Case report

Navigating the challenge: Selecting the optimal assay for serum albumin measurement

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Article Info

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Keywords

serum albumin, nephrotic syndrome, Bromocresol green, Bromocresol purple

Abstract

Background: Photometric techniques are the most common methods for measuring serum albumin, where albumin binds with an organic dye to form a complex. These methods are popular due to their simplicity, automation potential, speed, and cost-effectiveness, with bromocresol green (BCG) and bromocresol purple (BCP) being the most frequently used dyes.

Case presentation: A 2-year-old boy presented with facial swelling, starting around the eyes in the morning and gradually spreading to the face, improving by evening, and accompanied by reduced urine output. He was diagnosed with nephrotic syndrome and treated with a high-calorie, high-protein diet, oral prednisolone, furosemide, and intravenous albumin. Despite treatment, his local laboratory's serum albumin level remained consistently low. However, tests from a private lab showed levels higher than the state lab. The nephrology team was informed of this discrepancy and chose to rely on the private lab's results.

Conclusion: A comparison study between BCP and BCG methods found a good correlation overall, but Bland-Altman analysis revealed that BCG had a significant positive bias compared to BCP, explaining the lab discrepancies. The study underscored the importance of clinician awareness of different serum albumin measurement methods, noting that BCP is more specific and does not overestimate albumin in kidney disease patients like BCG does.

Introduction

Serum albumin is a key biomarker for assessing nutritional status, liver function, and kidney health [1,2]. Accurate measurement is vital for proper diagnosis and management of various conditions. Photometric methods, using dyes like Bromocresol Green (BCG) and Bromocresol Purple (BCP), are widely used due to their efficiency and cost-effectiveness [3,4]. While both dyes are commonly employed, the choice between BCG and BCP can affect result accuracy, particularly in patients with conditions such as kidney disease [5]. Understanding these methods helps ensure precise diagnosis and treatment.

Case presentation

A 2-year-old male patient presented with facial swelling, first noticed around the peri-orbital region upon waking. The swelling gradually spread across the face throughout the day but lessened by evening. In addition, the child had a marked decrease in urine output, suggesting potential renal pathology. Aside from the facial swelling, other general and systemic examinations were normal. Based on the clinical presentation and investigative findings, a diagnosis of nephrotic syndrome was made, and the child was admitted for further assessment and treatment.

Upon admission, the child was started on a comprehensive treatment plan aimed at addressing the nephrotic syndrome. This regimen included a high-calorie, high-protein diet to support his nutritional needs, along with oral prednisolone to reduce inflammation and manage the disease process. In addition, furosemide, a diuretic, was prescribed to help alleviate fluid retention, and intravenous albumin was administered to replenish the low serum albumin levels commonly associated with nephrotic syndrome.

Despite this aggressive treatment approach, the serum albumin levels, as measured by the local laboratory, remained critically low at 6 g/L (with a normal reference range of 35–50 g/L). This persistently low reading was concerning, as it suggested ongoing hypoalbuminemia despite therapeutic interventions. To investigate further, serum albumin levels were also assessed at a private laboratory, where the results indicated significantly higher levels, ranging between 15–20 g/L (35–50 g/L).

The nephrology team carefully reviewed the discrepancies between local and private lab results and, noting the impact of inaccurate albumin measurements on treatment, opted to rely on the private lab's results, which aligned with the clinical picture. A comparison study of the BCP and BCG methods was conducted to address this discrepancy.

However, based on the findings of the comparative study, the patient was provided with an additional albumin supplement, which resulted in improvements in oedema, proteinuria, and the overall clinical condition, that helped the nephrologist to decide on accurate treatment.

Differential Diagnosis

Given the diagnosis of nephrotic syndrome and the persistently low serum albumin levels, two main differential diagnoses were considered:

was excluded, as the prescribed dosages were appropriate and aligned with the standard treatment protocols.

Serum Albumin Assay Discrepancies

The other concern was the accuracy of the serum albumin measurements. The significant difference between the local laboratory and the private laboratory results led to the consideration of assay discrepancies. This was likely due to the use of different methods for measuring albumin, with the local lab potentially using a more specific but less reliable method for hypoalbuminemia cases (BCP), and the private lab using a method (BCG) that was more consistent with the clinical picture. After careful review, this assay discrepancy was deemed the likely explanation for the low serum albumin levels reported by the local lab.

Thus, the assay discrepancy was identified as the primary cause of the differing albumin results, rather than a suboptimal treatment regimen.

Diagnostic Workup

To evaluate the situation, the following steps were undertaken:

A total of 59 anonymized serum samples were randomly selected and analyzed using three analyzers: Dimension EXL 200 (BCP assay), Cobas c 311 (BCG assay), and Beckman Coulter AU 480 (BCG assay). The results were compared using linear regression and Bland-Altman methods. Additionally, 16 more samples were tested with the Dimension BCP method and compared with results from an external lab using the Abbott Architect Plus C8000 (BCP assay). The comparison was analyzed through linear regression, with statistical analysis performed in Excel (version 1808).

Results

Before testing patient samples, quality control checks were performed, with all results falling within acceptable ranges. The BCP method, serving as the reference standard, was compared with the BCG method to evaluate its accuracy.

The analytical measurement ranges for serum albumin are 6–80 g/L on the Dimension EXL 200, 2–60 g/L on the Cobas c 311, and 15–60 g/L on the Beckman AU 480. Our serum albumin samples ranged from 4–50 g/L. The comparison plots showed that these samples covered the entire analytical measurement range, demonstrating a linear relationship between the BCP and BCG methods within this range (Figure 1 and 2).

Bland-Altman plot (Figure 4) indicated that the Cobas c 311 BCG assay was positively biased compared with Dimension EXL 200 BCP method; producing results that were approximately 6 g/L higher.

Linear regression analysis showed good agreement ($y = 0.9065x + 1.315$, $R2 = 0.9848$) between the Dimension EXL 200 BCP results and external laboratory Abbott Architect Plus C8000 BCP results (Figure 3).

Figure 1: The Comparison Plot between BCP and BCG method between Cobas c 311 and Dimension EXL 200

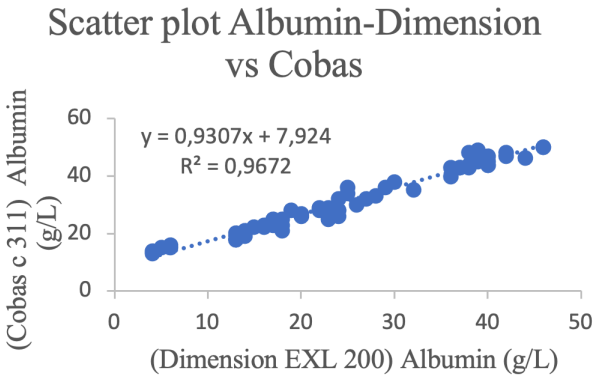


Figure 2: The Comparison Plot between BCP and BCG method between Beckman Coulter AU480 and Dimension EXL 200

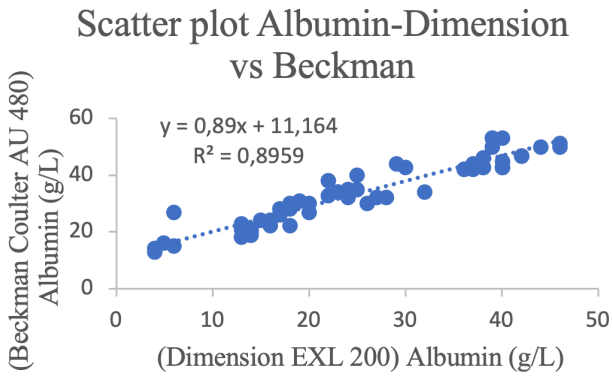


Figure 3: The Comparison Plot between Dimension and Abbot Architect BCP method

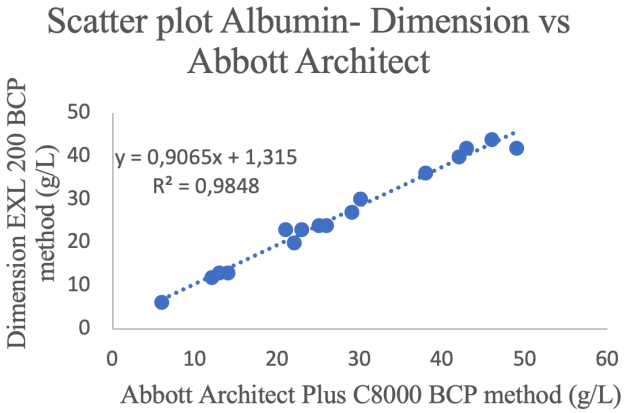


Figure 4: Bland-Altman plot comparison of albumin results for Dimension EXL200 BCP and Cobas c 311 BCG methods.

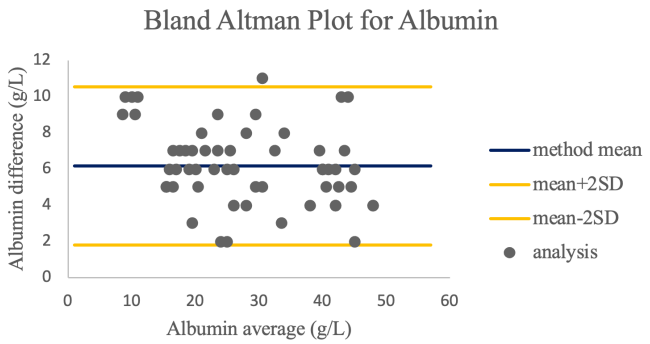
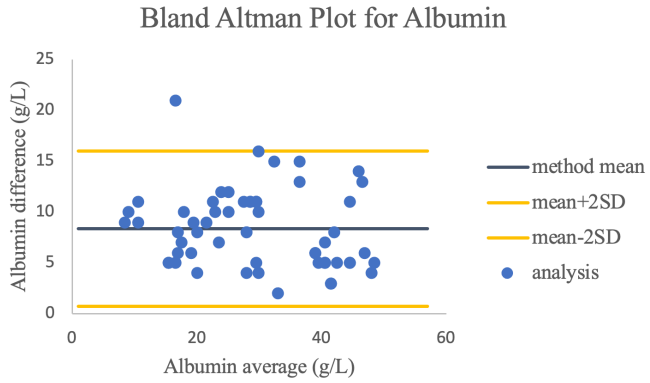


Figure 5: Bland-Altman plot comparison of albumin results for the Dimension BCP and Beckman Coulter AU480 BCG



The Bland-Altman plot (Figure 5) showed that the Beckman AU 480 BCG assay had a positive bias, yielding results approximately 8 g/L higher than the Dimension EXL 200 BCP method. Most results fell within the 95% confidence interval.

Discussion

Albumin is a crucial biomarker in kidney disease, as low serum albumin levels often indicate nephrotic syndrome or other forms of kidney dysfunction. Monitoring albumin levels helps assess the severity of kidney damage and guides treatment decisions to prevent further complications [6,7].

In this study, we compared serum albumin measurements obtained from three different analyzers in one laboratory: Dimension EXL 200, Cobas c 311, and Beckman AU 480. Values of serum albumin samples, which ranged from 4–50 g/L, effectively covered the concentration ranges of analyzers.

The comparison plots revealed a linear relationship between the BCP and BCG methods, indicating that both methods performed comparably within the tested concentration range. This linearity suggests that both methods can be used effectively within their respective ranges for measuring serum albumin levels.

Linear regression analysis showed a strong correlation between the Dimension EXL 200 BCP results and the external lab's Abbott Architect Plus C8000 BCP method, with an equation of $y = 0.9065x + 1.315$ and $R^2 = 0.9848$, confirming the accuracy of the Dimension EXL 200 analyzer.

Bland-Altman analysis revealed a positive bias in the Cobas c 311 and Beckman AU 480 BCG assays, with albumin results approximately 6 g/L and 8 g/L higher, respectively, than the Dimension EXL 200 BCP method. While most results fell within the 95% confidence interval, the BCG method tended to overestimate serum albumin levels compared to the BCP method, indicating consistent but clinically significant discrepancies.

This case report provides value in three key areas: clinical presentation and management of nephrotic syndrome, analytical challenges with serum albumin measurement, and the importance of statistical comparisons in laboratory medicine. It serves as an important lesson in ensuring the alignment of clinical signs with laboratory findings and recognizing the limitations of different diagnostic assays in medical practice [8,9].

Conclusion

This study highlights significant differences between serum albumin measurement methods, particularly between BCP and BCG techniques [3,4]. The BCP method showed excellent agreement across analyzers, supporting its reliability as a reference standard. In contrast, the BCG method exhibited positive biases, leading to higher albumin readings. Clinicians should be mindful of these biases when interpreting results, as accurate serum albumin measurement is critical for diagnosing and managing conditions like nephrotic syndrome [8,10]. The clinical team chose the BCP method to ensure more accurate patient assessments and better management outcomes.

There are certain limitations need attention. First, it focuses

on a single patient, which restricts the generalizability of its findings to broader populations or settings. The absence of a larger dataset further limits the robustness of the statistical analyses. Additionally, while the study compares the BCG and BCP methods, it does not include electrophoresis as a reference technique, which could have provided a more comprehensive evaluation of the methods' biases.

The lack of access to electrophoretic analysis, which is considered a more precise method for evaluating serum albumin, restricts the ability to provide a more comprehensive assessment of the biases between the two methods. Finally, the study was conducted in a single laboratory setting, which may limit the applicability of the findings to other laboratories with different equipment, reagents, and standard practices. Addressing these limitations in future research will provide a more comprehensive understanding of serum albumin measurement discrepancies and their clinical implications.

Learning Points

Importance of serum albumin in diagnostics: Serum albumin is a key biomarker for assessing nutritional status, liver function, and kidney health, crucial for diagnosing and managing various conditions.

Photometric methods: These are widely used for serum albumin measurement due to their efficiency, simplicity, and cost-effectiveness, relying on the interaction of albumin with a dye.

BCG vs BCP: The choice between BCG and BCP methods can impact accuracy, particularly in patients with kidney disease, as both are commonly used but may yield different results.

Clinical implications: Discrepancies in lab results, as seen in the case study, can complicate diagnosis and treatment, underscoring the need for accurate measurements.

Perspective of Laboratory Input

The clinical team recognizes the importance of understanding the differences between BCG and BCP methods for serum albumin measurement. The study's findings of a positive bias in BCG highlight potential inaccuracies that could affect patient management.

Discrepancies in lab results raise concerns about over- or under-treatment, especially in kidney disease management. As a result, the team is considering shifting to more reliable methods like BCP and exploring external lab verification for critical tests. They emphasize the need for collaboration with labs to ensure accurate diagnostics through regular reviews and protocol updates.

The team supports ongoing research to improve diagnostic methods and monitoring of serum albumin measurement practices. They believe further studies could refine current techniques and lead to more accurate tools, enhancing care for patients, especially those with conditions like nephrotic syndrome.

Conflicts of Interest

The authors whose names are listed immediately below certify that they have NO affiliations with or involvement in any organization or entity with any financial interest, or non-financial interest in the subject matter or materials discussed in this manuscript.

References

1. Pupim LB, Martin CJ, Ikizler TA. Chapter 10 - Assessment of Protein and Energy Nutritional Status. In: Kopple JD, Massry SG, Kalantar-Zadeh K, editors. Nutritional Management of Renal Disease (Third Edition) [Internet]. Academic Press; 2013. 137–158. DOI:10.1016/B978-0-12-391934-2.00010-2

2. Doweiko JP, Nompleggi DJ. Role of albumin in human physiology and pathophysiology. JPEN J Parenter Enteral Nutr. 1991;15(2):207–211. DOI: 10.1177/0148607191015002207

3. Brackeen GL, Dover JS, Long CL. Serum albumin. Differences in assay specificity. Nutr Clin Pract Off Publ Am Soc Parenter Enter Nutr. 1989;4(6):203–205 DOI: 10.1177/0115426589004006203

4. Logt AE van de, Rijpma SR, Vink CH, Prudon-Rosmulder E, Wetzels JF, Berkel M van. The bias between different albumin assays may affect clinical decision-making. Kidney Int. 2019;95(6):1514–1517. DOI: 10.1016/j.kint.2019.01.042

5. Lantman M van S, Logt AE van de, Prudon-Rosmulder E, Langelaan M, Demir AY, Kurstjens S, et al. Albumin determined by bromocresol green leads to erroneous results in routine evaluation of patients with chronic kidney disease. Clin Chem Lab Med CCLM. 2023;61(12):2167–2177. DOI: 10.1515/cclm-2023-0463

6. Lang J, Katz R, Ix JH, Gutierrez OM, Peralta CA, Parikh CR, et al. Association of serum albumin levels with kidney function decline and incident chronic kidney disease in elders. Nephrol Dial Transplant. 2018;33(6):986–992. DOI: 10.1093/ndt/gfx229

7. Gremese E, Bruno D, Varriano V, Perniola S, Petricca L, Ferraccioli G. Serum Albumin Levels: A Biomarker to Be Repurposed in Different Disease Settings in Clinical Practice. J Clin Med. 2023;12(18):6017. DOI: 10.3390/jcm12186017

8. Clase C, Pierre M, Churchill D. Conversion between bromcresol green- and bromcresol purple-measured albumin in renal disease. Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc. 2001;16:1925–1929. DOI: 10.1093/ndt/16.9.1925

9. Garcia Moreira V, Beridze Vaktangova N, Martinez Gago MD, Laborda Gonzalez B, Garcia Alonso S, Fernandez Rodriguez E. Overestimation of Albumin Measured by Bromocresol Green vs Bromocresol Purple Method: Influence of Acute-Phase Globulins. Lab Med. 2018 May 22

10. Filípek J, Illek J. Serum albumin assay – easy or problematic analysis? Acta Vet Brno. 2020;89(4):301–305. DOI: 10.2754/avb202089040301