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Lactate Dehydrogenase as Predictor for Severity in Sickle Cell Disease

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ABSTRACT

Introduction: Pyruvate to lactate in a glycolytic pathway is caused by enzyme lactate dehydrogenase (LDH) with the conversion of NADH TO NAD⁺. Lactate dehydrogenase can be found in different body tissues. For hemolysis marker lactate dehydrogenase levels can be used. In sickle cell anaemia patient those who are in the steady-state (SS) there will be an increase in the level of lactate dehydrogenase(LDH). In sickle cell disease, the life of the patient is hampered due to crisis and it is very difficult to predict the crisis. Hence in our study, we used a marker lactate dehydrogenase (LDH) to predict the severity of the crisis.

Objectives: To study the ability of serum LDH levels in predicting the severity of disease in sickle cell anaemia.

Methodology: To achieve the objective we assess serum LDH levels during steady-state and crisis and to correlate above with chronic complications (PH, Microalbuminuria, Liver functions) and severity of the crisis. Patients fulfilling selection criteria will be recruited after obtaining written consent. Detailed history including the age of onset, frequency and severity of the crisis, frequency of admissions and transfusions, quality of follow up, quality of treatment received will be taken. Detailed examination including anthropometry will be recorded. The severity of the acute crisis will be decided based on the duration of pain more than 2 days, need for admission & stay more than 3 days, death, need for surgery, need for support and need for other procedure.

Expected Results: We expect the LDH level to be significantly higher during the crisis. If steady-state patients are considered LDH level will be high in patients with moderate and severe disease (frequency more than 3/ year).

Key Words: Lactate Dehydrogenase, Sickle Cell Disease, Prediction

INTRODUCTION

Pyruvate to lactate in a glycolytic pathway is caused by enzyme lactate dehydrogenase (LDH) along with the conversion of nicotinamide adenine dinucleotide to nicotinamide adenine dinucleotide +. Lactate dehydrogenase can be found in all the body tissues. Lactate dehydrogenase is found in five different isoenzymes types 1-5 as by their electrophoretic motility.¹ Their distribution of all the types of LDH is different across different body tissues. 1, 2 can be found in RBC and heart smooth muscle; type 3 is found to be highest in lungs; type 4 is found to be highest in the kidney, placenta, pancreas; and type 5 is found in increased levels in skeletal muscle and liver.² The serum LDH routine evaluation includes all of the 5 types.

Along with increase reticulocyte count, increase in indirect bilirubin level, and decrease in serum haptoglobin,

Lactate dehydrogenase (LDH) also has been used as a marker of hemolysis. In sickle cell anaemia in the steady-state (SS) there will be an increase in the level of lactate dehydrogenase(LDH).³ And when painful vasoocclusive crises (VOCs) like dactylitis, sickle cell hepatopathy and abdominal crisis, and acute chest syndrome, the lactate dehydrogenase levels may further increase in some sickle cell patients due to increase in hemolysis⁴. In one study Neely et al found that increase in serum LDH was not correlated with plasma Hb level, indicating that the source of LDH is not secondary to hemolysis but rather to tissue damage.¹

In a forthcoming enlightening partner concentrate in youngsters between a half year to 18 years indicated that the LDH chemical level increments fundamentally during an emergency contrasted and consistent state esteems and that there is a critical positive relationship between's LDH levels and the seriousness of pain.⁵ however, raised LDH levels during

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the hour of affirmation confirmation for VOC was related with the extreme result, including, passing and exacerbating clinical state expecting the move to the emergency unit, the patients with sickle cell sickness (SCD).⁶

The predominance of microalbuminuria and proteinuria in the patients considered was 5% and 15%, separately. Univariate and multivariate investigations demonstrated a critical connection between LDH level, microalbuminuria, increment in unconjugated bilirubin levels and proteinuria.⁷ In an examination by Kato et al announced a relationship among hemolysis and subphenotypes of Sickle cell malady, including pneumonic hypertension (PH), yet the conclusion of hemolysis depended on Lactate dehydrogenase levels.⁸ In an examination by Autauga et al revealed a noteworthy connection between Pulmonary hypertension and microalbuminuria, yet no connection with hemolysis.⁹

This information proposes that it is the LDH level that is no doubt connected with PH and microalbuminuria regardless of the seriousness of hemolysis. In any case, except if the relationship among hemolysis and PH and different inconveniences of SCD is demonstrated by RBC endurance considers, this remaining parts speculation. Raised degrees of serum LDH is a marker of vague tissue harm. The clinical picture and the degree of LDH isoenzymes may give pieces of information to its source¹⁰. The results will be analysed with SPSS.

MATERIALS AND METHODS

Patients fulfilling selection criteria will be recruited after obtaining written consent. Detailed history including the age of onset, frequency and severity of the crisis, frequency of admissions and transfusions, quality of follow up, quality of treatment received will be taken. Detailed examination including anthropometry will be recorded. The information will be entered in a prevalidated pre-tested proforma.

Following investigations will be carried out

- Complete blood cell profile (Hb%, Total Leukocyte Count (TLC), Differential Leukocyte Count (DLC)
- Serum LDH levels
- Microalbuminuria, ECHO for pulmonary hypertension, SGPT, SGOT.
- Other investigations will be done as required.

Chronic disease will be called severe if any 1 of the major organ affected like kidney, heart or liver based on investigations (microalbuminuria, echo for pulmonary hypertension, SGPT, SGOT, serum bilirubin) and number of crisis in a year.

The severity of the acute crisis will be decided based on duration of pain more than 2 days, need for admission and stay more than 3 days, death, need for surgery, need for support and need for other procedure.

Study design

This is Prospective Cohort Study decided to carry at Acharya Vinoba Bhave Rural Hospital, Sawangi, Maharashtra, Located in Central India. Participants will be grouped as GROUP A which are diagnosed patients of sickle cell anaemia in steady-state for at least 6 weeks and GROUP B which are patients presenting with the acute crisis.

Inclusion criteria

Patients between 6 months to 18 years diagnosed to have sickle cell disease either in steady-state or crisis.

Exclusion criteria

Patients denying consent

Variables

- Hb%, TLC, DLC, PS-CBC
- Serum LDH levels
- Microalbuminuria, echo for pulmonary hypertension, SGPT, SGOT, SR. Creatinine

Study size:

The estimated sample size for one-sample comparison of proportion to the hypothesized value

Test Ho: $p = 0.4200$, where p is the proportion in the population

Assumptions

Alpha = 0.0500 (two-sided)

Power = 0.9000

Alternative $p = 0.2500$

Estimated required sample size (n): 81

Quantitative variables: LDH

Expected Outcomes/Results:

- 1) We expect the LDH level to be significantly higher during the crisis.
- 2) If steady-state patients are considered the LDH level will be high in patients with moderate and severe disease. (frequency more than 3/ year)
- 3) During crisis LDH levels will be high in severe crisis requiring transfusions, prolong stay or any other intervention.

DISCUSSION

Serum LDH is typically raised in sickle cell frailty in the consistent state (SS). During excruciating vasoocclusive emergencies (VOCs), the LDH may increment further in certain patients as a result of hyperhaemolysis, as appeared by RBC endurance considers. Information proposes that expansion in LDH level is in all likelihood connected with an expanded

number of emergency. Raised degrees of serum LDH is a marker of vague tissue harm. In this way serum, LDH levels are raised during an emergency. An imminent engaging partner concentrate in kids indicated that the LDH level increments fundamentally during VOCs contrasted and consistent state esteems and that there is a noteworthy positive connection between LDH levels and the seriousness of torment however not among LDH and Hb. Also, raised LDH levels at confirmation for VOCs were related to extreme result, including passing and declining clinical state expecting the move to the emergency unit, grown-up patients with sickle cell infection (SCD). Raised degrees of serum LDH is a marker of vague tissue harm. The clinical picture and the degree of LDH isoenzymes may give intimations to its source. Various articles in the neighbourhood setting identified with this examination were reviewed. Wasnik et al conducted an evaluation of serum zinc and antioxidant vitamins in adolescent homozygous sickle cell patients in Wardha.¹¹ Baliga et al studied malondialdehyde levels in serum and saliva of children affected with sickle cell anemia.¹² Similar child health-related studies were reported.¹³⁻¹⁷ Jaiswal et al reported a comparative study on peripapillary retinal nerve fibre layer thickness in patients with iron-deficiency anemia.¹⁸

CONCLUSION

Lactate Dehydrogenase level will be a useful diagnostic criterion for sickle cell disease cases.

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