

CLINICAL AND BIOCHEMICAL ALTERATIONS IN PATIENTS WITH VITAMIN B12 AND FOLATE DEFICIENCY ANEMIAS RESIDING IN ANDIJAN CITY

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Annotation

Megaloblastic anemias, driven by Vitamin B12 and folate deficiencies, present unique clinical and biochemical challenges, heavily influenced by regional dietary habits and gastrointestinal pathologies. This study characterizes these specific alterations in the urban population of Andijan. A cross-sectional study was conducted involving 80 patients (aged 18-65) diagnosed with megaloblastic anemia and 30 healthy controls. Comprehensive laboratory panels including complete blood count (CBC), serum B12, folate, lactate dehydrogenase (LDH), and homocysteine were analyzed. Patients exhibited significant macrocytosis (MCV 112 ± 5.4 fL vs. 88 ± 4.2 fL in controls, $p < 0.001$). Severe biochemical disruptions were noted, particularly elevated LDH (845 ± 120 U/L vs. 180 ± 25 U/L, $p < 0.001$) and hyperhomocysteinemia (24.5 ± 3.2 $\mu\text{mol/L}$ vs. 8.4 ± 1.5 $\mu\text{mol/L}$, $p < 0.01$), reflecting ineffective erythropoiesis and metabolic blockades. B12 and folate deficiencies in Andijan lead to profound systemic biochemical shifts beyond simple anemia, including severe hyperhomocysteinemia. Early laboratory differential diagnosis is essential to prevent irreversible neurological and cardiovascular complications.

Keywords

Megaloblastic anemia, Vitamin B12 deficiency, Folate deficiency, Macrocytosis, Homocysteine, Lactate dehydrogenase, Ineffective erythropoiesis.

Introduction

Vitamin B12 (cobalamin) and folate are essential micronutrients required for DNA synthesis and cellular energy metabolism. Deficiencies in either vitamin disrupt nuclear maturation, leading to megaloblastic anemia, a condition characterized by large, structurally abnormal red blood cells.

In the Central Asian region, including the Fergana Valley and specifically Andijan city, the prevalence of these deficiencies is strongly influenced by local nutritional patterns (high consumption of black tea which inhibits absorption, varied meat intake) and a high incidence of chronic atrophic gastritis associated with *Helicobacter pylori*. The clinical presentation often overlaps, but the biochemical pathways disrupted—specifically the accumulation of homocysteine and methylmalonic acid—pose independent risks for endothelial dysfunction and neurodegeneration. Identifying the specific biochemical phenotype of patients in Andijan is crucial for optimizing local diagnostic and therapeutic protocols.

Literature Review

Global literature extensively documents the systemic impact of megaloblastic anemias. Stabler (2013) established that B12 deficiency often presents with subtle neuropsychiatric symptoms

preceding severe hematological drops. Green (2017) highlighted the critical role of elevated LDH and indirect bilirubin as primary markers of intramedullary hemolysis (ineffective erythropoiesis) characteristic of these anemias. Furthermore, recent studies (Carmel, 2011) emphasize that isolated testing of serum B12 is often insufficient, advocating for homocysteine evaluation to detect tissue-level deficiency. Despite these global insights, there is a distinct lack of targeted biochemical profiling for populations in the Fergana Valley, making local epidemiological data highly necessary.

Materials and Methods

Study Design: A retrospective and prospective cross-sectional study was conducted at the Andijan State Medical Institute clinic.

Participants: 80 patients (45 females, 35 males) residing in Andijan, diagnosed with megaloblastic anemia, and 30 healthy age-matched controls.

Inclusion/Exclusion: Included adult patients (18-65 years) with confirmed macrocytic anemia (MCV > 100 fL). Excluded patients with active bleeding, hypothyroidism, liver cirrhosis, or a history of chemotherapy.

Ethics: The study was approved by the Local Bioethics Committee. All protocols complied with the Declaration of Helsinki.

Laboratory Methods: Fasting venous blood was analyzed for CBC (automated analyzer), serum B12, and serum folate (chemiluminescence immunoassay). LDH and homocysteine levels were measured using standard biochemical assays.

Statistics: Data are presented as mean \pm standard error ($M \pm m$). The Student's t-test was used to determine the statistical significance of differences between groups, with $p < 0.05$ considered significant.

Results

Clinical evaluation revealed that 85% of patients experienced profound fatigue, 40% reported glossitis (Hunter's glossitis), and 25% exhibited mild peripheral neuropathy (predominantly in the B12 deficient subgroup).

The biochemical and hematological findings are summarized in Table 1.

Table 1. Clinical and Biochemical Parameters of the Study Groups ($M \pm m$)

Parameter	Control Group (n=30)	Megaloblastic Anemia Group (n=80)	p-value
Hemoglobin (g/L)	138 \pm 8.5	82 \pm 6.4	< 0.001
MCV (fL)	88 \pm 4.2	112 \pm 5.4	< 0.001
Serum B12 (pg/mL)	450 \pm 45	115 \pm 20	< 0.001

Parameter	Control Group (n=30)	Megaloblastic Anemia Group (n=80)	p-value
Serum Folate (ng/mL)	12.5 ± 1.8	3.2 ± 0.8	< 0.01
LDH (U/L)	180 ± 25	845 ± 120	< 0.001
Homocysteine (µmol/L)	8.4 ± 1.5	24.5 ± 3.2	< 0.01

The laboratory profile confirms classic megaloblastic changes. Notably, the extreme elevation of LDH (845 ± 120 U/L) indicates a high rate of precursor cell destruction in the bone marrow. Additionally, the marked hyperhomocysteinemia (24.5 ± 3.2 µmol/L) serves as a critical biochemical indicator of the cellular metabolic block caused by the dual or isolated deficiency of these vitamins in the studied population.

Discussion

Our findings closely align with the biochemical patterns described by Green (2017), yet they underscore a severe degree of ineffective erythropoiesis (evidenced by LDH levels nearly 4-5 times the upper normal limit) specific to the Andijan cohort. The significant hyperhomocysteinemia observed is of particular clinical concern. Homocysteine is a known independent risk factor for atherothrombosis. Therefore, patients in Andijan suffering from prolonged, undiagnosed B12/folate deficiency are not only at risk for anemic hypoxia but also face an elevated risk of premature cardiovascular events. The high incidence may be tied to local agricultural diets leaning heavily on refined carbohydrates and specific tea consumption habits that interfere with micronutrient absorption.

Scientific Novelty

This is the first targeted clinical-biochemical study to quantify the severity of ineffective erythropoiesis (via LDH) and metabolic block (via homocysteine) in patients with megaloblastic anemia specifically residing in Andijan. The data establishes a baseline for local epidemiological monitoring.

Conclusion & Recommendations

- Conclusion:** Megaloblastic anemias in Andijan are characterized by severe macrocytosis, profound LDH elevation reflecting intramedullary hemolysis, and dangerous levels of homocysteine.
- Recommendations:** Standard diagnostic protocols for macrocytic anemias in regional polyclinics must be expanded to include obligatory LDH and homocysteine testing, preventing

misdiagnosis. Furthermore, public health initiatives should focus on targeted dietary education and aggressive *H. pylori* eradication to improve natural B12 absorption in the local population.

References

1. Stabler, S. P. (2013). Clinical practice. Vitamin B12 deficiency. *New England Journal of Medicine*, 368(2), 149-160. DOI: 10.1056/NEJMcp1113996
2. Green, R. (2017). Vitamin B12 deficiency from the perspective of a practicing hematologist. *Blood*, 129(19), 2603-2611. DOI: 10.1182/blood-2016-10-569186
3. Carmel, R. (2011). Biomarkers of cobalamin (vitamin B-12) status in the epidemiologic setting: a critical overview of context, applications, and performance characteristics of cobalamin, methylmalonic acid, and holotranscobalamin II. *The American Journal of Clinical Nutrition*, 94(1), 348S-358S. DOI: 10.3945/ajcn.111.013441
4. Devalia, V., Hamilton, M. S., & Dietz, V. C. (2014). Guidelines for the diagnosis and treatment of cobalamin and folate disorders. *British Journal of Haematology*, 166(4), 496-513. DOI: 10.1111/bjh.12959
5. Hannibal, L., Lysne, V., Bjørke-Monsen, A. L., Behringer, S., Grünert, S. C., Spiekerkoetter, U., ... & Blom, H. J. (2016). Biomarkers and algorithms for the diagnosis of vitamin B12 deficiency. *Frontiers in Molecular Biosciences*, 3, 27. DOI: 10.3389/fmolb.2016.00027
6. Andrès, E., Affenberger, S., Vinzio, S., Kurtz, J. E., Noel, E., Kaltenbach, G., ... & Schlienger, J. L. (2005). Food-cobalamin malabsorption in elderly patients: clinical manifestations and treatment. *The American Journal of Medicine*, 118(10), 1154-1159. DOI: 10.1016/j.amjmed.2005.02.026
7. Aslinia, F., Mazza, J. J., & Yale, S. H. (2006). Megaloblastic anemia and other causes of macrocytosis. *Clinical Medicine & Research*, 4(3), 236-241. DOI: 10.3121/cmr.4.3.236
8. Hunt, A., Harrington, D., & Robinson, S. (2014). Vitamin B12 deficiency. *BMJ*, 349, g5226. DOI: 10.1136/bmj.g5226
9. Reynolds, E. (2006). Vitamin B12, folic acid, and the nervous system. *The Lancet Neurology*, 5(11), 949-960. DOI: 10.1016/S1474-4422(06)70598-1
10. Allen, L. H. (2009). How common is vitamin B-12 deficiency?. *The American Journal of Clinical Nutrition*, 89(2), 693S-696S. DOI: 10.3945/ajcn.2008.26947A