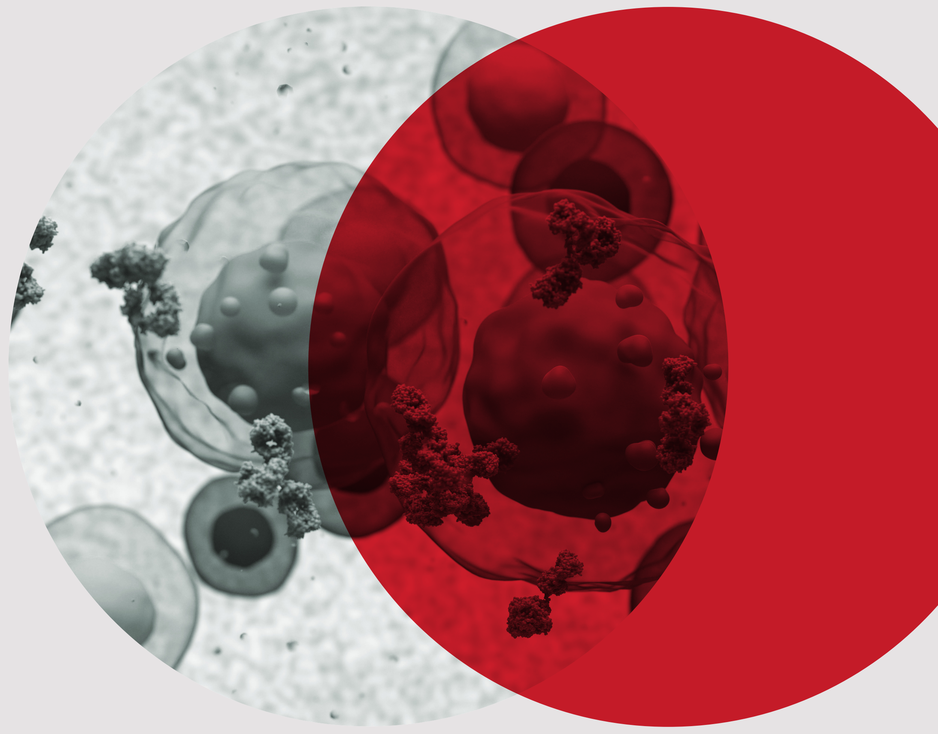
Variation in reporting of fractions in serum protein electrophoresis



Vraj Evans, Zoe Vayanos, Peter Graham

The Royal College of Pathologists of Australasia Quality Assurance Programs (RCPAQAP), St Leonards, Sydney

Introduction

Serum protein electrophoresis (EPG) is commonly requested to aid diagnosis of plasma cell dyscrasias and lymphoproliferative disorders through detection of monoclonal immunoglobulins[2]. In 2022, the RCPAQAP introduced reporting of serum protein electrophoresis fractions, albumin, alpha-1, alpha-2, beta, beta-1, beta-2, and gamma, in the Paraproteins program. A high variation in reporting results for certain fractions was noted. We sought to review this heterogeneity.

Method

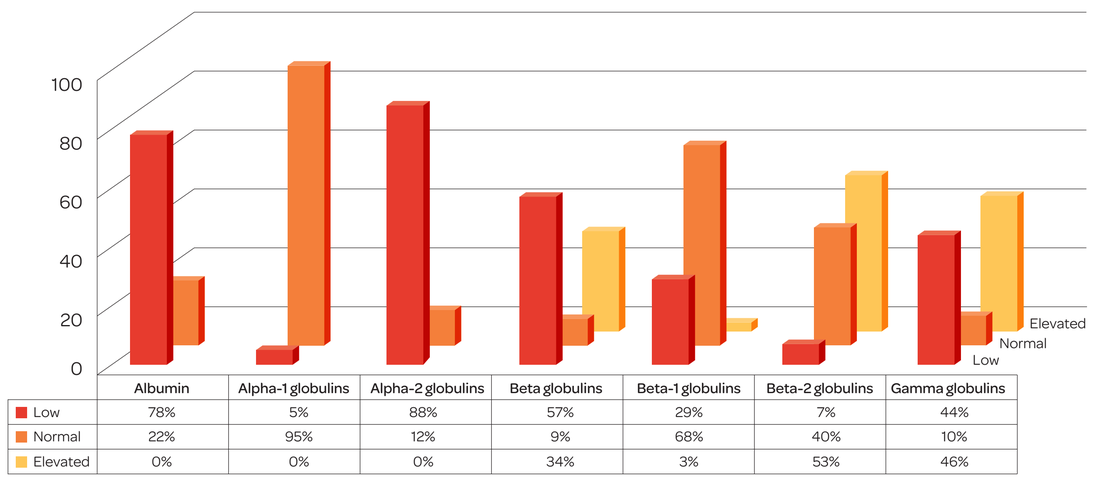
The qualitative results (low, normal or elevated) for protein fractions submitted by participating laboratories were compared and reviewed using RCPAQAP inhouse software. Results for samples containing monoclonal bands were further assessed given their clinical significance.

Results

Qualitative interpretations (on the same samples) varied across all fractions. The widest variation of results was found in a sample sourced from a consenting donor presenting with a monoclonal gammopathy (as reported in Survey 6). Table 1 and Figure 1 show the heterogenous reporting for Survey 6 for all protein fractions. This sample returned gamma result interpretations varying from "low" (n=26), "normal" (n=6), and "elevated" (n= 27). Beta 2 showed similar differences. The donor presented with an IgM Lambda monoclonal immunoglobulin band and was reported the same by >80% of all participants. No consensus (<80%) was reached for identification of the region/fraction of the paraprotein. Similar variation was noted for all other 2022 surveys, primarily in the beta, beta-2 and gamma regions, but when monoclonal bands were present, there was no evidence of identification of a band being missed from any of the three regions.

Table 1. Number of participants reporting protein fraction interpretations for sample IM-PP-22-06.

Survey 6 (IM-PP-22-06)	Low	Normal	Elevated	Consensus reached
Albumin	47	13	0	✗
Alpha-1 globulins	3	57	0	✓
Alpha-2 globulins	53	7	0	✓
Beta globulins	20	3	12	✗
Beta-1 globulins	9	21	1	✗
Beta-2 globulins	2	12	16	✗
Gamma globulins	26	6	27	✗



	Albumin	Alpha-1 globulins	Alpha-2 globulins	Beta globulins	Beta-1 globulins	Beta-2 globulins	Gamma globulins
Low	78%	5%	88%	57%	29%	7%	44%
Normal	22%	95%	12%	9%	68%	40%	10%
Elevated	0%	0%	0%	34%	3%	53%	46%

Figure 1. Variation in protein fraction results for sample IM-PP-22-06 as a percentage of the total number of participating laboratories.

Discussion

Qualitative reporting of paraproteins is an important component of patient diagnosis and management. Variation in RCPAQAP protein fraction results submitted for samples containing monoclonal bands is consistent with other studies on patient samples[2]. We propose three potential contributors to this lack of harmonisation:

1. The practice of reporting residual gamma (i.e. after subtracting the monoclonal immunoglobulins) versus total globulin. This may be intended to assist patients with hypogammaglobinaemia, who are at higher risk of infections, to meet the criteria for intravenous immune globulin (IVIG) therapy. To assist in identifying this further, we have since requested that our participants report total gamma, as well as enabling a residual gamma option in the 2023 Paraproteins program.
2. Method differences; e.g. capillary electrophoresis versus densitometric. We note a distinct variation in reporting protein fractions for these two methods.
3. Variation in methods should also reflect in the reference intervals being applied. Technically, appropriate reference intervals should serve to harmonise qualitative interpretations, however this still relies on consistent interpretation of the protein migration patterns.

Conclusion

Reporting of accurate total protein fractions is of important clinical significance to understand conditions like, inflammation, nephrotic syndrome, cirrhosis or chronic liver disease, malnutrition, alpha-1 antitrypsin deficiency, haemolysis and dehydration[1]. The practice of reporting residual versus total gamma globulin appears to be a contributing factor to the variation in reporting of protein electrophoresis fractions. Consideration should be given to options to minimise the potential sources of variation in paraprotein reporting as proposed by others[2,3].

References:

1. Ramanathan, S., Srinivas, C. N. Serum Protein Electrophoresis and Its Clinical Applications. In: Bobbarala, V., Zaman, G. S., Desa, M. N. M., Akim, A. M., editors. Biochemical Testing - Clinical Correlation and Diagnosis [Internet]. London: IntechOpen; 2019 [cited 2023 Jan 06]. Available from: https://www.intechopen.com/chapters/69537 doi: 10.5772/intechopen.88367.
2. Tate J, Caldwell G, Daly J, et al. Recommendations for standardized reporting of protein electrophoresis in Australia and New Zealand. Annals of Clinical Biochemistry. 2012;49(3):242-256. doi:10.1258/acb.2011.011158.
3. Wijeratne N, Tate JR, Wienholt L, et al. Report of the survey conducted by RCPAQAP on current practice for paraprotein and serum free light chain measurement and reporting: a need for harmonisation. Clin Biochem Rev 2019; 40: 31–42.

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