Content available at: https://www.ipinnovative.com/open-access-journals

Panacea Journal of Medical Sciences

Journal homepage: https://pjms.in/

Original Research Article

Role of lactate dehydrogenase in the diagnosis of Megaloblastic anemia-An observational study at tertiary care centre

Pallav Sharma[1], Shivani Dogra[2]*, Sindhu Sharma[2]

[1]Dept. of Biochemistry, Government Medical College, Jammu, Jammu and Kashmir, India
[2]Dept. of Pathology, Government Medical College, Jammu, Jammu and Kashmir, India

Abstract

Introduction: Megaloblastic anemia poses a significant health challenge in regions such as India. Peripheral blood smear shows macrocytic blood picture with hypersegmented neutrophils. Intramedullary hemolysis due to ineffective erythropoiesis is seen in patients of Megaloblastic Anemia leading to increased levels of certain enzymes including LDH. High serum LDH levels are seen in patients of Megaloblastic anemia.
Aim: Assessing the role of LDH in diagnosing megaloblastic anemia.
Materials and Methods: This observational study was conducted in the Department of Pathology, GMC Jammu, over a duration of one year. It involved the inclusion of 100 cases of megaloblastic anemia diagnosed through peripheral blood smear and bone marrow examination. A comprehensive assessment comprising detailed clinical history, physical examination, and investigations including CBC, MCV, MCH, MCHC, and serum LDH levels was performed.
Results: In the present study maximum number of cases of Megaloblastic anemia (30%) were in the age group of 21-30 years followed by 18% cases in 11-20 years. Males predominated the study with male to female ratio of 1.17: 1. MCV> 95 fl is found in majority of cases. Out of 100 cases maximum number of cases (35%) had serum LDH level of 2000-3000 U/L followed by 25% with serum LDH level of 3000-4000 U/L. Thus there is significant rise in serum LDH level in cases of megaloblastic anemia.
Conclusion: Serum LDH is a simple and non-invasive test. It can be used as a screening test before performing bone marrow aspiration thus provide an important means of diagnosis.

Keywords: Serum LDH, Megaloblastic anemia, Hemoglobin.

Received: 20-07-2024; **Accepted:** 26-03-2025; **Available Online**: 11-12-2025

1. Introduction

Megaloblastic anemia presents a significant health challenge in developing nations such as India. The notable responsiveness to treatment makes addressing these anemias particularly crucial.[1] Deficiency of vitamin B12 and folate accounts for over 95% of megaloblastic anemia cases.[2] Peripheral blood smear examination typically reveals macrocytes, macroovalocytes with hypersegmented neutrophils, thus providing supportive diagnostic evidence for megaloblastic anemia.[3] Macrocytosis is best detected by determination of MCV. Value exceeding 100fl are considered to establish the diagnosis of macrocytosis. MCH is also increased but MCHC is within normal limits. Bone marrow aspiration and evaluations of Vitamin B12 and red cell folate levels are the gold standard diagnostic techniques. However, the constraints associated with tests such as serum vitamin level measurements and the Schilling test have become evident. Their unavailability in peripheral medical centers has prompted increased interest in alternative simple biochemical investigations like assessing serum LDH levels.[4]

The significant increase in serum LDH levels in megaloblastic anemia was first documented by Hess B et al in 1955.[5] Since then this test did not became handy due to difficulties in assessment process. Now with advancement in technology, the assessments have been simplified. Elevation of Plasma LDH concentration is seen in patients of megaloblastic anemia. The normal range of LDH is between 140 to 280 U/L. LDH, an intracellular enzyme, facilitates the

*Corresponding author: Shivani Dogra
Email: shivanidogramani2@gmail.com

https://doi.org/10.18231/j.pjms.78117.1765436069

synthesis of lactate and pyruvate in a reversible reaction, commonly serving as a biomarker for cell damage and death. LDH is composed of five distinct isoenzymes, LDH1 through LDH5, each consisting of four subunits. It is distributed in various body tissues such as the heart, liver, skeletal muscle, kidney, and red blood cells (RBCs).[6] In patients with megaloblastic anemia, ineffective erythropoiesis leading to intramedullary hemolysis results in elevated levels of certain enzymes, particularly LDH. LDH serves as a marker of tissue breakdown and is notably abundant in RBCs. The release of LDH into circulation due to RBC lysis contributes to the observed high levels of LDH in megaloblastic anemia.[7] The higher LDH levels are linked not just to the increased turnover of megaloblastic cells within the bone marrow, but also to the elevated LDH content found within these cells.[8]

Serum LDH measurement serves as a potential screening tool for diagnosing megaloblastic anemia prior to resorting to bone marrow aspiration.[9] Early recognition of Megaloblastic anemia with simple investigations like serum LDH levels can also help in assessing the prognosis of Megaloblastic anemia.[10]

2. Aim and Objectives

To evaluate the role of LDH in the diagnosis of Megaloblastic anemia by studying serum LDH levels in cases of Megaloblastic anemia.

3. Materials and Methods

The study was conducted in the department of Pathology, GMC Jammu for a period of one year from October 31st, 2022 to November 1st 2023.

3.1. Study type

The Study commenced after obtaining Institutional Ethical Committee approval (IEC/GMCJ/2022/1129 dated 29/08/2022). The present study incorporated 100 cases of megaloblastic anemia diagnosed via examination of both peripheral blood smears and bone marrow.

3.2. Inclusion criteria

1. Clinically suspected cases of Megaloblastic anemia.
2. Patients with macrocytic anemia on peripheral blood smear with Mean corpuscular volume of >95 fl/100 fl.
3. Patients diagnosed on bone marrow examination with megaloblastic anemia.

3.3. Exclusion criteria

1. Other conditions that exhibit an increase in serum LDH activity, such as myocardial infarction, congestive heart failure, cirrhosis, pulmonary infarction, and leukemias.
2. Anemias due to other causes like iron deficiency anemia and hemolytic anemias.

A detailed clinical history and physical examination was done in all the cases. Following investigations were done to establish the diagnosis of Megaloblastic anemia i.e Complete blood count including Hemoglobin, MCV, MCH, MCHC, PCV, RBC count, peripheral blood smear; serum Vitamin B12 and folic acid levels and LDH estimation. Investigations like Retic count, Serum iron, Serum TIBC and bone marrow aspiration done whenever required to exclude other causes of anemia.

3.4. Method

Blood samples were collected for the analysis of hematological parameters such as.

1. Hemoglobin
2. MCV, MCH, MCHC, PCV, RBC count by automated cell counter.
3. Peripheral blood smears underwent staining with Leishman's stain and were observed under a light microscope to identify the type of anemia.
4. Bone marrow aspiration smears were stained with Leishman's stain and examined to confirm the diagnosis of Megaloblastic anemia.
5. Serum LDH level estimation by automated biochemistry analyser were done on all cases of megaloblastic anemias.

4. Results

For this study, we included 100 cases of megaloblastic anemia diagnosed via examination of both peripheral blood smears and bone marrow.

Table 1: Distribution of cases of Megaloblastic anemia by age

Age (in years)	No of cases	Percentage%
1-10	12	12
11-20	18	18
21-30	30	30
31-40	10	10
41-50	06	06
51-60	08	08
>60	16	16
Total	100	100

In the present study maximum number of cases 30(30%) were in the age group of 21-30 years followed by 18 (18%) cases in 11-20 years. Minimum number of cases i.e 6% and 8 % were in the age group of 41-50 years and 51-60 years respectively. (**Table 1**)

Table 2: Sex wise distribution of cases of Megaloblastic anemia.

Sex	No of cases	Percentage%
Male	54	54
Female	46	46
Total	100	100

In the present study males predominated the study comprising of 54 (54%) cases while females were 46 (46%) with narrow margin. Male to female ratio came out to be 1.17:1.(**Table 2**)

Table 3: Distribution of megaloblastic anemia cases based on hemoglobin levels.

Hb level (gm/dl)	No. of cases	Percentage (%)
<4	26	26
4-8	55	55
>8	19	19
Total	100	100

In this study, the highest proportion of cases, accounting for 55%, occurred when hemoglobin levels were between 4-8 g/dl. Following this, 26% of cases were observed with hemoglobin levels below 4 g/dl, while 19% of cases presented with hemoglobin levels exceeding 8 g/dl.(**Table 3**)

Table 4: Distribution of Red cell indices in patients with Megaloblastic Anemia.

MCV (fl)	No of cases	Percentage%
<95	03	03
95-100	37	37
>100	60	60
MCH (pg)		
<32	06	06
32-34	54	54
>34	40	40
MCHC(gm/dl)		
<30	06	06
30-32	26	26
32-34	56	56
34-36	12	12
Total	100	100

Out of 100 cases all the cases except 3 cases had MCV > 95 fl. 60 % of cases had MCV > 100 fl while 37 % of cases had MCV between 95-100 fl. Maximum number of cases i.e 54% had MCH between 32-34 pg followed by 40% of cases with MCH > 34 pg. Maximum number of cases i.e 94 % had MCHC within the normal limits (30- 36) gm /dl.(**Table 4**)

Table 5: Distribution of cases of Megaloblastic anemia based on serum LDH levels.

Serum LDH level (U/L)	No of cases	Percentage%
<250	0	0
250-1000	08	08
1000-2000	22	22
2000-3000	35	35
3000-4000	25	25
>4000	10	10
Total	100	100

Out of 100 cases maximum number of cases i.e 35% had serum LDH level of 2000-3000 U/L and 25% had serum LDH level of 3000-4000 U/L. Only few cases i.e 8% had serum LDH level of 250-1000 U/L. The serum LDH levels ranged from 482 to 4690 U/L, indicating a 2 to 20-fold increase in cases of Megaloblastic anemia.(**Table 5**)

5. Discussion

5.1. Age distribution

In this study, the largest proportion of cases (30%) fell within the age group of 21-30 years. Gaikwad AL et al[1] reported the highest occurrence of megaloblastic anemia in the age group of 11-40 years. Phurailatpam Madhubala Devi et al,[11] in their study of 50 cases, noted that the majority of cases were between 21-40 years old. Similarly, Gore B.P et al,[7] in a study involving 42 patients, found the mean age of patients to be 35.12 years. Mukibi et al,[12] 1992 in study of 100 cases reported 2 peaks one in the 3rd and 4th decade and other in 7th decade. In most of the studies the megaloblastic anemia was seen in adults.

5.2. Gender distribution

In this study, males were observed to be more affected than females, with a male to female ratio of 1.17:1. Chakravarty N et al[2] noted that among 20 cases, 55% were males and 45% were females, with a male to female ratio of 1.2:1. Prem Kumar M et al[13] reported a male to female ratio of 1.9:1 in their study involving 140 patients, indicating male predominance. Similarly, Phurailatpam Madhubala Devi et al[11] observed a male to female ratio of 1.5:1 in their study of 50 cases, also showing male predominance. Lakhotia M et al[14] reported a male predominance in cases of megaloblastic anemia, with 30% of the cases being males compared to 18.5% females.

This male preponderance may be attributed to the increased requirement for vitamin B12 and folic acid in them.

5.3. Hemoglobin level

In our study, the maximum number, that is 55% of cases, presented with a hemoglobin level ranging from 4 to 8 gm/dl. Gupta M et al[15] in study of 35 cases found that maximum number of cases (74.29%) presented with haemoglobin level of 4-7 gm/dl.

5.4. RBC indices

In our study maximum number of cases had MCV > 100 fl. Maximum number of cases i.e 54% had MCH between 32-34 pg followed by 40% cases with MCH > 34 pg. Maximum number of cases had MCHC within normal limits. This is in correspondence to study by Hallberg, 1965[16] and Hall, 1981.[17] Wilkinson,1949[18] had also reported macrocytosis with increase in MCV that precedes the development of anemia. Chakravarty N et al[2] found that out of 20 cases maximum number of cases i.e 90% had MCV > 100 fl. He

also found that maximum number of cases i.e 95% had MCH > 34 pg and all the 20 cases had MCHC within normal limits (30-36 gm/dl).

5.5. LDH level

In our study, the majority of cases (35%) exhibited serum LDH levels ranging from 2000-3000 U/L, followed by 25% of cases with serum LDH levels between 3000-4000 U/L. This indicates a notable increase in serum LDH levels, ranging from 2 to 20 times the normal range. Gaikwad AL et al[1] observed that the majority of megaloblastic anemia cases (80.49%) had LDH values exceeding 3000 U/L, representing a 19-fold increase in serum LDH values. Gronvall et al[19] and Jaswal et al[21] highlighted the diagnostic significance of serum LDH levels exceeding 3000 U/L in megaloblastic anemia. Stein ID[20] observed a significant elevation in serum LDH levels, ranging from 1.3 to 24 times higher than normal, in cases of megaloblastic anemia. Similarly, Hess B et al[5] reported a substantial increase in serum LDH activity, ranging from 5 to 21 times the normal range, in megaloblastic anemia.

Gupta M et al[15] found that the highest number of cases had LDH levels ranging from 3000-4000 U/L. Thus there was 2 to 20-fold rise in serum LDH levels in megaloblastic anemia which is primarily attributed to hemolysis occurring in the bone marrow due to ineffective erythropoiesis.

6. Conclusion

Serum LDH plays a crucial role in diagnosing megaloblastic anemia, offering a simple and non-invasive testing option. It can serve as a preliminary screening tool prior to further diagnostic procedures such as bone marrow examination.A simple investigation like serum LDH level helps in the early recognition of megaloblastic anemia. It has been seen that there is significant fall in serum LDH level with treatment so it is a cost effective tool in monitoring the response to treatment. We conclude that serum LDH levels can be used as a single discriminating marker to separate and diagnose Megaloblastic Anemias from other nutritional anemias.

7. Source of Funding

None.

8. Conflict of Interest

None.

References

1. Gaikwad AL, Jadhav DS. Utility of serum lactate dehydrogenase in the diagnosis of Megaloblastic anemia. *Int J Res Med Sci*. 2018;6(9):3051–6. https://doi.org/10.18203/2320-6012.ijrms20183643
2. Chakravarty N, Santhikiran D, Brahma A, Singh UR, Kol PC, Sen S. Study of serum lactate dehydrogenase level as diagnostic and prognostic indicator of Megaloblastic anemia. *Int J Adv Med*. 2019;6(4):1119–206. https://doi.org/10.18203/2349-3933.ijam20193271
3. Shubhangi Chaudhari and Suparna Bindu. Correlation of Lactate Dehydrogenase in Megaloblastic Anemia. *Int J Curr Med Appl Sci*. 2015;9(1):28–32.
4. Kumar V, Mirji G. Evaluation of Serum LDH levels in the diagnosis and immonitoring the response to the treatment in children with megaloblastic anemia. *Int J Pediatr Res*. 2019;6(05):217–20. https://doi.org/10.17511/ijpr.2019.i05.04
5. Hess B, Gehm E. Uber die Milchsäuredehydrogenase im menschlichen Serum [Lactic acid dehydrogenase in the human blood]. *Klin Wochenschr*. 1955;33(3-4):91–3. https://doi.org/10.1007/BF01473548.
6. Wickramasinghe SN. Diagnosis of Megaloblastic anemias. *Blood Rev*. 2006;20(6):299–18.
7. Gore B.P, Kurundkar G, Bhat S. Retrospective study of serum LDH in megaloblastic anemia. *Indian J Appl Res*. 2015;5(1):454–55.
8. Panteginini M, Bais R. Serum enzymes. In: Burtis C, Bruns D, eds. Teitz Fundamentals of clinical chemistry and molecular diagnostics. 7th ed. St Louis, MO: Elsevier Saunders; 2014:318–36.
9. Eivazi-Ziaei J, Dastgiri S, Sanaat Z. Estimation of the diagnostic value of myeloperoxidase index and lactate dehydrogenase in Megaloblastic Anemia. *J Clin of Diagn Res*. 2007;1(5):380–4. https://doi.org/10.7860/JCDR/2007/.122
10. Gupta A, Ravanagomagan, Sethi RS. The Role of Serum LDH level as an Early marker and Prognostic indicator for Megaloblastic Anemia in Children. *Indian J Public Health Res Dev*. 2021;12(1):7–12.
11. Phurailatpam Madhubala Devi et al. Clinicohematological profile of Pancytopenia in Manipur, India. *Kuwait Med J*. 2008;40(3):221–4.
12. Mukiibi JM, Makumbi FA, Gwanzura C. Megaloblastic anemia in Zimbabwe: Spectrum of clinical and haematological manifestations. *East Afr Med J*. 1992;69(2):83–7.
13. Premkumar M, Gupta N, Singh T, Velpandian T. Cobalamin and folic Acid status in relation to the etiopathogenesis of pancytopenia in adults at a tertiary care centre in north India. *Anemia*. 2012;2012:707402. https://doi.org/10.1155/2012/707402.
14. Lakhotia M, Shah PKD, Balani V, Gupta A, Saxena A, Sinha HV. Incidence of Megaloblastic anemia in Indian adults and the role of serum LDH as a diagnostic tool. *Indian J Haematol Blood Transf*. 1994;12:113–5.
15. Gupta M et al. Serum lactate dehydrogenase in diagnosis of Megaloblastic anemia- An observational study in central India. *JMSCR*. 2019;7(7):603–10. DOI:10.18535/jmscr/v7i7.106
16. Hallberg L. Blood Volume, hemolysis and regeneration of blood in pernicious anemia: study based on the endogenous formation of carbon monoxide and determinations of the total amount of hemoglobin. *Scand J Clin Lab Invest*. 1955;7(16):1-127.
17. Hall CA. Vitamin B12 deficiency and early rise in mean corpuscular volume. *JAMA*. 1981;245(11):1144-6.
18. Wilkinson J. Megalocytic anemias. *Lancet.* 1949;1(6548):249.
19. Gronvall C. On the serum activity of lactic acid dehydrogenase and phosphohexose isomerase in pernicious and hemolytic anemias. *Scand J Clin Lab Invest*. 1961;13:29–36. https://doi.org/10.3109/00365516109137245.
20. Stein ID. Elevated serum lactate dehydrogenase activity in megaloblastic anemia--some current explanations re-examined. *Am J Clin Pathol.* 1973;59(1):122–3. https://doi.org/10.1093/ajcp/59.1.122.
21. Jaswal TS, Mehta HC, Gupta V, Singh M, Singh S. Serum Lactate dehydrogenase in diagnosis of Megaloblastic anemia. *Indian J Pathol Microbiol*. 2000;43(3):325–9.

Cite this article: Sharma P, Dogra S, Sharma S. Role of lactate dehydrogenase in the diagnosis of Megaloblastic anemia-An observational study at tertiary care centre. *Panacea J Med Sci*. 2025;15(3):551-554.