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BACKGROUND AND IMPORTANCE

Valproic acid (VA) binds strongly to albumin. In hypoalbuminaemia, the free valproic acid fraction (FVPA) — the pharmacologically active form — increases, raising efficacy and toxicity risks. Determining FVPA concentration is therefore crucial for monitoring, dose adjustment, and treatment safety.

AIM AND OBJECTIVES

The primary objective was to evaluate the influence of hypoalbuminaemia on the relationship between total VA and FVPA concentrations. Secondly, a proposed formula for the theoretical calculation of FVPA was compared with measured values (1)

MATERIAL AND METHODS



A retrospective observational and descriptive study

Electronic medical record
Laboratory programme

Patients treated with VA
01/2024 and 09/2025
Tertiary hospital

Analysed variables:

- Demographic: sex, age
- Anthropometric: weight, height
- Biochemical parameters: VA, FVPA, albumin, and total proteins

Classification

Target therapeutic range established at:

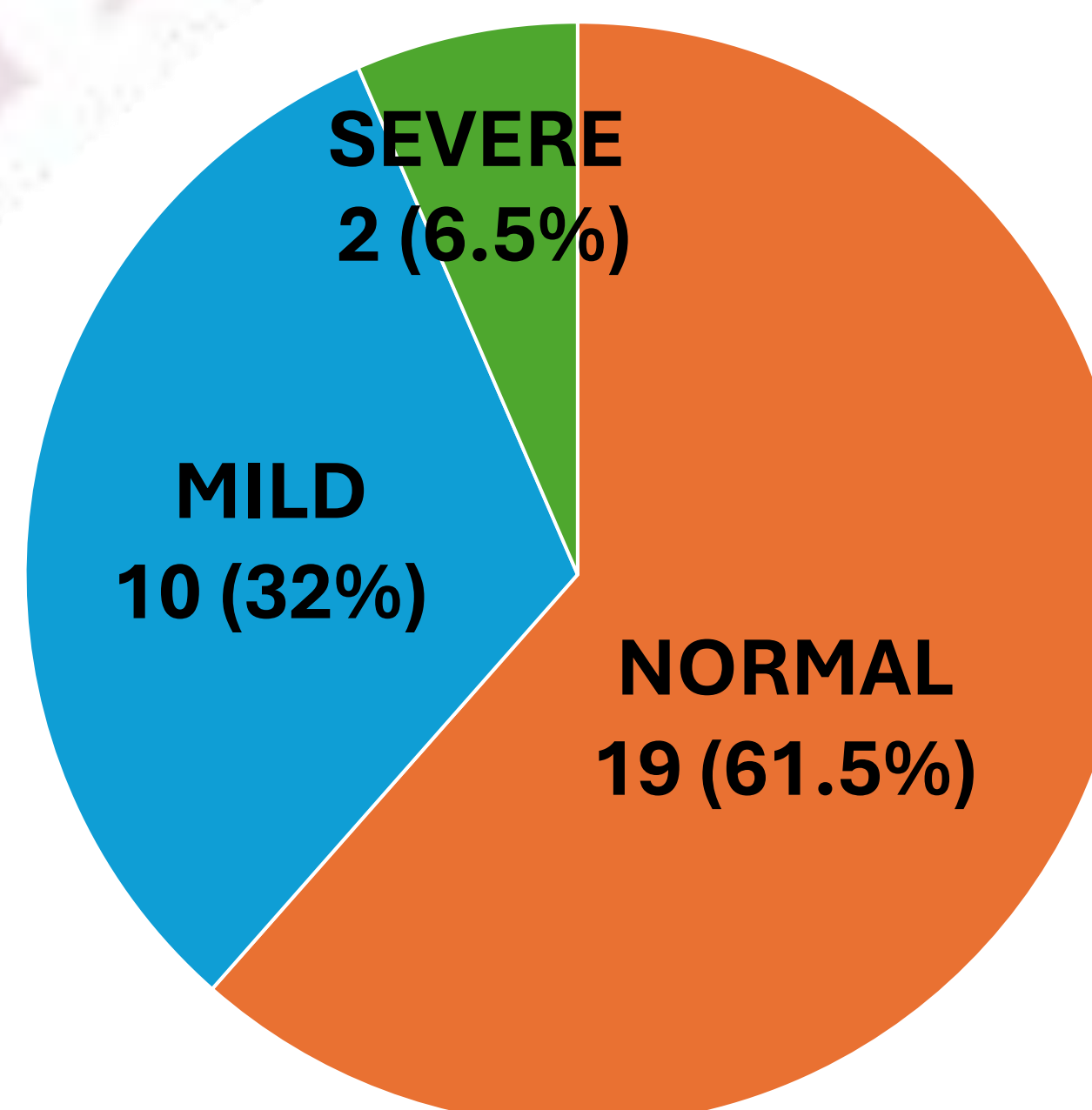
- FVPA: 5-15 mcg/mL
- VA: 50-100 mcg/mL

Normoalbuminaemic: ≥ 3.5 g/dL
Mildly hypoalbuminaemic: 2.5–3.4 g/dL
Severely hypoalbuminaemic: < 2.5 g/dL

RESULTS

31 patients
11 (35%)
20 (65%)
Mean age: 58 ± 17 years

Distribution by albumin status



FVPA concentration
Supratherapeutic levels were observed in 13 (41.9%) of patients

Hypoalbuminaemic 69.2% (9)
Mildly 7 (53.8%)
Severely 2 (15.4%)

- 3 (9.7%) patients exhibited FVPA levels above the therapeutic range despite total VA concentrations below the recommended range.
- 4 (30.8%) patients had total VA concentrations at the lower limit or subtherapeutic range, with FVPA concentrations even above the range.
- Comparison of measured versus calculated FVPA revealed an average difference of $\pm 4.96\%$ between the actual and theoretical values derived from the proposed formula.

CONCLUSION AND RELEVANCE

Over half of patients with supratherapeutic FVPA levels were hypoalbuminaemic, often showing total VA concentrations below target. In all cases of severe hypoalbuminaemia, FVPA levels were high. These results highlight the need to measure FVPA directly in hypoalbuminaemic patients to ensure accurate interpretation, optimal dosing, and prevent toxicity, in addition to the difference obtained in its theoretical measurement.

