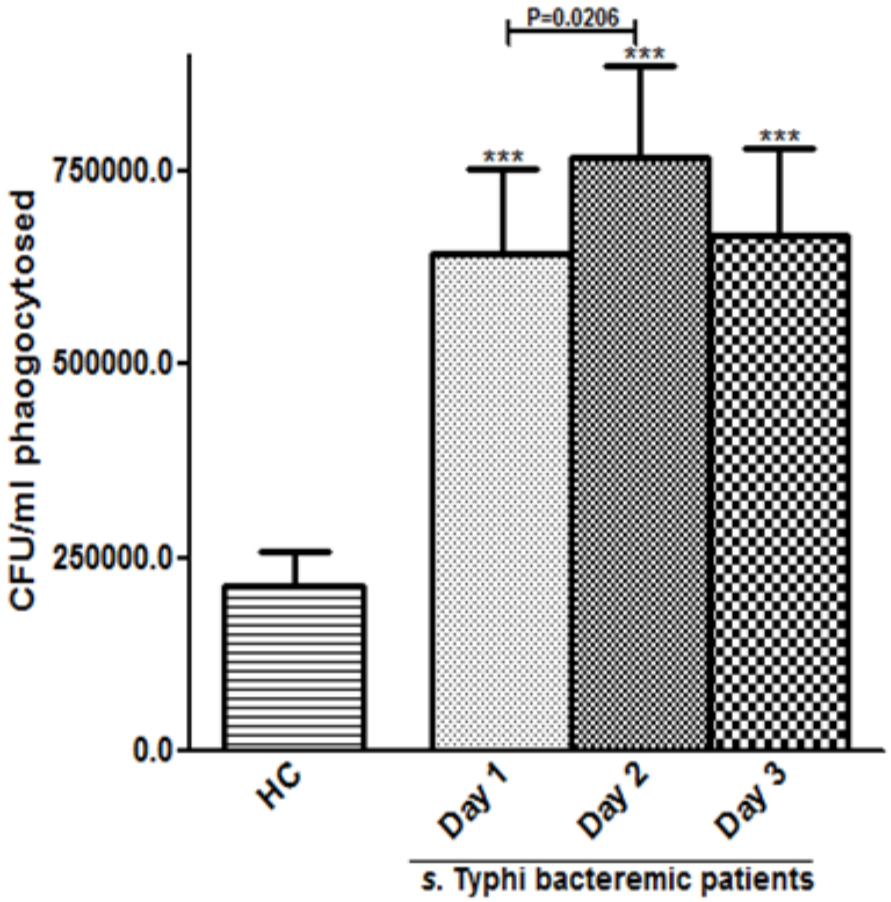
and in children vaccinated with the Ty21a live oral vaccine

Comparison of bactericidal antibody responses among typhoid fever patients



Opsonophagocytosis in vaccinees and typhoid fever patients





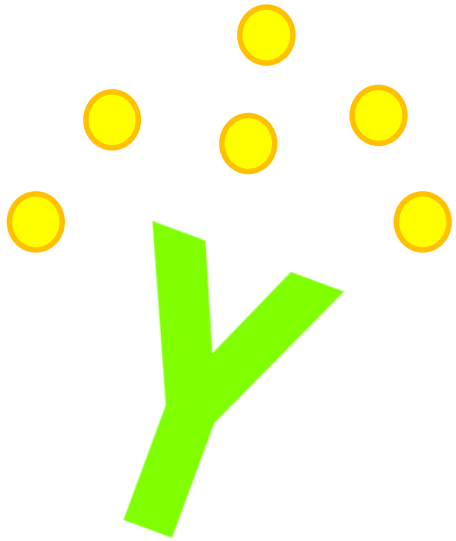
What is Avidity ?

Affinity

Avidity

Affinity
strength of interaction between a single epitope and a single paratope

Avidity
a measure of the overall strength of an antibody-antigen complex



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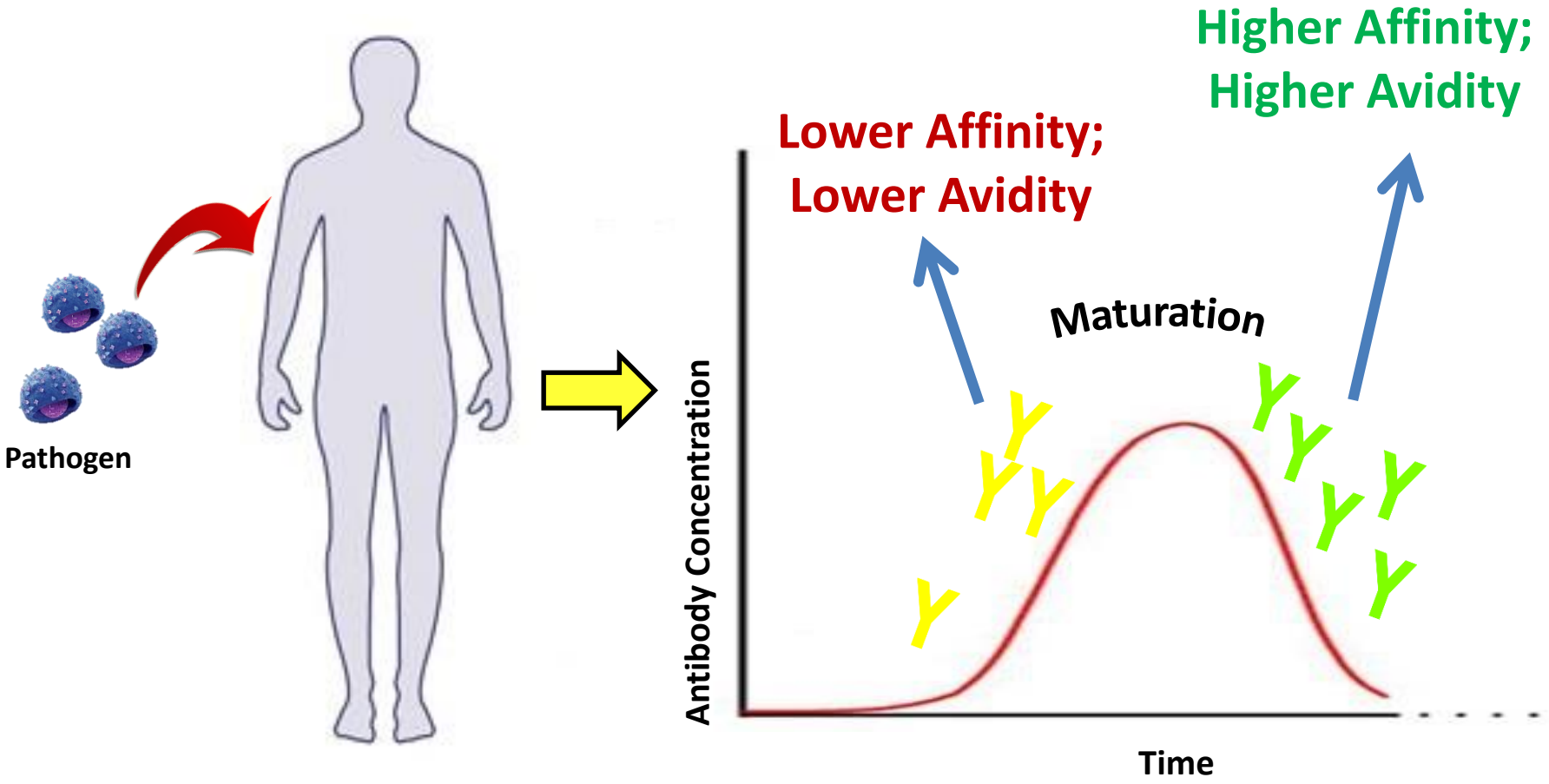
Avidity ELISA: The General Perspective



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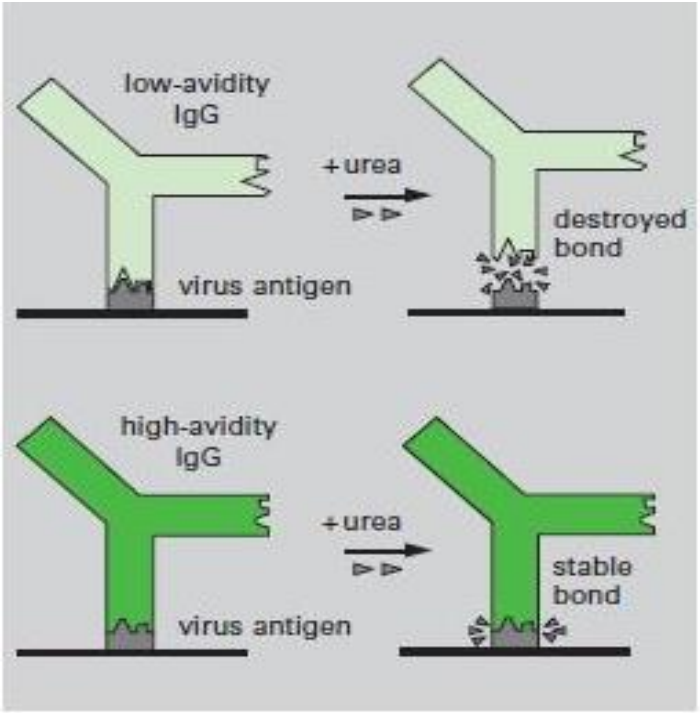
Avidity ELISA: The General Perspective

- During ELISA, treatment with chaotropic agents (like **urea** or **NaSCN**) can selectively dissociate the low-avidity antibodies generated early in the course of infection

- Such assays can be used as a tool to differentiate between acute and chronic infection



Avidity measurements in natural infections

- Distinguishing between a newly acquired (primary) and a preexisting (prolonged) infection in:

  - ❑ Cytomegalovirus (CMV) infection
  - ❑ Rubella Virus Infection
  - ❑ Human Immunodeficiency Virus (HIV)
  - ❑ *Neospora caninum* infection
  - ❑ *Toxoplasma gondii* infection
  - ❑ Dengue Virus Infection
  - ❑ Cholera and ETEC diarrheal patients

- To elucidate the efficacy of vaccination

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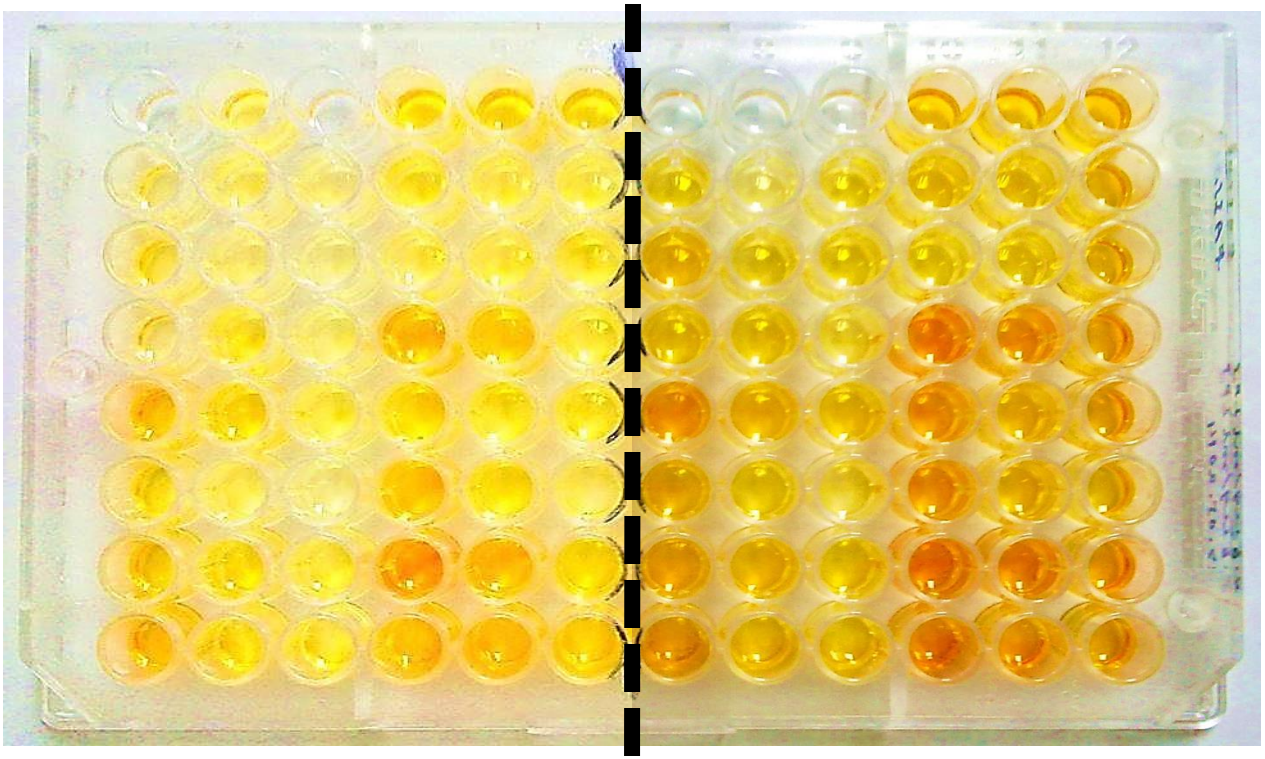
Avidity ELISA

2M NaSCN in 0.3% Tween PBS



Only 0.3% Tween PBS

The Avidity Index is the percentage of antibodies that remains bound at the antigen coat after the treatment with NaSCN

$$\text{A. I.} = \frac{\text{Optical density of the wells treated with chaotropic agent}}{\text{Optical density of the wells without treatment}} \text{ X 100}$$

Study Participants and specimens

Plasma from the *S*. Typhi bacteremic patients of three age groups **(young children: 1-5 years; older children: 6-17 years; and adults: 18-59 years)** at day of enrolment (day 1) and then day 7 (day 2) and 21 days later (day 3)

Plasma from the Vivotif vaccinees **(2-5 years)** immediately before the first immunization (day 1) and then 7 (day 2) and 21 days (day3) after the third vaccination

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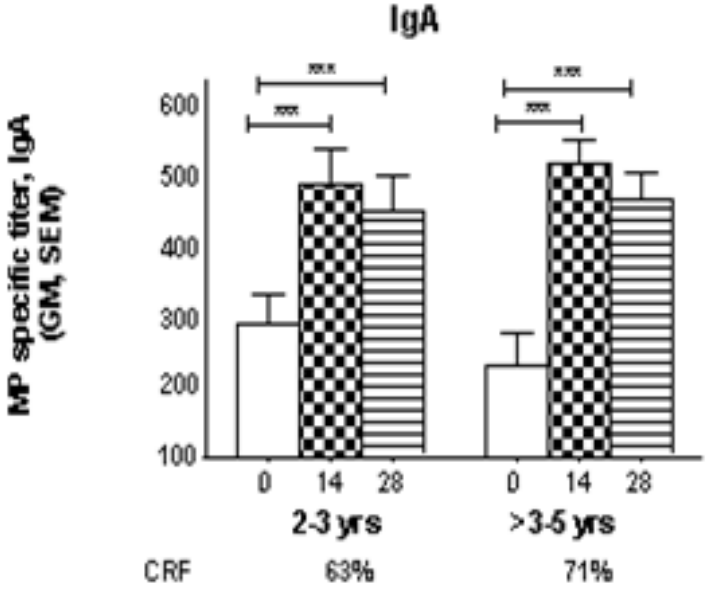
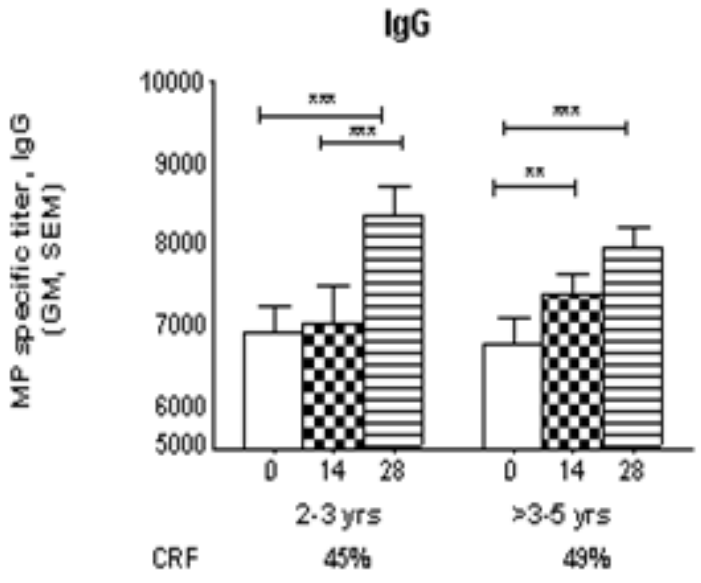
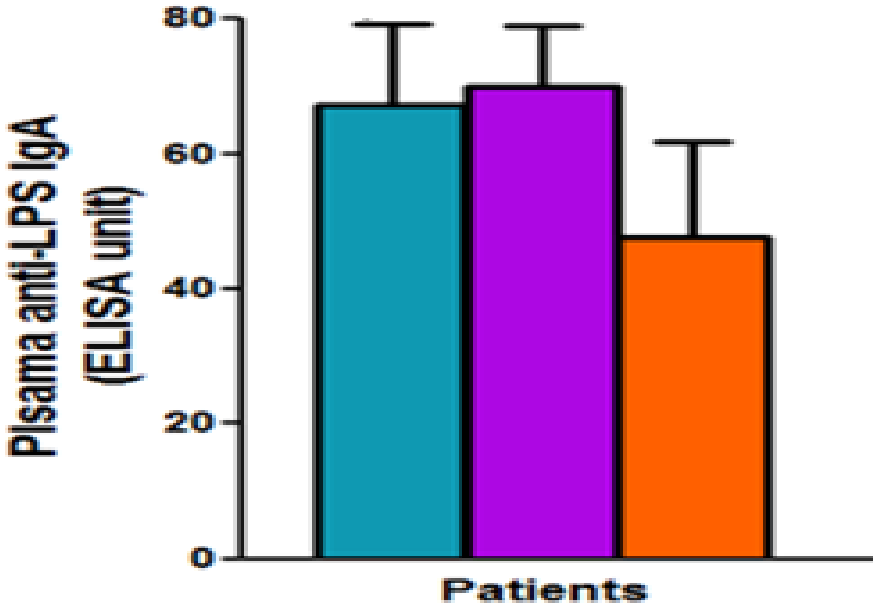
Result

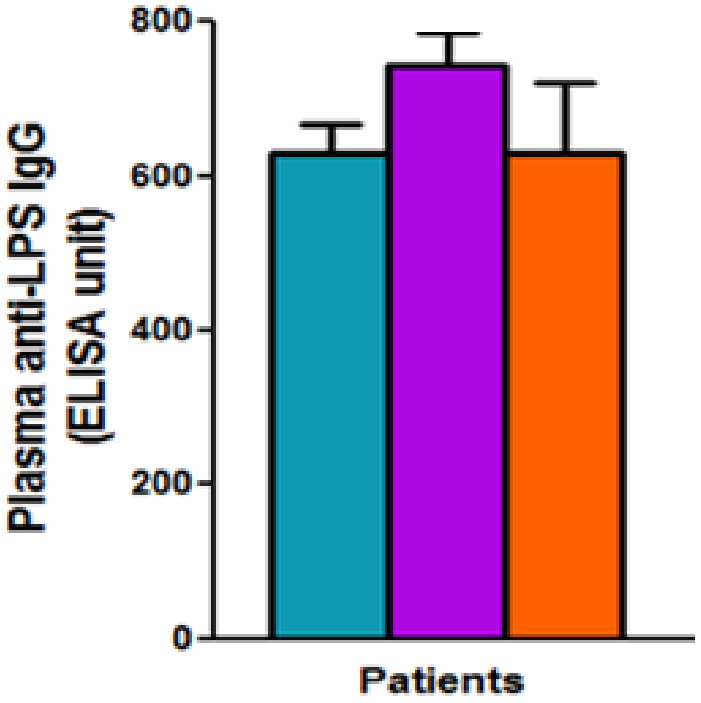
Plasma antibody responses in vaccinees



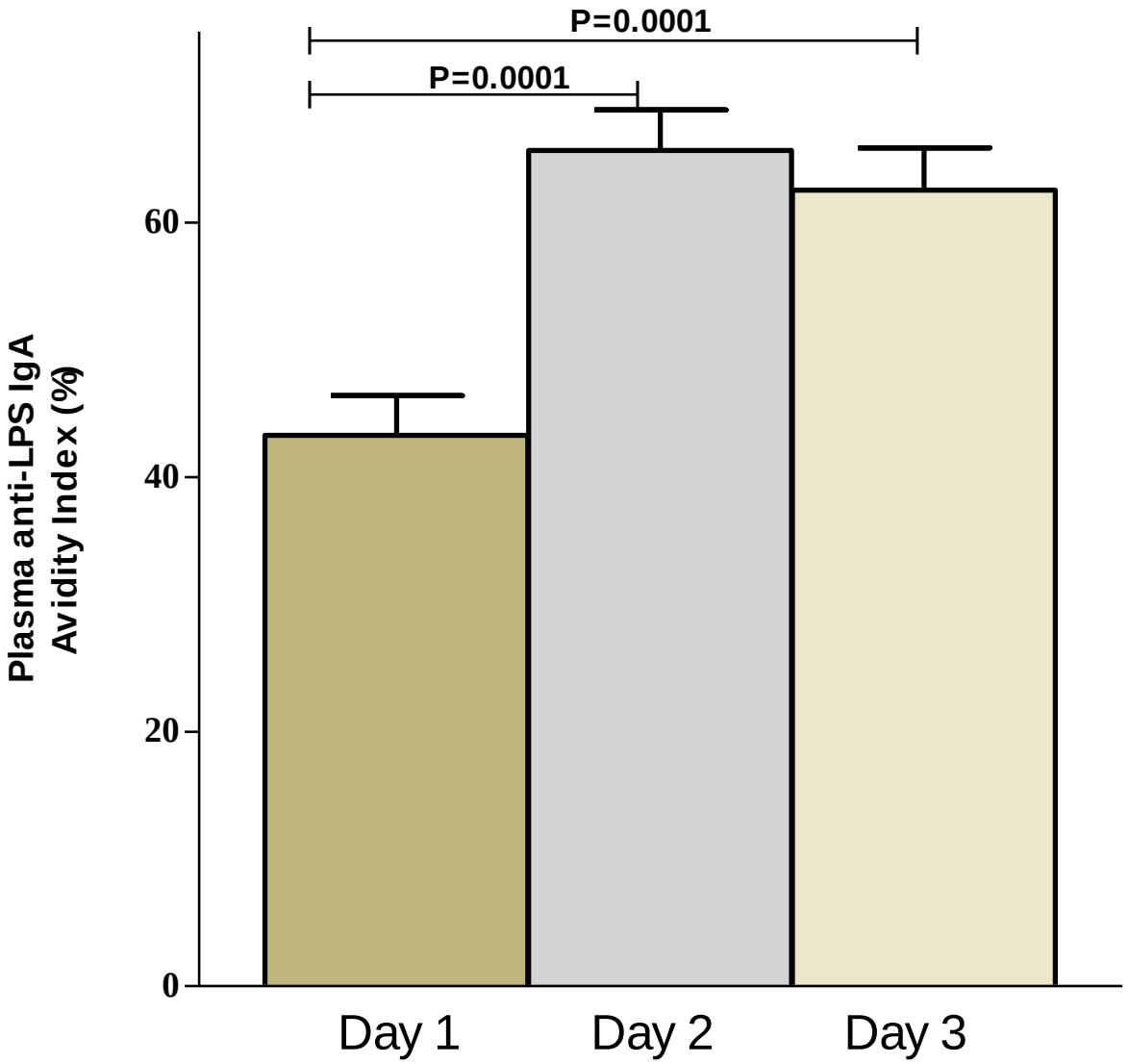


Plasma antibody responses in patients

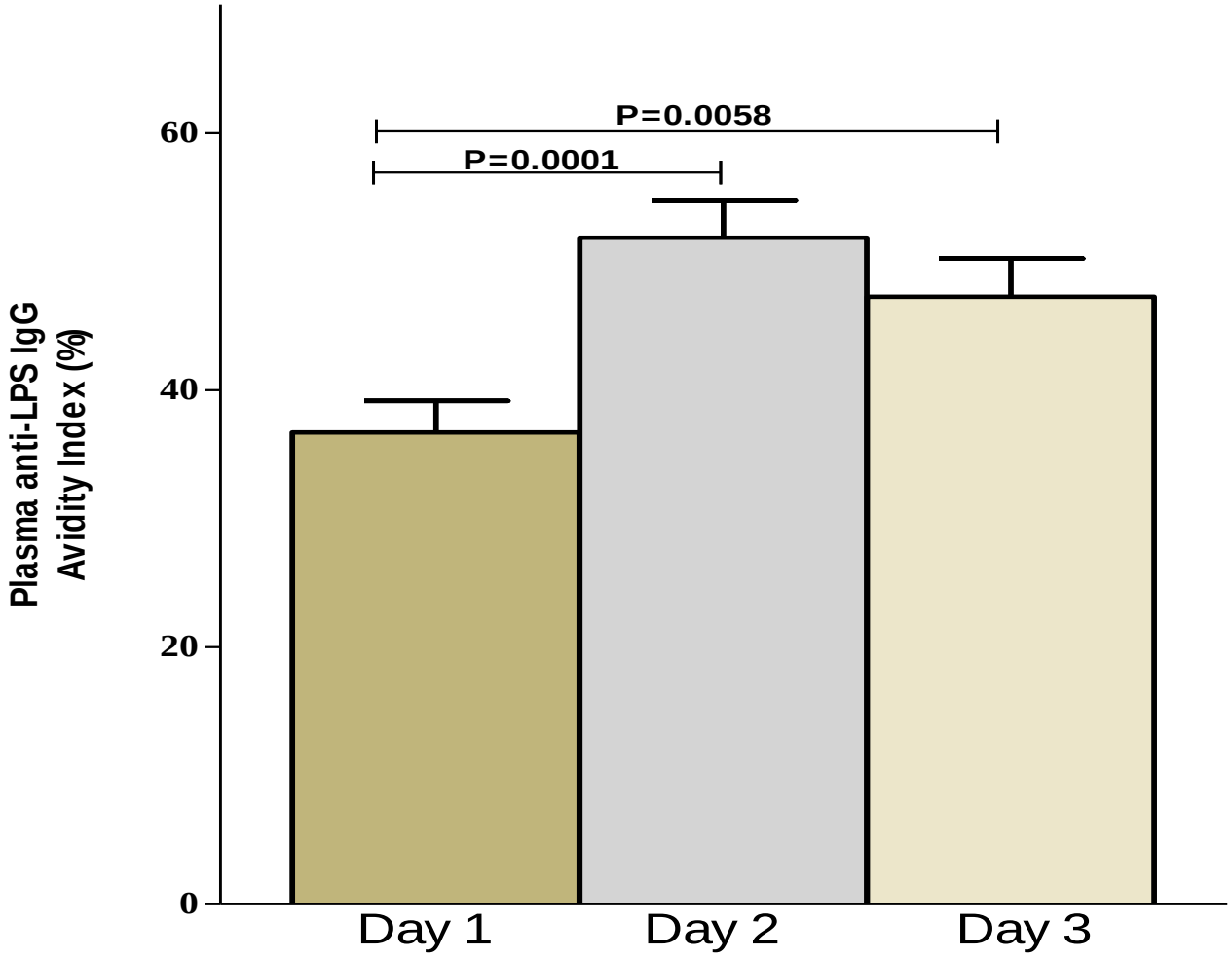




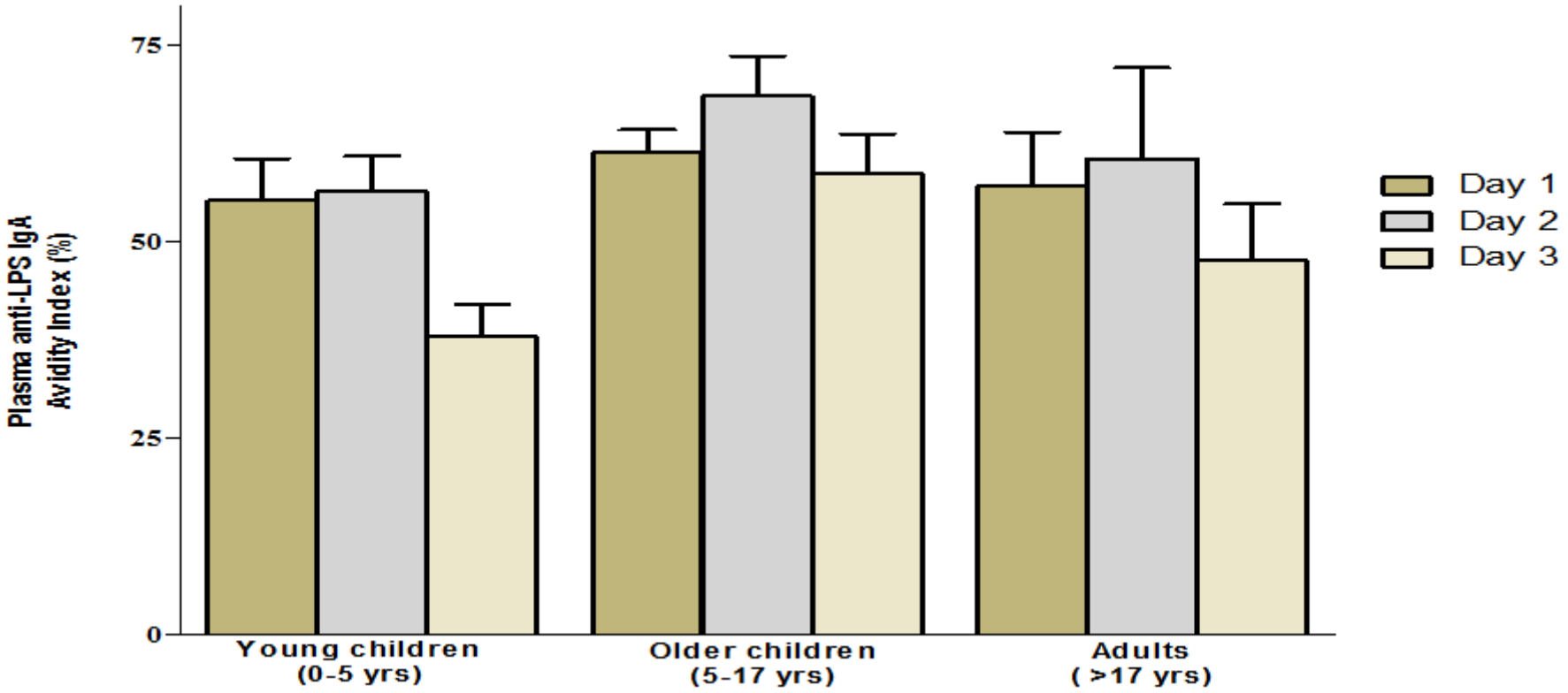
LPS-IgA avidity indices in vaccinees



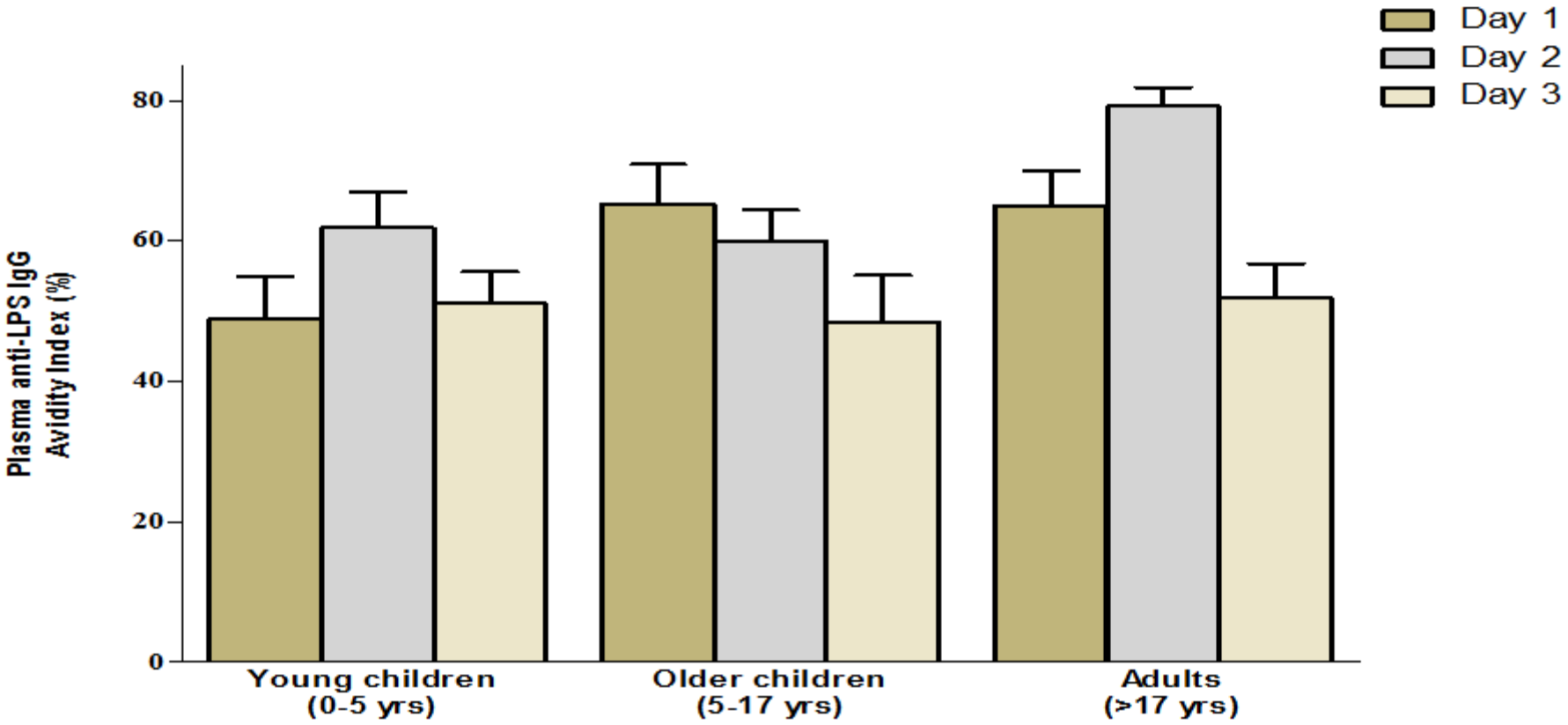
LPS-IgG avidity indices in vaccinees



LPS-IgA avidity indices in *S.* Typhi bacteremic patients



LPS-IgG avidity indices in *S.* Typhi bacteremic patients



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Conclusion

The patients mounted LPS-IgA and IgG antibodies with high avidity

The vaccinees had significant higher antibody avidity after vaccination

The avidity ELISA can be helpful to evaluate immunogenicity of the upcoming conjugate vaccines

We plan to analyze other immunological parameters to better understand the functional role of these antibodies

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