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Warburg-Effect Driven Lactic Acidosis is Associated with Early Death in Patients with Lymphoma

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INTRODUCTION

The capacity of shifting glucose metabolism to anaerobic pathway despite the presence of adequate oxygen and producing more lactate, is a well-defined phenomenon in malignant cell metabolism, and is called the Warburg Effect (WE).

A systemic rise in lactate and lactic acidosis has been reported in hematologic malignancies and less commonly in solid tumors, and is thought to occur as a consequence of both increased production of lactate- reflecting high malignancy burden, and impaired lactate turnover or elimination by liver or kidney.

AIM

We aimed to characterize the incidence and clinical impact of Warburg-driven lactic acidosis on outcome including early death.

METHOD

A retrospective study of patients admitted to the haemato-oncology department in a large tertiary medical center between the years 2013- 2022, that presented with elevated lactate levels during the first week of admission.

Patients with hematologic diseases other than lymphoma were excluded.

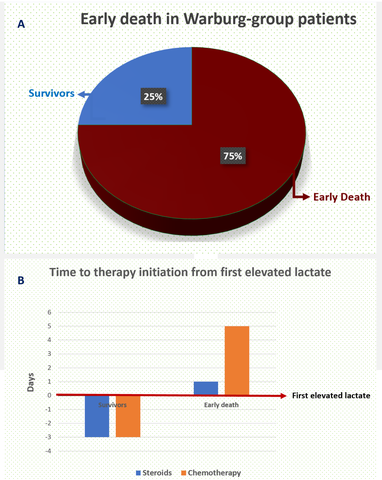
Medical records were retrieved and reviewed for a recognizable cause for elevated lactate, or non (assigned as the WE group). Early-death was defined as death of any cause within 4 weeks of admission.

RESULTS

19 patients had lymphoma and elevated lactate levels within the first week of admission. Of these, 12 patients fulfilled the criteria for WE and 7 patients had their high lactate attributed to other causes.

Early-death rate was 75% (9 patients) among patients with WE. (A)

Both steroid and chemotherapy were initiated earlier in surviving patients as compared to those who died early (within 4 weeks of admission); in surviving patients, chemotherapy was initiated at a median of 3 days **before** first elevated lactate was detected (range (-)7-1), and steroids at median of 3 days before first elevated lactate was detected, while in those who died early, chemotherapy was initiated at median of 5 days **after** first elevated lactate was detected (range (-)2-18) and steroids at median 1 day after first elevated lactate (p=0.29 and 0.05 for steroids and chemo, respectively).(B)



	Warburg group – EARLY DEATH (n=9)	Warburg group- SURVIVORS** (n=3)	P value
Age (median)	72	73	0.96
Male N(%)	5 (55.6%)	0 (3 Female)	0.1
Aggressive lymphoma N(%)	8 (88.9%)	3 (100%)	0.09
IPI (median)	4	4	0.99
Newly diagnosed	9 (100%)	1 (33%)	0.007
Lactate (mg/dL, range)	30 (22-39)	37 (30-64)	0.2
LDH (U/L, range)	1035 (645-4339)	700 (455-3906)	0.81
Glucose (mg/dL, range)	159 (81-455)	172 (165-338)	0.92
Time to anti-lymphoma therapy*	Chemo 5 ((-)2-18) Steroids 1 ((-)10-6)	Chemo (-)3 ((-)7-1) Steroids (-)3 ((-)4-1)	0.05 0.29

* Median days from first elevated lactate (steroids/chemotherapy) (range)

** Patients who survived 4 weeks of admission and discharged.

CONCLUSIONS

Warburg driven lactic acidosis is a marker of 'acute cancer' in lymphoma patients and is associated with a very high mortality rate.

Early recognition of this very high-risk clinical scenario is of utmost importance and should prompt immediate anti-lymphoma therapy that may improve outcome.

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