Prognostic Significance of Hypercobalaminemia in Medically Hospitalized Patients: A Prospective Study

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Abstract

Objectives: Hypercobalaminemia has been increasingly recognized as a marker of systemic diseases rather than only a nutritional excess. While it has been linked to malignancy, liver dysfunction, and inflammation, its prognostic value in general hospitalized patients remains underexplored. This study aimed to evaluate the prevalence of hypercobalaminemia, its clinical correlations, and its association with in-hospital outcomes.

Methods: We conducted a prospective cohort study of 351 adult patients admitted to the General Internal Medicine Unit at Sultan Qaboos University Hospital, Oman, between May 25 and September 30, 2023. Vitamin B12 levels were classified as deficient (<138 pmol/L), normal (138–663 pmol/L), or high (>663 pmol/L). Demographics, comorbidities, laboratory parameters, and outcomes were analyzed. The primary endpoints were ICU admission and in-hospital mortality.

Results: Normal B12 levels were observed in 78.1% of patients, while 16.8% had hypercobalaminemia and 5.1% were deficient. Elevated B12 correlated positively with CRP, liver enzymes, and age, and negatively with albumin and eGFR. Patients with hypercobalaminemia were significantly older and had higher rates of ICU admission (25.9% vs. 12.4% vs. 16.7%; $p = 0.031$) and in-hospital mortality (25.9% vs. 4.7% vs. 11.1%; $p < 0.001$) compared to those with normal or low levels. In multivariate logistic regression, hypercobalaminemia remained an independent predictor of mortality (OR 3.04, 95% CI 1.13–8.22, $p = 0.028$), alongside inotrope/vasopressor use, invasive respiratory support, and do-not-resuscitate status. The model showed excellent predictive performance (AUC = 0.931).

Conclusion: Hypercobalaminemia is common in hospitalized patients and independently predicts poor outcomes, including ICU admission and in-hospital mortality. Elevated B12 appears to reflect systemic illness, inflammation, and organ dysfunction rather than nutritional status. Routine measurement may help identify high-risk patients, though multicenter studies are warranted to confirm its prognostic utility.

Keywords: Hypercobalaminemia; Vitamin B12; Hospitalized patients; Prognosis; ICU admission; Mortality

Introduction

Vitamin B12 is obtained from animal-derived foods and is released from dietary proteins in the stomach, binding to intrinsic factor for absorption in the ileum. Once absorbed, it is transported in the bloodstream bound to proteins like haptocorrin and transcobalamin. Transcobalamin-bound vitamin B12 (holotranscobalamin) is taken up by cells and converted into active coenzymes: methylcobalamin and adenosylcobalamin, essential for DNA synthesis and energy metabolism.[1,2] Vitamin B12 acts as a cofactor for methionine synthase and methylmalonyl-CoA mutase, involved in remethylation of homocysteine to methionine, crucial for DNA methylation and synthesis of S-adenosylmethionine, a universal methyl donor.[2]

Vitamin B12 deficiency is a significant health concern due to its role in cellular metabolism, DNA synthesis, and neurological function.[3] It can lead to megaloblastic anemia, characterized by large, abnormal red blood cells, causing fatigue and weakness.[4] Neurological symptoms include sensory and motor disturbances, cognitive decline, and psychiatric disorders, which can occur even without anemia.[5] The deficiency disrupts the metabolism of homocysteine and methylmalonic acid, increasing cardiovascular risk. Many individuals have subclinical deficiency, with subtle symptoms and elevated homocysteine and methylmalonic acid levels, despite normal serum B12 levels. The deficiency is prevalent globally, especially in populations with limited animal-derived food intake, affecting the elderly, vegetarians, and those with absorption issues due to gastrointestinal disorders.[4,6]

Hypercobalaminemia, or elevated levels of vitamin B12 in the blood, can be caused by a variety of underlying conditions. It is often an indicator of more serious health issues rather than excessive intake of vitamin B12.[7] Hypercobalaminemia is often linked to solid

tumors and hematological disorders like chronic myelomonocytic leukemia, myelodysplastic syndromes, and acute leukemias, serving as a non-specific early marker for these conditions.[7 8] Liver disorders and renal failure commonly cause elevated vitamin B12 levels due to affected metabolism and clearance, leading to accumulation in the blood.[8] Inflammatory and autoimmune diseases, such as monoclonal gammopathy of undetermined significance, can also increase serum cobalamin levels.[7 9] Excessive vitamin B12 intake, though less common, can cause hypercobalaminemia, but is usually not the primary cause when high levels are detected.[8]

Current literature indicates that hypercobalaminemia is linked to poor prognosis in hospitalized patients, particularly those with cancer. It is associated with higher mortality and unplanned hospitalizations.[10] Cancer patients with elevated B12 levels (>800 pmol/L) have lower survival probabilities, and there is a higher risk of developing hematological cancers within five years.[11] In older cancer patients, a high serum vitamin B12-C-reactive protein index is a prognostic factor for early death and unplanned hospitalizations, suggesting its use as a marker to assess frailty and adapt care.[12]

Research on hypercobalaminemia primarily focuses on specific conditions like cancer, liver, and hematologic disorders, where it is linked to poor prognosis.[13] Although evidence suggests its potential as a prognostic marker in a broader inpatient population, further studies are needed to understand its implications in general medical settings.

This study aims to evaluate the prevalence of hypercobalaminemia, identify factors associated with elevated levels, and assess their impact on health outcomes among medically hospitalized patients .

Methods

This is a prospective cohort study conducted at Sultan Qaboos University Hospital (SQUH), a 600-bed tertiary care hospital in Oman.[14,15] The study included consecutive adult patients (≥18 years old) admitted under the General Internal Medicine Unit from 25/05/2023 to 30/09/2023 . Patients with missing outcome or follow-up data were excluded from the study.

Vitamin B12 levels were measured within 24 hours of admission for all included patients . Data were collected using a structured case report form and extracted from electronic medical records, recording variables such as demographic and clinical data (age, sex, BMI, functional status, primary diagnosis), comorbidities (diabetes, heart failure, chronic kidney and liver diseases, hypertension, COPD, malignancy, neurological diseases, autoimmune disorders), and laboratory parameters (hematological markers like hemoglobin, hematocrit, MCV; biochemical markers like albumin, liver function tests, inflammatory markers, renal function). Hospitalization outcomes included primary outcomes (length of stay, in-hospital mortality, ICU/high-dependency ward admission)

Previous studies have reported a prevalence of hypercobalaminemia in hospitalized patients ranging between 15% and 40%.[16 17] Based on this, we estimated that a sample size of 380 patients would be required to determine the prevalence of hypercobalaminemia in medically hospitalized patients with 95% confidence and a 5% margin of error.

Vitamin B12 status is categorized by our laboratory reference range as deficiency (< 138 pmol/L), normal (138 – 663 pmol/L), and high (> 663 pmol/L).

Continuous variables were expressed as means with standard deviations for normally distributed data and medians with interquartile ranges (IQRs) for non-normally distributed data. Categorical variables were presented as frequencies and percentages. The distribution of continuous variables across vitamin B12 categories was compared using the Kruskal-Wallis test due to non-normal distribution of most variables. For categorical variables, associations with vitamin B12 categories were analyzed using the Chi-square test or Fisher's exact test when expected cell counts were less than 5. Univariate logistic regression analysis was performed to identify variables associated with in-hospital mortality. Variables with p-values <0.20 in univariate analysis were considered for inclusion in the multivariate model. Multivariate logistic regression was conducted using a stepwise approach to identify independent predictors of mortality.

The final multivariate model included clinically relevant variables: inotrope/vasopressor use, invasive respiratory support, do-not-resuscitate (DNR) status, and high vitamin B12 levels. Model performance was evaluated using the area under the receiver operating characteristic curve (AUC). Odds ratios (OR) with 95% confidence intervals (CI) were calculated for all variables in the final model.

Statistical significance was assessed using the Mann-Whitney U test for comparing B12 levels between groups with and without specific clinical characteristics. Correlations between vitamin B12 levels and continuous variables were evaluated using Spearman's rank correlation coefficient due to non-normal distribution of the data. Statistical analyses were performed using Python (version 3.x; Python Software Foundation, Beaverton, Oregon, USA) within the Julius AI cloud-based data science platform (Julius AI, San Francisco, California, USA).

This study was approved by the Medical Research Ethics Committee, College of Medicine & Health Sciences, Sultan Qaboos University (REF. NO. SQU-EC/074/2023, MREC #2982).

Results

The study cohort included 351 patients hospitalized during the study period, with a median age of 63 years (IQR: 48.0–75.5), 48.72% male patients, and a median BMI of 27.68 kg/m² (IQR: 23.52–30.26). The most common comorbidities included hypertension (57.83%), diabetes mellitus (45.01%), and dyslipidemia (33.05%), while 14.81% of patients required ICU admission, and in-hospital mortality was 8.55%. Median vitamin B12 levels were 350.0 pmol/L (IQR: 248.5–523.5), and polypharmacy was present in 45.87% of patients, with 82.62% receiving enteral feeding (mouth or tube feeding) during hospitalization (Table 1).

Regarding vitamin B12 levels, 78.1% of hospitalized patients (95% CI: 73.4%–82.3%) had normal levels (138-663 pmol/L). Elevated vitamin B12 levels were present in 16.8% of patients (95% CI: 13.0%–21.1%), while deficient levels were the least common, observed in 5.13% of patients (95% CI: 3.07%–7.98%).

Table 1: Comprehensive Patient Characteristics, Laboratory Parameters, Comorbidities, Medications, and Outcomes (n = 351).

Characteristics	**n(%) unless specified otherwise**
Demographics	
Age, IQR; (years)	63.0 (48.0–75.5)
Gender, IQR; (Male)	171 (48.72%)
Weight, IQR; (kg)	72.27 (61 - 77.05)
Height, IQR; (m)	1.66 (1.56–15.70)
Body Mass Index, IQR; (BMI, kg/m²)	27.68 (23.52–30.26)
Lifestyle Factors	
Substance Abuse	7 (1.99%)
Smoking	45 (12.82%)
Alcohol Status	32 (9.12%)
Drug Use	5 (1.42%)
Feeding & Nutrition	
Feeding Status (Parenteral)	12 (3.42%)
Feeding Status (Enteral)	290 (82.62%)
Diet Type - Normal	339 (96.58%)
Diet Type - Vegetarian	4 (1.14%)
Functional Status	
Independent	187 (53.28%)
Partially Dependent	71 (20.23%)
Fully Dependent	93 (26.50%)
Comorbidities	
Hypertension (HTN)	203 (57.83%)
Diabetes Mellitus (DM)	158 (45.01%)
Chronic Kidney Disease (CKD)	65 (18.52%)
Heart Failure (HF)	55 (15.67%)
Liver Cirrhosis	10 (2.85%)
Dyslipidemia (DLP)	116 (33.05%)
Anemia	25 (7.12%)
Dementia	20 (5.70%)
History of stroke or transiet ischemic stroke (TIA)	54 (15.38%)
Parkinson’s Disease	9 (2.56%)
Epilepsy	10 (2.85%)
Autoimmune Disease	1 (0.28%)
Solid Tumors	21 (5.98%)
Leukemia	1 (0.28%)
Lymphoma	2 (0.57%)
Myeloproliferative Disorders	1 (0.28%)
End-Stage Renal Disease (ESRD)	5 (1.42%)
Hemiplegia	5 (1.42%)
AIDS	1 (0.28%)
No Comorbidities	37 (10.54%)
Laboratory Parameters	
Chloride, IQR; (mmol/L)	101.0 (98.0–104.0)
Random glouse lucose Level, IQR; (mmol/L)	8.2 (6.3–12.1)
C-Reactive Protein, IQR; (CRP, mg/L)	24.0 (6.0–91.0)
Vitamin B12, IQR; (B12, pmol/L)	350.0 (248.5–523.5)
Hematocrit, IQR; (HCT, L/L)	0.372 (0.3165–0.423)
Hemoglobin, IQR; (g/dL)	11.9 (10.35–13.5)
Mean Corpuscular Volume, IQR; (MCV, fL)	77.1 (70.5–83.8)

Estimated Glomerular Filtration Rate, IQR; (eGFR, mL/min)	77.0 (47.0–90.0)
Albumin, IQR; (g/L)	36.4 (31.0–42.0)
Alanine Aminotransferase, IQR; (ALT, U/L)	19.0 (11.0–43.7)
Aspartate Aminotransferase, IQR; (AST, U/L)	23.0 (15.0–50.3)
Alkaline Phosphatase, IQR; (ALP, U/L)	92.0 (70.5–129.5)
Diagnosis classified as per ICD-10	
Infectious & Parasitic Diseases (A00-B99)	42 (12.0%)
Blood Disorders & Immune Diseases (D50-D89)	16 (4.6%)
Endocrine, Nutritional, & Metabolic Diseases (E00-E90)	33 (9.4%)
Nervous System Diseases (G00-G99)	26 (7.4%)
Circulatory System Diseases (I00-I99)	48 (13.7%)
Respiratory System Diseases (J00-J99)	65 (18.5%)
Diagnosis classified as per ICD-10	
Infectious & Parasitic Diseases (A00-B99)	42 (12.0%)
Blood Disorders & Immune Diseases (D50-D89)	16 (4.6%)
Endocrine, Nutritional, & Metabolic Diseases (E00-E90)	33 (9.4%)
Nervous System Diseases (G00-G99)	26 (7.4%)
Circulatory System Diseases (I00-I99)	48 (13.7%)
Respiratory System Diseases (J00-J99)	65 (18.5%)
Polypharmacy	161 (45.87%)
Multivitamins	21 (5.98%)
Neurobion	15 (4.27%)
Metformin	62 (17.66%)
Proton Pump Inhibitors (PPI)	128 (36.47%)
H2 Blockers	22 (6.27%)
Colchicine	3 (0.85%)
Chloramphenicol	2 (0.57%)
Vitamin Injections in the Last Year	13 (3.70%)
Respiratory Support and circulatory support	
Invasive Respiratory Support	15 (4.27%)
Non-Invasive Respiratory Support (NIV)	48 (13.68%)
No Respiratory Support	270 (76.92%)
Inotropic or Vasopressor Support	36 (10.26%)
Number of Inotropic or Vasopressor Agents	340 (96.87%)
Hospitalization Outcomes	
ICU Admission	52 (14.81%)
Death in Hospital	30 (8.55%)
Length of Stay, IQR; (hours)	118.0 (75.6–206.6)

Spearman correlation analysis revealed significant associations between vitamin B12 levels and several clinical parameters. Positive correlations were observed with alkaline phosphatase (rho = 0.1833, p = 0.0006), aspartate aminotransferase (rho = 0.1414, p = 0.008), and C-reactive protein (rho = 0.1587, p = 0.0029). Negative correlations were found with albumin (rho = -0.1835, p = 0.0006) and estimated glomerular filtration rate (rho = -0.172, p = 0.0012) (Table 2, Figure 1).

Table 2: Top Positive and Negative Correlations Between Vitamin B12 Levels and Clinical Parameters in Hospitalized Patients.

Variable	Correlation	*p*-value
Age (years)	0.1297	0.015
Weight (kg)	-0.0884	0.0984
Height (cm)	0.0211	0.6943

Body Mass Index (BMI, kg/m²)	-0.0794	0.1378
Length of Stay (days)	0.0466	0.3841
Number of Regular Medications (count)	0.1188	0.026
Chloride Levels (mmol/L)	-0.083	0.1205
Glucose Levels (mmol/L)	0.0797	0.1362
Highest Blood Sugar (mmol/L)	0.0635	0.2351
Lowest Blood Sugar (mmol/L)	0.0351	0.5121
C-Reactive Protein (CRP, mg/L)	0.1587	0.0029
Hematocrit (HCT, %)	-0.0401	0.4535
Hemoglobin Levels (g/dL)	-0.0541	0.3122
Mean Corpuscular Volume (MCV, fL)	-0.0094	0.8608
Estimated Glomerular Filtration Rate (eGFR, mL/min/1.73m²)	-0.172	0.0012
Albumin Levels (g/L)	-0.1835	0.0006
Alanine Transaminase (ALT, U/L)	0.1269	0.0174
Aspartate Transaminase (AST, U/L)	0.1414	0.008
Alkaline Phosphatase (ALP, U/L)	0.1833	0.0006

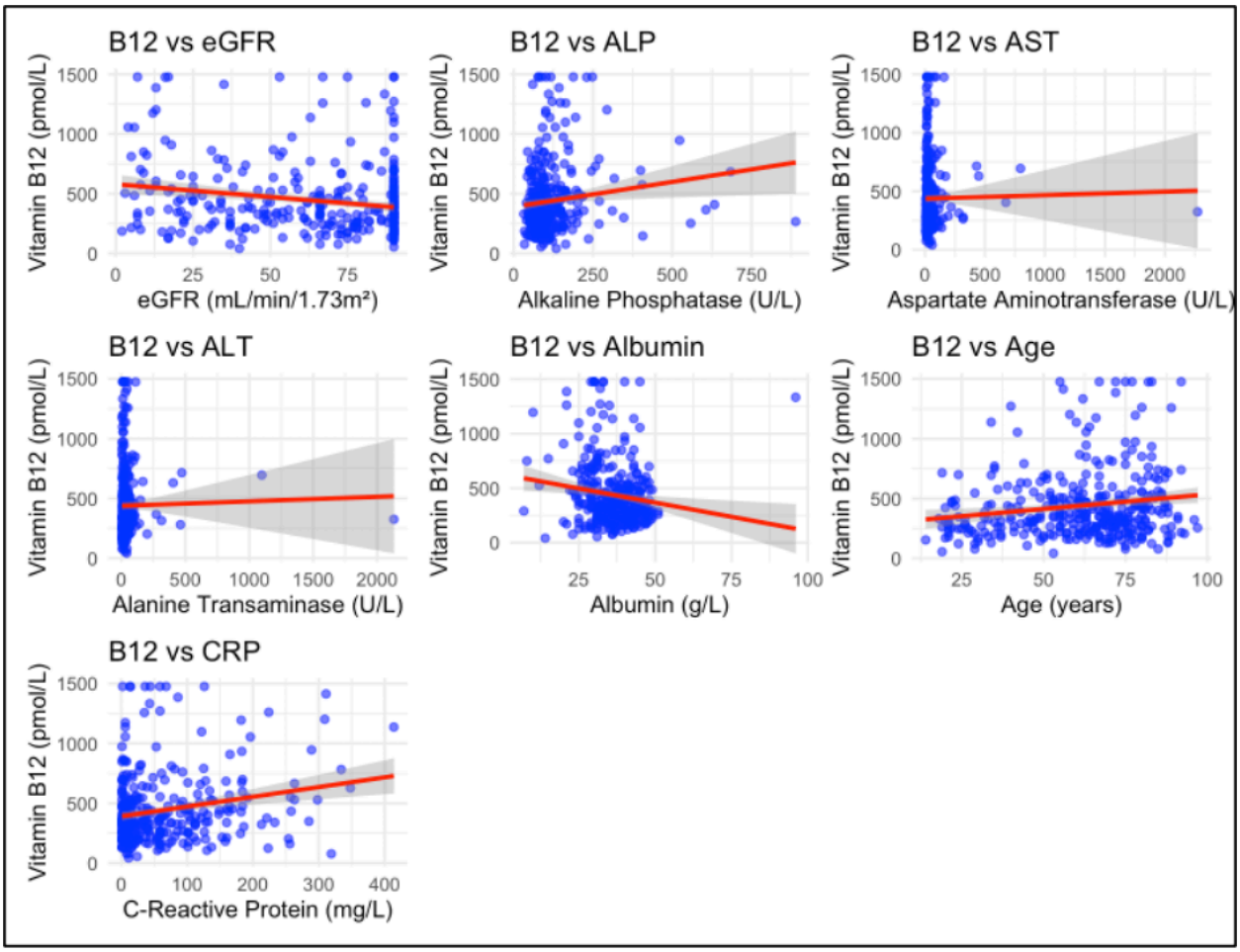

Figure 1: Spearman correlation analysis showed a positive correlation between Vitamin B12 and alkaline phosphatase ($\rho = 0.183$, $p = 0.0006$), aspartate aminotransferase ($\rho = 0.141$, $p = 0.008$), alanine aminotransferase ($\rho = 0.127$, $p = 0.017$), C-reactive protein ($\rho = 0.159$, $p = 0.0029$), and age ($\rho = 0.130$, $p = 0.015$), Negative correlations were observed with albumin ($\rho = -0.183$, $p = 0.0006$) and eGFR ($\rho = -0.172$, $p = 0.0012$).

When stratified by vitamin B12 concentrations, patients with high B12 levels (>663 pmol/L), and low vitamin B12 levels were significantly older compared to those with normal (69.5 vs. 63.0 vs. 68.5 years; p = 0.0388). ICU admissions were more frequent among patients with high B12 (25.9% vs. 12.4% vs. 16.7%; p = 0.0307), and in-hospital mortality was significantly higher in this group (25.9% vs. 4.7% vs. 11.1%; p< 0.0001) (Table 3).

Table 3: Comparison of Clinical Characteristics, Laboratory Markers, Comorbidities, and Outcomes Based on Vitamin B12 Levels in Hospitalized Patients.

Variable **n(%) unless specified otherwise**	**Low vitamin B12**	**Normal vitamin B12**	**High Vitamin B12**	***p*-value**
Demographics				
Age (years)	69.5 (36.8 - 77.2)	63.0 (47.0 - 74.0)	68.5 (56.5 - 80.0)	0.0388
Gender (Male)	8 (44.4%)	130 (47.3%)	33 (56.9%)	0.3840
Body Mass Index (BMI) (kg/m²)	16.3 (0.0 - 29.4)	21.9 (0.0 - 28.8)	22.6 (17.3 - 28.6)	0.6172
Lifestyle Factors				
Smoking	0 (0.0%)	40 (14.5%)	5 (8.6%)	0.1168
Alcohol Use	0 (0.0%)	28 (10.2%)	4 (6.9%)	0.2826
Comorbidities				
Hypertension (HTN)	10 (55.6%)	152 (55.3%)	41 (70.7%)	0.0949
Diabetes Mellitus (DM)	6 (33.3%)	122 (44.4%)	30 (51.7%)	0.3509
Chronic Kidney Disease (CKD)	3 (16.7%)	45 (16.4%)	17 (29.3%)	0.0684
Heart Failure (HF)	4 (22.2%)	39 (14.2%)	12 (20.7%)	0.3410
Dementia	2 (11.1%)	13 (4.7%)	5 (8.6%)	0.3033
Dyslipidemia (DLP)	5 (27.8%)	87 (31.6%)	24 (41.4%)	0.3177
History of stroke or transient ischemic stroke (TIA)	3 (16.7%)	44 (16.0%)	7 (12.1%)	0.7436
Liver Cirrhosis	1 (5.6%)	7 (2.5%)	2 (3.4%)	0.7250
Laboratory Parameters				
Albumin (g/L)	34.0 (29.2 - 36.8)	38.0 (33.0 - 43.0)	31.0 (29.0 - 36.0)	<0.0001
Alkaline Phosphatase (ALP) (U/L)	97.5 (77.2 - 115.0)	86.0 (70.0 - 118.5)	109.0 (79.2 - 170.0)	0.0098
Alanine Aminotransferase (ALT) (U/L)	13.5 (11.5 - 26.5)	20.0 (11.0 - 43.7)	21.0 (11.0 - 43.5)	0.2911
Aspartate Aminotransferase (AST) (U/L)	19.5 (14.2 - 26.0)	24.0 (15.0 - 50.3)	23.5 (16.0 - 47.0)	0.3286
C-Reactive Protein (CRP) (mg/L)	20.0 (8.8 - 92.8)	21.0 (5.0 - 78.5)	50.5 (6.5 - 127.5)	0.0619
Estimated Glomerular Filtration Rate (eGFR) (mL/min/1.73 m²)	69.0 (40.2 - 89.8)	79.0 (51.0 - 90.0)	63.0 (21.2 - 88.5)	0.0041
Diagnosis classified as per ICD-10				0.2947961
Infectious & Parasitic Diseases (A00-B99)	2 (11.1%)	36 (13.1%)	6 (10.3%)	
Blood Disorders & Immune Diseases (D50-D89)	1 (5.6%)	12 (4.4%)	3 (5.2%)	
Endocrine, Nutritional, & Metabolic Diseases (E00-E90)	1 (5.6%)	26 (9.5%)	6 (10.3%)	
Nervous System Diseases (G00-G99)	3 (16.7%)	22 (8.0%)	1 (1.7%)	
Circulatory System Diseases (I00-I99)	5 (27.8%)	33 (12.0%)	12 (20.7%)	
Respiratory System Diseases (J00-J99)	1 (5.6%)	57 (20.7%)	8 (13.8%)	
Others	5 (27.8%)	89 (32.4%)	22 (37.9%)	
Medications and Treatments				
Polypharmacy	7 (38.9%)	121 (44.0%)	33 (56.9%)	0.1669
Insulin Use	6 (33.3%)	122 (44.4%)	30 (51.7%)	0.3509

Metformin Use	2 (11.1%)	46 (16.7%)	14 (24.1%)	0.3059
Proton Pump Inhibitors (PPI)	9 (50.0%)	97 (35.3%)	22 (37.9%)	0.4392
Neurobion	1 (5.6%)	5 (1.8%)	9 (15.5%)	<0.0001
Vitamin Injections (Last Year)	5 (27.8%)	7 (2.5%)	1 (1.7%)	<0.0001
Feeding				
Enteral Feeding	16 (88.9%)	223 (81.1%)	51 (87.9%)	0.3535
Parenteral Feeding	0 (0.0%)	6 (2.2%)	6 (10.3%)	0.0057
Hemodialysis	0 (0.0%)	9 (3.3%)	10 (17.2%)	0.0001
Respiratory Support and circulatory support				
Inotropic/Vasopressor Use	3 (16.7%)	19 (6.9%)	14 (24.1%)	0.0003
Invasive Respiratory Support	2 (11.1%)	7 (2.5%)	6 (10.3%)	0.0096
Hospitalization Outcomes				
Length of Stay (days)	124.8 (93.7 - 270.5)	118.0 (74.0 - 190.1)	122.4 (77.5 - 323.3)	0.1350
ICU Admission	3 (16.7%)	34 (12.4%)	15 (25.9%)	0.0307
Death in Hospital	2 (11.1%)	13 (4.7%)	15 (25.9%)	<0.0001

Univariate logistic regression analysis identified several variables significantly associated with in-hospital mortality, including high vitamin B12 levels (OR 6.89, 95% CI: 2.89-16.42, $p < 0.001$), inotrope/vasopressor use (OR 15.75, 95% CI: 6.89-35.98, $p < 0.001$), invasive respiratory support (OR 8.40, 95% CI: 3.59-19.66, $p < 0.001$), and DNR status (OR 12.25, 95% CI: 5.35-28.04, $p < 0.001$). Variables with p-values < 0.20 in univariate analysis were considered for inclusion in the multivariate model.

Multivariate logistic regression analysis identified four independent predictors of in-hospital mortality. Inotrope/vasopressor use showed the strongest association with mortality (OR 8.051, 95% CI: 2.568-25.242, $p = 0.0003$), followed by DNR status (OR 6.575, 95% CI: 2.273-19.019, $p = 0.0005$), invasive respiratory support (OR 5.552, 95% CI: 1.156-26.666, $p = 0.0323$), and elevated vitamin B12 levels >663 pmol/L (OR 3.041, 95% CI: 1.125-8.220, $p = 0.0283$). The final multivariate model demonstrated excellent discriminative ability with an area under the receiver operating characteristic curve (AUC) of 0.931, indicating strong predictive performance for in-hospital mortality (Table 4).

Table 4: Multivariate Logistic Regression Analysis of Independent Predictors of In-Hospital Mortality.

Variable	**Odds Ratio**	**95% CI**	***p*-value**
Inotrope/Vasopressor Use	8.051	(2.568-25.242)	0.0003
Invasive Respiratory Support	5.552	(1.156-26.666)	0.0323
Resuscitation Status (not for resuscitation)	6.575	(2.273-19.019)	0.0005
High B12 (>663 pmol/L)	3.041	(1.125-8.220)	0.0283

Discussion

Hypercobalaminemia is increasingly seen as a marker of systemic diseases. Linked to hematological and hepatic disorders, its prognostic value in general inpatients is under investigation. This study explores its clinical and laboratory associations, suggesting its role as a biomarker for adverse outcomes.

This study found that in hospitalized patients, 78.1% had normal vitamin B12 levels, 16.8% had elevated levels, and 5.13% had deficient levels.There are no previous studies assessed the prevelence of hypercobalaminemia among hospitalized medical patients.

The relationship between age and vitamin B12 is influenced by factors like absorption efficiency and dietary intake. Although levels don't necessarily decline with age, older adults are at a higher risk of deficiency due to absorption challenges, such as those caused by atrophic gastritis, leading to conditions like cognitive decline and musculoskeletal issues.[17,18] In addition, this study found that patients with high vitamin B12 levels were often older well. This may be because elderly hospitalized patients are at greater risk of deterioration, liver damage, and acute kidney injury, which can elevate vitamin B12 levels.

Vitamin B12 has anti-inflammatory properties, with higher levels linked to reduced inflammatory markers like interleukin-6 and C-reactive protein. Also, Higher vitamin B12 levels are linked to lower CRP and other inflammatory markers, suggesting an anti-inflammatory effect.[19] In cancer patients, elevated B12 levels correlate with increased mortality risk, while CRP remains a key prognostic factor.[20] Post-bariatric surgery, vitamin B12 supplementation reduces CRP levels, highlighting its role in inflammation management.levels, suggesting that vitamin supplementation could influence inflammation.[21] This study found that CRP levels correlate with vitamin B12 levels . This suggests that hypercobalaminemia may reflect an acute-phase response rather than a direct nutritional excess, especially in hospitalized patients with inflammatory conditions.

This study found a negative correlation between albumin levels and vitamin B12, indicating that higher B12 levels were associated with lower albumin concentrations. Patients with elevated B12 had significantly lower median albumin levels compared to those with normal or low B12. Very few studies have evaulationed the relationship betweeb low albumin and high vitamin B12 levels are linked to increased mortality in patients with acute kidney injury and other hospitalized patients, indicating they are independent mortality predictors.[22,23] Elevated B12 levels are associated with reduced kidney function and albuminuria, especially in those with high homocysteine levels.[24] This findings of our stduy suggests that hypercobalaminemia may be linked to disease severity, malnutrition, or hepatic dysfunction, where decreased albumin synthesis reflects an underlying systemic illness rather than a direct excess.

This study found a negative correlation between vitamin B12 levels and kidney function, as measured by estimated glomerular filtration rate (eGFR). Patients with elevated B12 levels had significantly lower median eGFR compared to those with normal or low B12. This suggests that impaired renal function may contribute to hypercobalaminemia due to reduced clearance of vitamin B12 and its binding proteins, supporting the role of B12 as a marker of underlying disease severity. Previous studies suggest that the relationship between renal dysfunction and vitamin B12 levels is complex, with both elevated and deficient levels observed in patients with kidney issues.[25] Elevated B12 levels, often seen in acute kidney injury, may indicate kidney stress or damage due to impaired excretion.[26] Conversely, vitamin B12 deficiency is common in chronic kidney disease and end-stage renal disease, attributed to dietary restrictions and dialysis losses, contributing to anemia and other issues.[27]

This study showed a positive correlation between elevated vitamin B12 levels and liver enzyme levels (ALT, AST, and ALP), suggesting a potential link between hypercobalaminemia and hepatic dysfunction. This association supports the hypothesis that liver disease or increased hepatocellular turnover may contribute to elevated B12 levels.

Elevated liver enzymes and vitamin B12 levels are often observed in patients with liver diseases.. Previous studies demonstrated that elevated vitamin B12 levels in patients with liver disease often indicate liver damage and correlate with disease severity, serving as prognostic markers, especially in chronic liver disease and acute-on-chronic liver failure.[16,28] These elevated levels are associated with increased liver enzyme levels, reflecting underlying liver dysfunction.[29] In this study, The association between elevated vitamin B12 levels and increased liver enzymes reflects hepatic dysfunction and altered B12 metabolism. Liver damage can release stored B12 into circulation, while impaired clearance and increased production of B12-binding proteins can elevate serum levels.

This study found that elevated vitamin B12 levels were associated with worse health outcomes, including higher ICU admission rates and increased in-hospital mortality. Patients with high B12 levels had a significantly greater likelihood of requiring intensive care and experiencing higher in-hospital death rates compared to those with normal or low B12 levels. These findings suggest that hypercobalaminemia may serve as a marker of disease severity and poor prognosis. This association could be related to the fact that

hypercobalaminemiais linked to serious conditions like tumors, liver, and kidney diseases, serving as an early diagnostic marker. [30,31]

This study's strengths include its prospective design, enhancing data reliability, comprehensive data collection with multiple comorbidities, laboratory markers, and outcomes, a large sample size providing sufficient power to detect significant associations, and statistical rigor through appropriate methods like correlation analysis and stratification by B12 levels. However, limitations include its single-center nature, limiting generalizability, lack of long-term follow-up with outcomes limited to in-hospital events, and the inability to establish causality, leaving it unclear whether high B12 is a marker or causative factor for poor prognosis.

Conclusion

This study finds that hypercobalaminemia is common among hospitalized patients and is associated with poor outcomes, including ICU admission and mortality. Elevated B12 levels likely indicate systemic illness, inflammation, or organ dysfunction rather than nutritional status. Routine B12 measurement may help identify high-risk patients, but further multicenter research is needed to confirm its prognostic value.

Disclosure

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