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Evaluating The Glycolytic Shifts In Respiratory Diseases: A Correlative Study

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ABSTRACT

Objective: To examine the possible correlation between the glycolytic profile which include glucose and lactate level in various respiratory condition like asthma, pneumonia, cystic fibrosis, tuberculosis etc.

Result: A study examining the relationship between glucose and lactate levels among 100 patients with respiratory conditions found considerable variability in glucose levels and lactate levels. Elevated glucose levels were observed in some patients, while normal ranges were 70-99 mg/dL (fasting) or up to 125 mg/dL (non-fasting). A weak positive linear association was found, suggesting a slight rise in lactate levels as glucose levels rose. Fisher's z-transformation showed a 95% confidence interval for the correlation coefficient, suggesting a minimal and clinically not relevant correlation. A scatter plot showed no obvious trend, indicating that elevated glucose levels may be an accurate measure of lactate buildup.

Novelty: In order to provide insight into metabolic adaptations and the impact of variables such as medicine, lifestyle choices, and the severity of the disease on glucose and lactate levels, this study investigates the weak relationship between glucose and lactate metabolism in respiratory patients.

Keywords: *Glucose, Lactate, Respiratory Diseases, respiratory disorders, glycolysis, shifts, Metabolism, Hypoxia, Biomarkers, Asthma, Tuberculosis, COPD, ARDS, hypoxia, inflammation*

1. INTRODUCTION

The lungs are a metabolically active organ that plays a central role in maintaining cellular homeostasis by regulating glucose and lactate levels. Glucose metabolism in lung tissue is essential for cellular energy production, with oxygen being a critical factor in balancing anaerobic and aerobic glycolysis **(Ashcroft et al, 1970).** In healthy cells, when oxygen levels are adequate, oxidative phosphorylation is the primary means of ATP production. However, in hypoxic conditions or when oxygen is scarce, cells shift to glycolysis as the main energy source. This metabolic shift is particularly prominent in tissues with high metabolic demands or limited oxygen supply **(Glancy et al., 2020)**. Lung cells also interact with various metabolic pathways to regulate energy production. Whereas, Carbon dioxide (CO_2), a consequence of cellular metabolism, including glycolysis and the tricarboxylic acid cycle (TCA cycle), is eliminated via the lungs. Acid-base imbalances, including respiratory acidosis, can result from CO_2 accumulation and impact metabolic pathways and enzyme performance. Glycolytic enzymes work well when pH levels are maintained by the lungs' effective CO_2 removal ***(Gupta et al., 2022)***. For example, glycolysis in the cytoplasm converts glucose to pyruvate, a process governed by enzymes like hexokinase (HK), phosphofructokinase (PFK), and pyruvate kinase (PK). These enzymes are tightly regulated to ensure proper glycolytic flux, and in response to hyperglycemia, cells may upregulate glycolysis and glycogen synthesis **(Wilson et al, 1979).** Additionally, the pentose phosphate pathway works in parallel with glycolysis to produce NADPH and ribose for cellular functions **(Higo et al., 2022)**.

When oxygen availability is compromised, lactate is produced as a byproduct of glycolysis. This occurs because pyruvate is converted to lactate by lactate dehydrogenase (LDH) rather than entering the tricarboxylic acid (TCA) cycle for further oxidation **(Bennis et al., 2020)**. In conditions of low oxygen or compromised mitochondrial function, such as in various respiratory diseases, lactate can accumulate in the blood, leading to lactic acidosis. This metabolic shift is crucial in maintaining energy production during stress but also requires efficient lactate elimination via the lungs **(Adar et al., 2023)**. Respiratory diseases like chronic obstructive pulmonary disease (COPD), asthma, and cystic fibrosis can disrupt these metabolic processes, leading to altered glucose and lactate levels. In hyperglycemia, for instance, the liver increases glucose production, while peripheral glucose utilization decreases. Conversely, in hypoglycemia, prolonged hypoxia may deplete glucose stores, resulting in pyruvate accumulation and lactate production **(Clyne et al, 2021).** The Cori cycle, which facilitates the conversion of lactate back to glucose in the liver, may also be impaired in respiratory diseases, further exacerbating metabolic disturbances **(Wang et al., 2020).** In conclusion of the finding, the lungs play an integral role in regulating glucose and lactate metabolism, and disruptions in respiratory function can significantly impact these metabolic pathways, influencing overall cellular homeostasis and energy balance in the body.

But there are studies on these topics which also shows that various factors like environment, age, gender etc are also a part of the elevation in levels of glycolytic shifts. However, this study hypothesizes that whether the patients or individual affected with various respiratory conditions have any correlative effect in their elevated levels of lactate and glucose levels in body.

2. METHODOLOGY:

2.1 Study Design

The prospective study was conducted based on ABG (Arterial Blood Gas) test preferred heparized sample and was conducted at NABL Accredited Lab in the Delhi NCR region. This study includes the patients with respiratory conditions like asthma, tuberculosis, cystic fibrosis, pneumonia.

2.2 Sample Size

A total of 100 patient heparinized blood sample were collected from NABL Accredited lab in Delhi NCR region.

2.3 Ethical Approval and Patient Consent

Ethical approval for this study was obtained from a relevant independent committee priorly. Additionally, written informed consent was obtained from all study participants before the study commence.

2.4 Study Eligibility Criteria

- **Inclusive Criteria**

The study includes patient in ICU with various respiratory disorders like asthma, tuberculosis, cystic fibrosis, pneumonia of both genders aged between 35-70 years.

- **Exclusive Criteria**

To ensure the findings' reliability and accuracy, the results of the participants who were on medication or taking medicines that could significantly change glucose or lactate metabolism were excluded to participate. Furthermore, people who smoke or drink too much alcohol were not included because these habits can directly affect the respiratory system and metabolic processes. Possible influences were also thought to include lifestyle variables including poor eating habits and constant stress. As stress and inadequate nutritional intake can impact glucose regulation and obesity can result in insulin resistance, which might alter metabolic pathways. The study intends to concentrate on a more uniform sample by eliminating participants with these traits, which will lower variability and guarantee that the findings are more correctly defined to the physiological relationships between glucose and lactate metabolism in respiratory disorders.

3. RESULTS AND DISCUSSION

A correlative analysis was conducted to investigate the relationship between glucose (mg/dl) and lactate levels (mmol/l) among 100 patients with respiratory conditions. The statistics revealed considerable variability in glucose levels ranging from 34 -434 mg/dL whereas the lactate levels ranging from 0.4-14.6 mmol/l. There was several patients, showing the elevated levels in both parameters, notably the normal ranges for glucose is 70-99 mg/dL (fasting) or upto 125 mg/dL (non-fasting) and normal range of lactate levels is below 2.0 mmol/L.

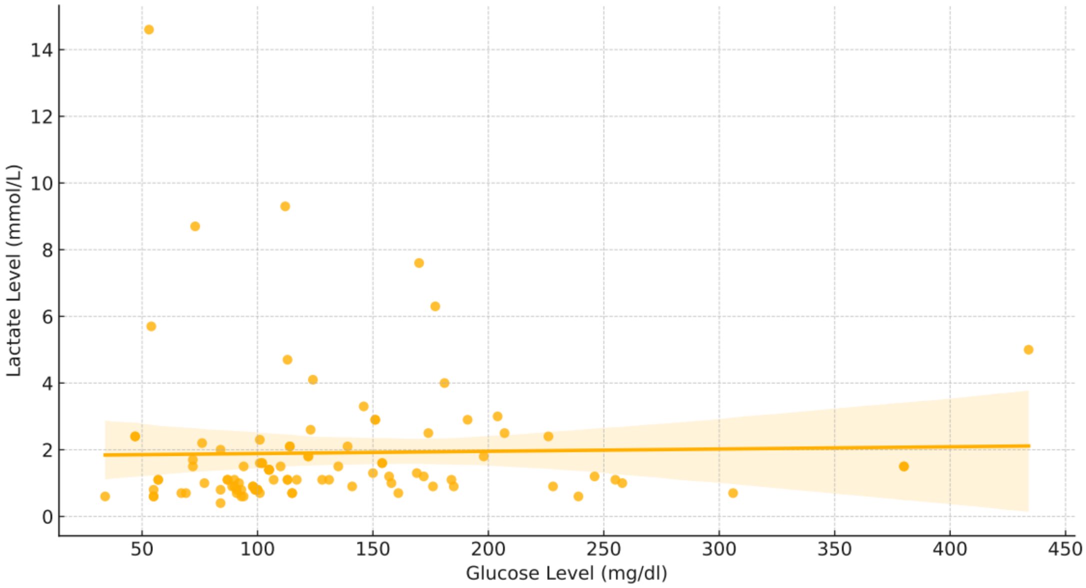

Fig.1: Glucose vs Lactate Correlative Report using Pearson Correlation. Where r=0.023, p=0.8192 and 95% CI = (-0.174,0.219)

A very weak positive linear association as mentioned in Fig. 1, found when the relationship between glucose and lactate levels was analyzed; the Pearson correlation value (r) was 0.078. This suggests a weak correlation, indicating that lactate levels likely to rise slightly as glucose levels rise, but the relationship is not extremely strong. A two-tailed hypothesis test was used to determine the statistical significance of this link, and the p-value was 0.4537. Which are unable to reject the null hypothesis since this result is greater than the traditional significance level of 0.05. Consequently, we get the conclusion that there is not a statistically significant connection between the levels of lactate and glucose in this sample.

	SO2 (Oxygen Saturation %)	*pH*	*pCO2 (mmHg)*	*pO2 (mmHg)*	*Glu (mg/dL)*	*Lac (mmol/L)*
SO2 (Oxygen Saturation %)	1					
pH	-0.2299	1				
pCO2 (mmHg)	-0.15249	0.018205	1			
pO2 (mmHg)	0.543891	-0.0357	0.160728	1		
Glu (mg/dL)	0.034323	-0.079	-0.11082	-0.0377	1	
Lac (mmol/L)	-0.14254	-0.04043	-0.11145	0.038623	-0.05337	1

Table 1: Represents the weak linear association using Pearson Correlation Coefficient.

Fisher's z-transformation was used to compute a 95% confidence interval for the correlation coefficient, which further supports this finding. The true correlation may be zero or even negative, as the interval, which crossed zero, varied from -0.127 to 0.279. This implies that any possible correlation between lactate and glucose in the respiratory population is probably minimal and clinically unimportant. The data was visually represented using a scatter plot, which included a linear regression line and its 95% confidence range. The graphic supported the statistical conclusions by demonstrating that there was no obvious trend and that the data points were widely dispersed around the regression line. The minimal correlation was further highlighted by the regression line's shallow slope. In conclusion, there is no evident linear link between glucose and lactate levels in this particular category of respiratory patients. In this cohort, elevated glucose levels are probably to be an accurate measure of lactate buildup which also indicate that other factors may be impacting lactate levels apart from glycemic status.

4. LIMITATION

The study focused on a small cohort of respiratory patients, limiting its generalizability to the broader population. It did not account for confounding factors like medication use, smoking, alcohol consumption, or poor lifestyle habits. Other factors like genetic differences, metabolic disorders, or stress levels may also influence glucose and lactate levels. The study was cross-sectional, capturing data at a single point in time, and could not establish causal relationships or track changes over time. Longitudinal studies are needed to observe the interaction of these variables in respiratory diseases.

5. CONCLUSION

The study examines how lactate and glucose metabolism relate to respiratory health, emphasizing the function of the lungs in preserving cellular homeostasis. Factors such as medication use, lifestyle decisions, and underlying disorders can affect glucose and lactate metabolism; however, this study did not include these factors because they were excluded despite the finding of a modest positive connection. The results provide insight into metabolic changes brought on by respiratory distress and recommend more study to fully comprehend their function in respiratory disorders and their potential as biomarkers.

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