When "Corrected Calcium" Is Not Correct: Age-Specific Interpretation of Total and Albumin-Adjusted Calcium in Neonates and Children

Manivannan Kandasamy[1], Alan Rice[1], Stephanie Gill[1], Salah Mansy[1], Guna Sameera Chevireddy[2], Ahmed Osman[3*]

[1]Consultant Paediatrician, Department of Paediatrics, East Sussex Healthcare NHS Trust (ESHT), United Kingdom

[2]Paediatrics Speciality Trainee, Department of Paediatrics, East Sussex Healthcare NHS Trust (ESHT), United Kingdom

[3]Speciality Doctor in Paediatrics, Department of Paediatrics, East Sussex Healthcare NHS Trust (ESHT), United Kingdom

[3]https://orcid.org/0009-0000-6343-9078

***Corresponding Author**

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ABSTRACT

Background: Total serum calcium is influenced by protein binding principally to albumin whereas ionised calcium represents the biologically active fraction. When direct ionised calcium is unavailable, automated laboratory systems routinely apply the adult-derived Payne equation anchored to an adult reference albumin target of 40 g/L. In neonates and infants, whose physiological albumin concentrations are substantially lower, this practice creates diagnostic misclassification and patient safety risks.

Objective & Design: To evaluate the clinical mechanisms of spurious hypercalcaemia flagging in paediatric biochemistry, present a retrospective clinical practice review alongside a structured quality improvement (QI) framework, and establish a prospective validation protocol using age-specific albumin midpoint adjustment.

Setting & Participants: Special Care Baby Unit (SCBU) and general paediatric wards at East Sussex Healthcare NHS Trust (ESHT), United Kingdom. Routine paired serum total calcium and albumin biochemistry profiles from neonates and children were reviewed; specimens with severe acid–base disturbances or missing paired albumin values were excluded.

Intervention & Analytical Framework: Pragmatic recalculation using locally established age-stratified albumin reference midpoints—preterm neonates at 27 weeks: 27.0 g/L (interval 21–33 g/L); preterm neonates at 28–35 weeks: 29.0 g/L (22–36 g/L); term neonates ≤28 days: 32.0 g/L (24–40 g/L); infants 1–12 months: 37.0 g/L (25–49 g/L); and children >12 months: 41.5 g/L (35–48 g/L)via the formula: Age-Specific Adjusted Calcium (mmol/L) = Total Calcium + 0.02 × (Age-Specific Albumin Midpoint − Measured Albumin), benchmarked against standard automated adult reporting (40 g/L target) and contextualised against published UK multicentre findings.

Results & Practice Findings: Automated application of the adult albumin reference target of 40 g/L may systematically overestimate neonatal albumin-adjusted calcium concentrations, potentially generating false-positive hypercalcaemia flags despite unremarkable unadjusted total calcium. Published UK multicentre data demonstrated a 6.8–9.0% relative difference between adult-derived and age-specific adjustment equations in neonates younger than one month. In our local clinical review, recalculation using age-specific reference interval

midpoints reclassified some apparently elevated adjusted calcium results as being within age-appropriate limits. This approach helped avoid potentially unnecessary repeat blood sampling and downstream investigations, including parathyroid hormone and vitamin D testing.

Conclusions: Adult-derived albumin-adjustment formulas may overestimate calcium levels in neonates, potentially leading to inaccurate results and unnecessary investigations. Direct ionised calcium measurement remains the gold standard when accurate assessment of calcium status is required. Where it is unavailable, using a laboratory-verified, age-specific albumin reference midpoint within a structured clinical assessment may provide a safer alternative. However, this approach requires further validation against ionised calcium measurements in future prospective studies.

Keywords: Albumin; Calcium; Corrected Calcium; Diagnostic Reliability; Hypercalcaemia; Ionised Calcium; Neonates.

INTRODUCTION AND LITERATURE REVIEW

Physicochemical Fractions of Calcium and the Conventional Payne Equation

Calcium circulates in human plasma in three distinct physicochemical fractions: free ionised calcium (approximately 50%), protein-bound calcium—predominantly bound to albumin (approximately 40%)—and calcium complexed to small diffusible anions such as citrate, phosphate, and bicarbonate (approximately 10%) [2,6]. Ionised calcium is the sole biologically active fraction governing neuromuscular excitability, myocardial contractility, coagulation, and cellular signalling, whereas total serum calcium quantifies all three fractions combined [2,6]. Because the equilibrium between protein-bound and free calcium depends heavily on circulating albumin concentration, blood pH, and competing anions, interpreting total serum calcium without accounting for protein status can obscure true calcium homeostasis [2,9].

Because direct measurement of ionised calcium requires strict anaerobic sample collection and rapid analysis, clinical laboratories have relied for over five decades on albumin-adjusted ("corrected") calcium formulas as a pragmatic surrogate [1,2]. The most widely used formula was derived by Payne et al. in 1973 through linear regression of total calcium on albumin across 200 consecutive adult clinical chemistry specimens with abnormal serum protein concentrations [1]. Expressed in conventional units, the original Payne equation is:

Adjusted Calcium (mg/100 mL) = Total Calcium (mg/100 mL) − Albumin (g/100 mL) + 4.0

In standard International System (SI) units used across United Kingdom (UK) clinical laboratories, this relationship is routinely approximated as:

Adjusted Calcium (mmol/L) = Total Calcium (mmol/L) + 0.02 × [40 − Measured Albumin (g/L)]

Crucially, the original Payne study was conducted exclusively in an adult cohort and did not validate albumin-adjusted calcium against direct ionised calcium measurements [1,6]. Applying this adult-derived equation to neonatal and paediatric populations introduces a fundamental physiological mismatch. Serum albumin rises progressively from early preterm gestation through infancy and childhood, while total calcium reference intervals simultaneously undergo marked developmental shifts during the neonatal period [3–5].

Diagnostic Reliability, Clinical Decision-Making, and Healthcare Quality Improvement

Contemporary clinical pathology and healthcare quality literature increasingly highlights how automated laboratory reporting defaults shape clinical decision-making, diagnostic reliability, and patient safety [6–8,11,12]. Cognitive heuristics and automation bias predispose clinicians to act upon asterisked "abnormal" flags generated by laboratory information management systems (LIMS), even when the underlying physiological assumptions are invalid for the specific patient subgroup [11,12]. In vulnerable neonatal populations, false-positive biochemical flags carry tangible clinical and iatrogenic risks: repeated venepuncture or heel-prick

sampling causes procedural pain, cumulative iatrogenic blood loss, parental anxiety, delayed discharge, and cascading specialist endocrine referrals [11,13].

From an evidence-based healthcare management and diagnostic stewardship perspective, eliminating low-value testing and preventing overdiagnosis are core pillars of modern patient safety [6,12,13]. Recent large-scale empirical studies have challenged the routine diagnostic utility of albumin-adjusted calcium across clinical settings. Kenny et al. concluded that direct ionised calcium should be prioritised whenever calcium status is clinically consequential, whereas unadjusted total calcium provides an adequate initial screen in low-risk patients [6]. In a 2025 population-based cohort study of 22,658 adults, Desgagnés et al. demonstrated that albumin-adjusted calcium correlated only modestly with ionised calcium, performed no better than unadjusted total calcium, and systematically overestimated true hypercalcaemia while underestimating true hypocalcaemia [7]. Similarly, a 2026 prospective intensive care study by Özdemir et al. comparing multiple albumin-correction equations against ionised calcium confirmed poor diagnostic concordance in physiologically unstable patients [8].

Within paediatrics specifically, Jassam et al. evaluated adult versus age-specific calcium adjustment equations across three UK teaching hospitals and demonstrated that the divergence between equations was greatest in neonates and infants younger than one year [2]. In neonates under one month of age, the reported relative bias between adult and age-specific adjusted calcium was approximately 6.8% to 9.0% across the three centres [2]. Importantly, in a neonatal subgroup (n = 61), Jassam et al. found that neither unadjusted total calcium nor the age-specific adjusted calcium equation consistently agreed with directly measured ionised calcium. These findings support the use of direct ionised calcium measurement when accurate assessment of calcium status is clinically important, particularly in infants. They also highlight that paediatrics calcium-adjustment formulas should be interpreted within a risk-stratified clinical framework rather than used as standalone diagnostic tools [2].

METHODOLOGY AND CLINICAL EVALUATION FRAMEWORK

Study Design, Setting, and Ethical Governance

This initiative was structured as a two-phase observational quality improvement (QI) project and clinical practice evaluation conducted within the Special Care Baby Unit (SCBU) and general paediatric inpatient wards at East Sussex Healthcare NHS Trust (ESHT), United Kingdom. Phase 1 comprised a retrospective clinical practice review of routine neonatal and paediatric bone profile biochemistry reports to characterise the mechanism and clinical consequences of automated hypercalcaemia flagging. Phase 2 established a standardised clinical interpretive pathway alongside a formal prospective validation protocol.

In accordance with UK National Health Service (NHS) Health Research Authority (HRA) governance criteria, Phase 1 constituted an internal clinical service evaluation and quality improvement review utilising anonymised routine clinical biochemistry data generated during standard care; therefore, formal Research Ethics Committee (REC) review and individual parental consent were not required. All patient identifiers were removed from illustrative clinical pathology excerpts prior to analysis and publication.

Patient Selection Criteria and Specimen Handling

During the retrospective clinical practice review, routine inpatient and neonatal unit biochemical profiles containing paired serum total calcium and serum albumin measurements were examined. Because Phase 1 was conducted as an exploratory, hypothesis-generating clinical practice audit rather than a powered epidemiological cohort study, a consecutive formal cohort denominator and universal paired ionised calcium sampling were not captured across all historic episodes—a methodological limitation explicitly addressed in our prospective validation design. Specimens were excluded from interpretive evaluation if they lacked a paired serum albumin measurement or were obtained during documented severe acid–base disturbance (blood pH <7.25 or >7.50), given the direct competitive effect of hydrogen ions on calcium–albumin binding [9].

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Analytical Methodology and Age-Specific Recalculation

Routine central laboratory biochemistry profiles were analysed on automated clinical chemistry platforms using standard colorimetric total calcium and albumin assays, with automated LIMS middleware calculating "corrected calcium" via the adult SI Payne formula anchored at 40 g/L and flagging results against an adult reference interval (2.17–2.44 mmol/L). To mitigate systematic upward bias in paediatric patients when direct ionised calcium was unavailable, we applied a pragmatic recalculation substituting the mathematical midpoint of locally established, age-stratified serum albumin reference intervals:

Age-Specific Adjusted Calcium (mmol/L) = Total Calcium (mmol/L) + 0.02 × [Age-Specific Albumin Midpoint (g/L) − Measured Albumin (g/L)]

Recalculated values were subsequently interpreted against age-appropriate paediatric calcium reference intervals rather than the adult 2.17–2.44 mmol/L range [3–5]. Table 1 details the age-stratified albumin reference intervals and target midpoints used in our local clinical evaluation.

Table 1. Age-stratified serum albumin reference intervals and target midpoints used in the local pragmatic calcium adjustment approach [14–15].

Paediatric Group	Age / Gestational Stratification	Local Albumin Reference Interval (g/L)	Target Midpoint Used (g/L)	Maximum Upward Bias if Adult 40 g/L Formula Used at Lower Albumin Limit
Preterm neonate	27 weeks' gestation	21–33	27.0	+0.38 mmol/L (at 21 g/L)
Preterm neonate	28–35 weeks' gestation	22–36	29.0	+0.36 mmol/L (at 22 g/L)
Term neonate	Birth to 28 days	24–40	32.0	+0.32 mmol/L (at 24 g/L)
Infant	1–12 months	25–49	37.0	+0.30 mmol/L (at 25 g/L)
Child	>12 months	35–48	41.5*	+0.10 mmol/L (at 35 g/L)

**Note: The mathematical midpoint of the 35–48 g/L reference interval for children >12 months is 41.5 g/L. If a clinical laboratory operationally applies 41.0 g/L, this should be explicitly documented as an operational target rather than a mathematical midpoint. Local reference intervals were derived from internal clinical biochemistry guidance and require formal platform-specific verification prior to wider institutional adoption.*

Prospective Validation Protocol and Statistical Analysis Plan

To establish rigorous diagnostic validity beyond preliminary observational findings, we designed a prospective validation protocol (Phase 2) for implementation across our neonatal and paediatric services. In this prospective study, temporally matched arterial or venous whole-blood and serum specimens (collected within ≤15 minutes

under anaerobic conditions) will be analysed simultaneously for central laboratory total serum calcium, serum albumin, and point-of-care/laboratory direct ionised calcium alongside blood pH [9,10].

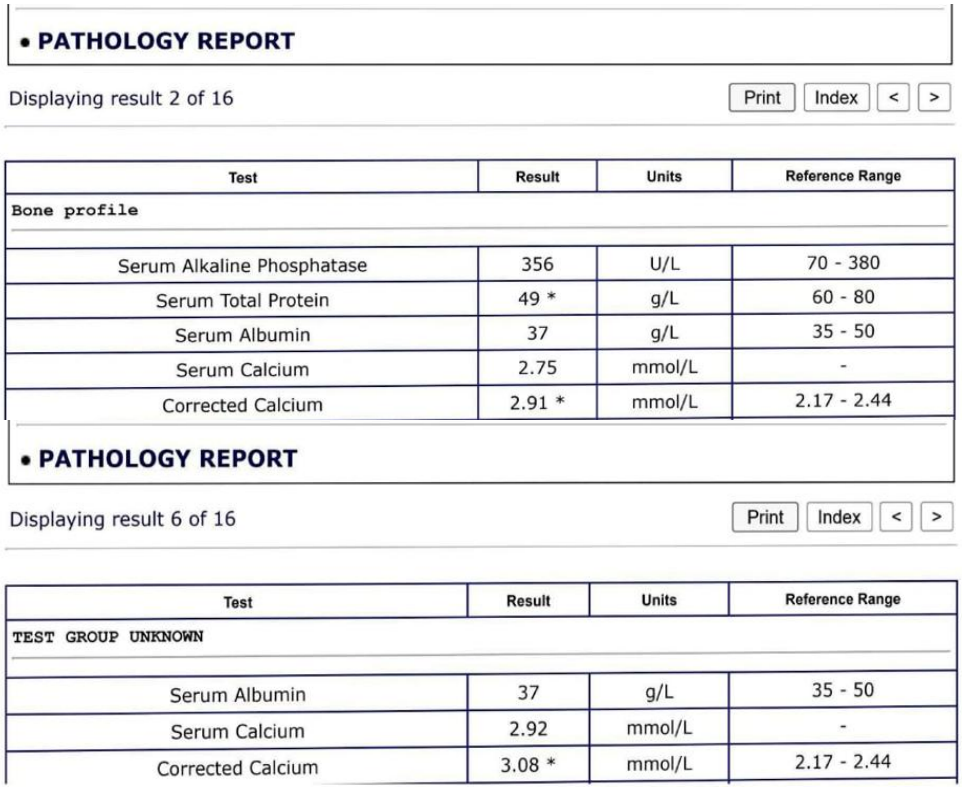
Rather than relying solely on linear correlation coefficients which measure association rather than agreement statistical validation will employ Bland–Altman analysis to quantify mean bias and 95% limits of agreement between direct ionised calcium and three comparators: (1) unadjusted total calcium, (2) conventional adult-adjusted calcium (40 g/L target), and (3) age-specific midpoint-adjusted calcium [7,8]. Diagnostic performance for detecting true hypocalcaemia and hypercalcaemia (defined by age-specific ionised calcium reference limits) will be evaluated using sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), area under the receiver operating characteristic curve (AUC-ROC), and overall diagnostic misclassification rates, stratified by gestational age, postnatal age, albumin concentration, and acid–base status.

CLINICAL PRACTICE OBSERVATIONS AND QUANTITATIVE CASE ILLUSTRATIONS

Mechanism of Artefactual Hypercalcaemia in Neonatal Reporting

In our retrospective clinical practice review, automated LIMS reporting repeatedly flagged apparently elevated corrected calcium concentrations in clinically asymptomatic neonates whose unadjusted total calcium values were unremarkable for age. Investigation with clinical biochemistry confirmed two compounding sources of error: first, applying an adult albumin target of 40 g/L to neonates whose physiological albumin typically spans 21–36 g/L added an artificial upward adjustment of +0.08 to +0.38 mmol/L; second, automated LIMS flags compared the resulting value against an adult reference interval (2.17–2.44 mmol/L) rather than neonatal intervals (which extend up to ~2.80 mmol/L in the first weeks of life) [4,5].

In our unit's observational experience, recalculating flagged results using the age-specific albumin midpoint reclassified the majority of apparent hypercalcaemia episodes into expected neonatal ranges mirroring the 6.8% to 9.0% neonatal relative bias quantified in the three-centre UK cohort study by Jassam et al. [2] and prevented clinicians from initiating unnecessary secondary endocrine investigations (such as serum parathyroid hormone [PTH], 25-hydroxyvitamin D, and urinary calcium-to-creatinine ratios).



• PATHOLOGY REPORT

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Test	Result	Units	Reference Range
Bone profile			
Serum Alkaline Phosphatase	356	U/L	70 - 380
Serum Total Protein	49 *	g/L	60 - 80
Serum Albumin	37	g/L	35 - 50
Serum Calcium	2.75	mmol/L	-
Corrected Calcium	2.91 *	mmol/L	2.17 - 2.44

• PATHOLOGY REPORT

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Test	Result	Units	Reference Range
TEST GROUP UNKNOWN			
Serum Albumin	37	g/L	35 - 50
Serum Calcium	2.92	mmol/L	-
Corrected Calcium	3.08 *	mmol/L	2.17 - 2.44

Figures 1 and 2. Sequential electronic pathology reports from a preterm neonate (33+3 weeks' gestation) illustrating automated hypercalcaemia flagging caused by adult reference parameters. In Figure 1 (top), total serum calcium is 2.75 mmol/L and serum albumin is 37 g/L; the automated adult LIMS formula (using a 45 g/L adult albumin target: 2.75 + 0.02 × [45 − 37] = 2.91 mmol/L) flags Corrected Calcium at 2.91 mmol/L (*) against an adult reference range (2.17–2.44 mmol/L). In Figure 2 (bottom), total calcium is 2.92 mmol/L and albumin is 37 g/L, yielding an automated Corrected Calcium of 3.08 mmol/L (*). Recalculating with the preterm gestational age-appropriate albumin midpoint of 29 g/L lowers the adjusted values by −0.16 mmol/L (to 2.59 mmol/L and 2.76 mmol/L, respectively), bringing both within the age-specific neonatal upper threshold of 2.80 mmol/L.

Worked Clinical Examples and Resolution of Formula Discrepancies

Comparison of the illustrative pathology reports (Figures 1 and 2) and routine neonatal cases highlights an important operational nuance in UK clinical laboratories: while the standard textbook SI Payne formula uses a reference albumin of 40 g/L, some UK laboratory middleware systems apply a locally derived adult reference target (such as 45 g/L, which explains why a total calcium of 2.75 mmol/L with an albumin of 37 g/L produced an automated report of 2.91 mmol/L in Figure 1: 2.75 + 0.02 × [45 − 37] = 2.91 mmol/L, whereas the 40 g/L formula yields 2.75 + 0.02 × [40 − 37] = 2.81 mmol/L). Regardless of whether 40 g/L or 45 g/L is embedded in the adult middleware, both targets substantially overestimate neonatal baseline albumin.

Consider a second worked example from a 10-day-old term neonate with a measured total serum calcium of 2.71 mmol/L and serum albumin of 37 g/L. Under the standard 40 g/L adult SI Payne equation, the calculated corrected calcium is:

Adult-Adjusted Calcium (40 g/L target) = 2.71 + 0.02 × (40 − 37) = 2.71 + 0.06 = 2.77 mmol/L

(Note: Under middleware anchored at 45 g/L, the reported value rises further to 2.71 + 0.02 × [45 − 37] = 2.87 mmol/L, both of which trigger automated abnormal flags against the adult upper limit of 2.44 mmol/L.) Recalculating the same specimen using the term-neonate albumin midpoint of 32.0 g/L yields:

Age-Specific Adjusted Calcium (32 g/L target) = 2.71 + 0.02 × (32 − 37) = 2.71 − 0.10 = 2.61 mmol/L

Using the age-appropriate albumin midpoint reduces the calculated value by 0.16 to 0.26 mmol/L (to 2.61 mmol/L), placing it well within published term-neonatal reference intervals [4,5]. While a single universal upper cut-off (such as 2.80 mmol/L) should not be applied indiscriminately across all gestational and postnatal ages, this worked calculation illustrates how adult reference assumptions systematically inflate neonatal results. Crucially, the recalculated figure remains an albumin-adjusted estimate and cannot replace direct ionised calcium measurement when clinically indicated.

PRIMACY OF IONISED CALCIUM AND RISK-STRATIFIED CLINICAL PATHWAY

Whenever calcium homeostasis is clinically in question, when an abnormal result will alter clinical management, or when physiological derangements disrupt calcium–protein binding, direct measurement of ionised calcium is unequivocally superior to any adjustment equation [6–9]. Blood pH exerts a major acute effect on calcium binding because hydrogen ions compete directly with calcium ions for negatively charged binding sites on albumin; acidaemia increases ionised calcium while alkalaemia decreases it without altering total calcium concentration [9].

In neonatal and paediatric inpatient settings, point-of-care blood gas analysers provide rapid access to ionised calcium alongside simultaneous blood pH measurement. Previous large-scale comparative work by our group demonstrated clinically acceptable analytical agreement between blood gas analyser and central laboratory electrolyte and calcium measurements, supporting timely bedside clinical decision-making provided strict pre-analytical sample handling protocols are observed [10].

To translate these principles into safe, consistent bedside practice and reduce diagnostic error, we developed a seven-step clinical decision pathway for interpreting neonatal and paediatric calcium results (Table 2).

Table 2. Risk-stratified seven-step clinical pathway for interpreting serum calcium in neonates and children.

Step	Clinical Action	Diagnostic Reliability & Patient Safety Rationale
1	**Assess clinical context and pre-test probability**	Evaluate symptoms, signs, and risk factors for calcium disturbance (e.g., extreme prematurity, parenteral nutrition, vitamin D therapy, renal impairment, or endocrine disorders).
2	**Review unadjusted total serum calcium**	Interpret measured total calcium directly against validated, age-specific paediatric laboratory reference intervals before reviewing automated adjusted values [4–6].
3	**Obtain direct ionised calcium when indicated**	Whenever calcium homeostasis is clinically in question or results will alter management, measure direct ionised calcium (the biological gold standard) [2,6–9].
4	**Interpret ionised calcium alongside blood pH**	Account for acid–base status when reviewing blood-gas ionised calcium, as acidaemia and alkalaemia directly shift protein-bound calcium equilibrium [9,10].
5	**Apply age-specific adjustment (only if iCa unavailable)**	When ionised calcium cannot be obtained and protein adjustment is warranted, recalculate using the locally verified age-specific albumin midpoint rather than adult targets (40–45 g/L).
6	**Do not diagnose hypercalcaemia on adjusted values alone**	Prevent overdiagnosis and iatrogenic harm: never initiate invasive endocrine workups or treatment based solely on an albumin-adjusted calculation without ionised calcium confirmation [6–8,12].
7	**Investigate confirmed true hypercalcaemia**	Once hypercalcaemia is confirmed on direct ionised calcium, execute targeted diagnostic investigation (PTH, phosphate, vitamin D

		metabolites, renal function, and urinary calcium).

DISCUSSION

Clinical Implications of Age-Specific Albumin Targets Versus the Adult Payne Equation

The central laboratory medicine challenge illustrated by our clinical evaluation is the interaction between a mathematical adjustment formula and the reference population embedded within it. By anchoring adjustment to an adult albumin concentration of 40 g/L (or 45 g/L on certain analytical platforms), the conventional Payne equation answers a clinically irrelevant hypothetical question for a neonate: what the infant's calcium concentration would be if they possessed adult serum albumin levels [1–3]. Because normal serum albumin increases markedly from 21–33 g/L at 27 weeks' gestation to 24–40 g/L in term neonates and 35–48 g/L after one year of age, applying an adult target systematically introduces positive bias across the entire neonatal period [2,3].

In daily clinical practice, this bias directly impacts clinical risk assessment and resource stewardship. When automated LIMS middleware flags an adjusted calcium of 2.87–3.08 mmol/L with an abnormal asterisk against an adult reference interval, junior and senior clinicians alike face cognitive pressure to exclude pathology [11,12]. In neonates, pursuing apparent hypercalcaemia frequently triggers repeat venepuncture, cessation of routine vitamin D or calcium supplementation in parenteral/enteral nutrition, and costly secondary endocrine assays (PTH, 1,25-dihydroxyvitamin D, and renal ultrasonography). Recalculating with an age-specific albumin midpoint removes this artificial upward shift, aligning biochemical interpretation with developmental physiology and supporting high-value, harm-free care [12,13].

Validity of the 0.02 Correction Coefficient and Analytical Platform Variation

A critical biochemical question is whether the conventional slope coefficient of 0.02 mmol/g (0.8 mg/dL per g/dL) remains valid across neonatal and paediatric age groups. In the original Payne regression, 0.02 represented the average change in total calcium per 1 g/L change in albumin across 200 adult specimens [1]. However, subsequent laboratory medicine studies have demonstrated that calcium–albumin binding stoichiometry varies substantially depending on the analytical assay used for albumin specifically bromocresol green (BCG) versus bromocresol purple (BCP) dye-binding methods as well as across different patient populations [2,3,6]. BCG methods tend to overestimate serum albumin in neonates due to non-specific binding to alpha- and beta-globulins, whereas BCP methods yield lower, more specific albumin values, thereby altering the apparent regression slope [2,3].

Indeed, Jassam et al. derived population-specific paediatric regression slopes across three UK hospital laboratories and found that locally derived coefficients differed from 0.02 and varied across sites depending on analytical instrumentation [2]. Consequently, while retaining the 0.02 coefficient alongside an age-specific albumin midpoint offers a practical, zero-cost bedside interim adjustment, clinical biochemistry departments seeking to implement automated paediatric adjustment formulas must derive and validate platform-specific regression slopes and age-stratified reference intervals locally rather than importing universal constants uncritically [2,3].

Governance Recommendations for Laboratory Reporting and Patient Safety

From a healthcare quality improvement and clinical governance perspective, transparency in laboratory reporting is essential to prevent diagnostic error [11,12]. Clinical pathology reports displaying adjusted calcium should explicitly state: (1) the exact equation and slope coefficient applied, (2) the assumed reference albumin target, (3) the age-appropriate calcium reference interval, and (4) whether the formula is validated for patients under one year of age. Where laboratory middleware cannot support age-stratified equations and paediatric reference intervals, suppressing automated adult-adjusted calcium reporting in infants under 12 months and defaulting instead to age-specific unadjusted total calcium alongside direct ionised calcium represents a safer systems-level intervention than reporting misleading adult-adjusted results [2,6,12].

METHODOLOGICAL LIMITATIONS

Several methodological limitations must be considered when interpreting this evaluation. First, our local clinical observations were derived from a retrospective clinical practice review and lack a formal consecutive patient denominator, hypothesis-testing statistics, and universal paired ionised calcium measurements across all reviewed episodes. The 6.8% to 9.0% neonatal relative bias reduction cited herein reflects published multicentre UK findings by Jassam et al. [2] rather than an original cohort rate calculated from our local dataset. Second, our pragmatic calculation retains the adult-derived 0.02 mmol/g slope coefficient, which may not reflect true calcium–albumin binding affinity across preterm and term neonates or between BCG and BCP albumin assays [1,2]. Third, the age-stratified albumin intervals in Table 1 were compiled from internal clinical biochemistry guidance and require formal local laboratory verification prior to wider institutional implementation. Finally, albumin-adjusted calcium remains an indirect estimate that can diverge substantially from biologically active ionised calcium in the presence of acid–base disturbances, renal dysfunction, critical illness, hyperbilirubinaemia, or intravenous lipid/citrate infusions [2,6–9].

CONCLUSION

Automated calcium adjustment formulas anchored to adult reference albumin targets (40–45 g/L) systematically overestimate adjusted calcium in neonates and young infants due to physiologically lower baseline serum albumin concentrations, generating spurious hypercalcaemia flags and unnecessary secondary investigations [2,3]. Integrating a locally verified, age-specific albumin reference midpoint into a structured, seven-step clinical pathway provides a pragmatic bedside safeguard when direct ionised calcium is unavailable. However, age-adjusted calcium cannot replace direct ionised calcium measurement; clinicians must continue to prioritise direct ionised calcium whenever calcium homeostasis is clinically in question or will materially influence patient management [2,6–8].

KEY CLINICAL & QUALITY IMPROVEMENT MESSAGES

- Direct ionised calcium is the unequivocal clinical gold standard whenever calcium homeostasis is in question or results will alter neonatal or paediatric management [2,6–9].
- Automated adult-derived calcium equations (anchored at 40–45 g/L) introduce systematic upward bias in neonates due to physiologically lower serum albumin concentrations, driving false-positive hypercalcaemia flags [2,3].
- Substituting an age-specific albumin reference midpoint provides a pragmatic, harm-reducing interim estimate when ionised calcium is unavailable, though the 0.02 slope coefficient requires local analytical verification.
- To protect patient safety and prevent diagnostic cascades, clinicians must never diagnose hypercalcaemia or initiate endocrine investigations based solely on an albumin-adjusted calculation without ionised calcium confirmation [6–8,12].

AUTHOR STATEMENTS AND DECLARATIONS

Authors' Contributions: AO conceived the clinical evaluation, performed the retrospective clinical review, drafted the manuscript, and led revisions. AR contributed to clinical biochemistry data review, assay evaluation, and methodological oversight. MK contributed to clinical protocol development and departmental governance review. SG contributed to manuscript revision and clinical data interpretation. SM and GSC provided senior clinical oversight, structural editing, and final supervision. All authors approved the final manuscript.

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Ethics Approval and Patient Consent: In accordance with UK NHS Health Research Authority (HRA) guidance, this project was conducted as an internal clinical quality improvement and service evaluation review using anonymised routine clinical biochemistry data; formal Research Ethics Committee approval and individual patient consent were not required. All patient identifiers were removed from illustrative pathology reports.

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