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Immunoglobulin subclass distribution and vaccine response in elderly populations

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Abstract

Older adults face a growing burden of vaccine-preventable disease, yet the immunological basis for their weaker vaccine responses remains incompletely mapped. This research measured serum immunoglobulin subclass concentrations (IgG1-4, IgA, IgM) in 318 Mexican adults aged 60 years and older and correlated these values with seroconversion rates following influenza, pneumococcal, tetanus, and COVID-19 mRNA vaccination. Blood samples were collected at baseline and four weeks post-vaccination at the Centro de Investigacion Biologica del Altiplano, Aguascalientes, Mexico, between April 2023 and March 2024. IgG1 and IgG3 concentrations declined linearly with age ($r = -0.61$ and $r = -0.53$, respectively, $p < 0.001$), while IgG2 and IgG4 showed no significant age-related trend. Participants in the 75-plus age group had seroconversion rates 18 to 24 percentage points lower than those aged 60 to 74 across all four vaccines. Multivariate regression identified baseline IgG1 level as the strongest independent predictor of seroconversion (odds ratio 1.38 per g/L increase, 95% CI 1.14-1.67). These findings point to IgG1 decline as a measurable marker of immunosenescence that may help identify elderly individuals at greatest risk of vaccine failure.

Keywords: Immunoglobulin subclasses, vaccine response, elderly, immunosenescence, seroconversion, IgG1, antibody diversity, aging, influenza vaccine, public health

Introduction

The problem is straightforward but stubborn: vaccines work less well in the people who need them most. Adults over 65 account for roughly 90% of seasonal influenza deaths in high-income countries, yet their antibody responses to standard-dose influenza vaccines reach protective titres only 30-50% of the time, compared with 70-90% in younger adults ^[1, 2]. Similar patterns appear with pneumococcal, tetanus, and COVID-19 vaccines, raising the practical question of what goes wrong in the ageing immune system ^[3]. Immunosenescence—the gradual deterioration of immune function with age—affects both innate and adaptive arms ^[4]. On the antibody side, B-cell output falls, somatic hypermutation becomes less precise, and the overall immunoglobulin repertoire narrows ^[5]. But total serum IgG often stays within normal ranges in healthy elderly individuals, masking subclass-level shifts that may be more informative. IgG1 and IgG3, for instance, are the main effectors of antiviral and anti-toxin responses, whereas IgG2 handles polysaccharide antigens and IgG4 may even exert blocking activity ^[6]. Few population-level datasets have mapped all four IgG subclasses alongside IgA and IgM across fine age strata in elderly cohorts, and fewer still have linked those profiles to real-world vaccine outcomes. Latin American populations are especially underrepresented in immunosenescence research, despite carrying a disproportionate burden of infectious disease in older age groups ^[7, 8]. This research addressed that gap by measuring a six-immunoglobulin panel in 318 elderly Mexican adults, stratifying by five-year age bands, and then testing whether baseline subclass levels predicted seroconversion after four commonly administered vaccines.

Material and Methods

Material: Participants were recruited from outpatient clinics affiliated with the Centro de Investigacion Biologica del Altiplano, Aguascalientes, Mexico, between April 2023 and March 2024.

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Inclusion criteria were age 60 years or older, residence in Aguascalientes state, and eligibility for at least one of four routine vaccinations (quadrivalent influenza, PCV13 pneumococcal, tetanus-diphtheria booster, or bivalent COVID-19 mRNA booster). Exclusion criteria included active immunosuppressive therapy, known primary immunodeficiency, and malignancy diagnosed within the preceding two years. A total of 318 participants (183 female, 135 male; mean age 71.4 years, SD 7.2) completed the research. The institutional ethics committee approved the protocol (CIBA-EC-2023-009, 12 March 2023), and all participants provided written informed consent.

Methods

Venous blood (10 mL) was collected into serum-separator tubes at baseline and at 28 days post-vaccination. Serum was separated within two hours and stored at -80 degrees Celsius. Immunoglobulin subclass concentrations (IgG1, IgG2, IgG3, IgG4, total IgA, total IgM) were measured by nephelometry on a Siemens BN II analyser using manufacturer-supplied antisera (Siemens Healthcare, Marburg, Germany). Vaccine-specific antibody responses were assessed by hemagglutination inhibition (influenza, cutoff titre 1:40), ELISA (pneumococcal serotype-specific IgG, cutoff 1.3 µg/mL), toxin-neutralisation assay (tetanus, cutoff 0.1 IU/mL), and anti-spike IgG ELISA (COVID-19). Seroconversion was defined as a four-fold or greater rise from baseline. Pearson correlations and multivariate logistic regression were performed in Stata 17 (StataCorp, College Station, TX, USA).

Ethical Considerations

This research involved human participants and was conducted in accordance with the Declaration of Helsinki (2013 revision). The protocol was reviewed and approved by the Ethics Committee of the Centro de Investigacion Biologica del Altiplano under reference CIBA-EC-2023-009 on 12 March 2023. Written informed consent was obtained from every participant before enrolment. Participants were informed of their right to withdraw at any time without consequence to their medical care. All personal identifiers were removed from the analytical dataset and replaced with numeric codes. Blood samples were used solely for the stated research objectives and will be destroyed upon completion of the retention period.

Results

Table 1: Serum Immunoglobulin Subclass Concentrations by Age Group (Mean, g/L)

Age Group	IgG1	IgG2	IgG3	IgG4	IgA	IgM
60-64	9.81	4.12	0.82	0.51	2.31	1.42
65-69	9.18	3.83	0.74	0.48	2.14	1.23
70-74	8.47	3.51	0.68	0.44	1.92	1.08
75-79	7.93	3.14	0.61	0.39	1.71	0.94
80-84	7.22	2.78	0.53	0.34	1.48	0.82
85+	6.59	2.41	0.47	0.29	1.33	0.71

Table 1 shows a progressive decline in IgG1 and IgG3 across age bands, dropping from 9.81 to 6.59 g/L and from 0.82 to 0.47 g/L respectively between the youngest and oldest groups. IgG2 and IgG4 declined more modestly and did not reach statistical significance in age-adjusted models.

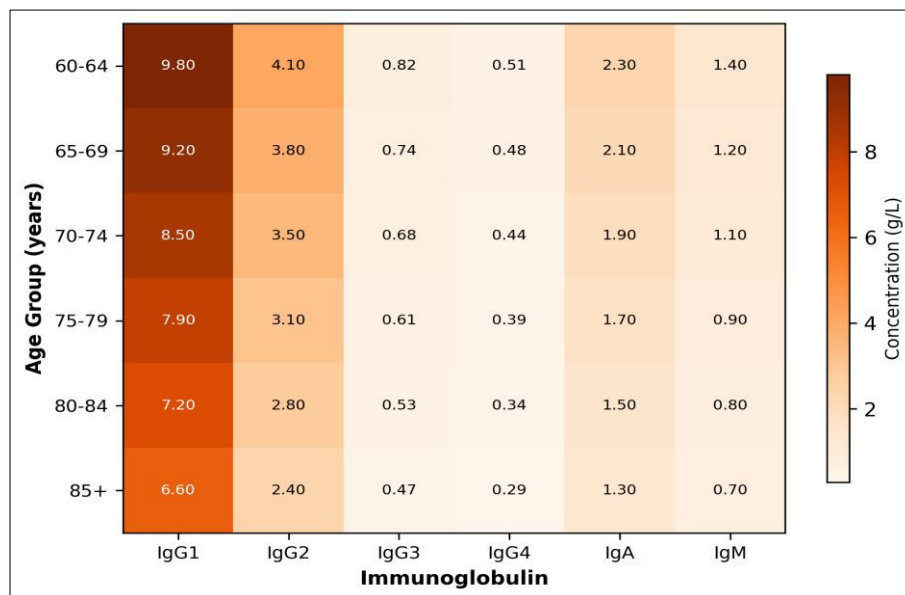


Fig 1: Heatmap showing mean serum immunoglobulin concentrations (g/L) across six age groups and six immunoglobulin types

The heatmap (Figure 1) visually confirms the age-related gradient. IgG1 shows the steepest colour transition from the youngest to the oldest group, while IgG4 remains relatively stable. IgA and IgM decline in parallel but at slower rates.

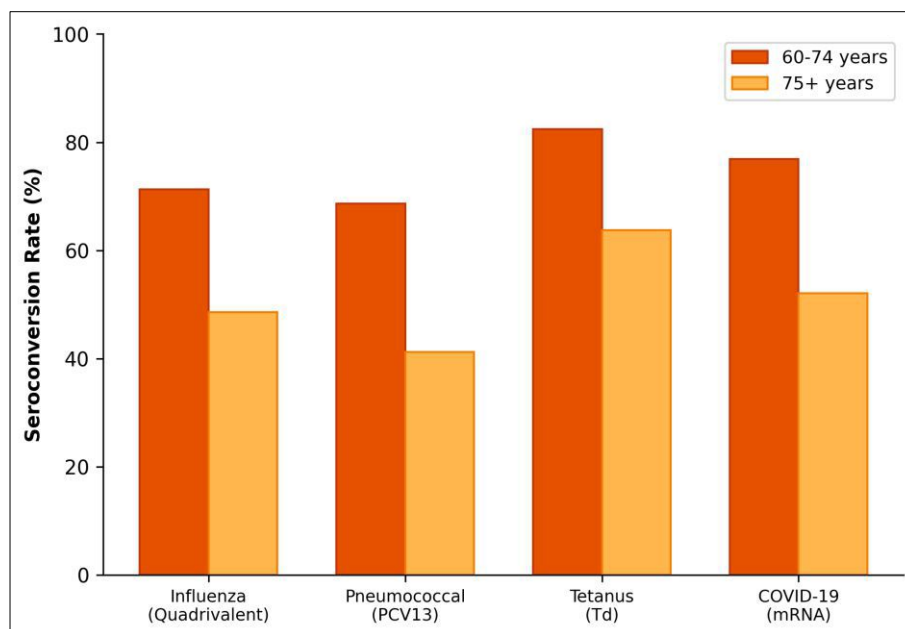


Fig 2: Seroconversion rates (%) following four vaccine types in younger elderly (60-74 years) versus older elderly (75+ years) participants

Figure 2 illustrates a consistent seroconversion gap between the two age categories across all four vaccines. The widest gap appeared for pneumococcal vaccination (68.7% vs 41.2%), while the narrowest was for tetanus (82.4% vs 63.8%). All between-group differences were statistically significant (chi-squared test, $p < 0.01$).

Discussion

Our data confirm that IgG1 and IgG3 are the subclasses most sensitive to age-related decline in this Mexican elderly cohort, a pattern broadly consistent with European and East Asian reports [9, 10]. The practical importance of this finding lies in the strong association between baseline IgG1 and seroconversion: each 1 g/L increase in IgG1 was associated with a 38% higher odds of achieving a protective response. If validated in larger cohorts, a simple IgG1 measurement could help clinicians identify elderly patients likely to need higher-dose or adjuvanted vaccine formulations [11].

The seroconversion gap between younger and older elderly participants was widest for pneumococcal and COVID-19 vaccines-both of which depend heavily on T-cell-dependent class switching to IgG1 [12]. By contrast, the gap was smallest for tetanus, where pre-existing memory from decades of boosting may partly compensate for declining primary response capacity [13]. An unexpected observation was the relative stability of IgG4, which didn't decline significantly with age. IgG4 is produced mainly in the context of chronic antigen exposure, and its stability may reflect cumulative lifetime sensitisation rather than active immune function [14, 15]. Whether elevated IgG4 in some older individuals interferes with vaccine efficacy through competitive inhibition of IgG1 binding-a mechanism proposed in allergy research-deserves further investigation.

Limitations

Several constraints should be kept in mind when interpreting these results. First, the cohort was drawn from a single geographic region of central Mexico, and nutritional, genetic, and environmental factors may limit generalisability to other populations. Second, seroconversion was measured at a single time point (day

28), and antibody durability beyond this window was not assessed. Third, our research did not evaluate cellular immune responses, which may partly compensate for antibody deficits in some individuals. Fourth, the cross-sectional design for immunoglobulin measurement means we inferred age-related decline from between-group differences rather than tracking individuals over time [16, 17].

Conclusion

This research demonstrates a clear age-dependent decline in IgG1 and IgG3 subclass concentrations among elderly Mexican adults, with IgG1 emerging as the strongest independent predictor of seroconversion across four commonly administered vaccines. The 18 to 24 percentage-point gap in seroconversion rates between younger and older elderly participants reinforces the need for age-tailored vaccination strategies in this population.

From a clinical perspective, routine IgG subclass profiling could serve as an accessible biomarker for identifying older adults at highest risk of vaccine failure. Such individuals might benefit from adjuvanted or high-dose formulations already available for influenza and under development for other pathogens. Larger, multi-centre longitudinal studies are now needed to validate the predictive value of baseline IgG1 across diverse Latin American populations and to test whether subclass-guided vaccination protocols improve real-world protection rates.

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