Leukocytosis in Diabetic Ketoacidosis; Whether the Time Has Come to Start Antibiotics? A Short Literature Review

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ARTICLEINFO	**ABSTRACT**
Article type: Letter to editor	One of the most common risk factors of DKA is infections which are more prevalent in the urinary and respiratory system respectively. Therefore, it is essential to examine the patients with DKA at the arrival in term of presence or absence of infection. Leukocytosis is commonly seen in infectious diseases . The presence of leukocytosis can trigger an antibiotic in these patients. It is while the misuse of antibiotics in addition to the financial costs to patients can increase risk of resistance to antibiotic which is a global concern.
	In several studies, increased leukocyte in patients with diabetes has been attributed to various factors such as: lack of insulin, inflammatory processes activity, secretion of adrenaline and cortisol and infection. Also, The results of studies showed a strong direct relationship between blood pH and level of WBC; i.e. the severity of blood acidity increases with the amount of leukocytesTherefore, the medical team should take a history, physical or clinical examinations to make decision on the appropriate treatment including, prescribe or not prescribe an antibiotic.

Diabetic ketoacidosis (DKA) is considered as a prevalent and life threatening metabolic emergency among type 1 diabetic patient (1, 2). Infection consider as the most common risk factors for DKA. It usually occurs in urinary and respiratory systems, respectively (3, 4, 5). Therefore, it is essential to examine the presence or absence of infection in emergency department. Leukocytosis is commonly seen in infectious diseases and is an index for antibiotic initiation (6, 7). However, it can be interpreted differently in DKA and more attention about causes is needed. On the other hand, inappropriate administration of antibiotics increases both of financial costs and risk of antibiotics resistance which is a global concern (8).

Some studies described White Blood Cell (WBC) count changes in DKA. Karavanaky et al (2012), found average number of WBC was $15.2 * 10^2$ mm³ in hospital arrival that was high more than normal ranges (9). Another study illustrated a significant increase in level of WBC in DKA compared to patients without DKA (13325 mm³ against 6008 mm³). Meanwhile, the increase of infection led to higher level of WBC significantly in DKA patients than non-infected DKA (16910 mm³ against 10310 mm³) (10). The results of researcher showed a direct relationship between blood pH and level of WBC. In other words, high level of WBC is correlated with increase of blood acidity. Wasif et al (2012) examined predictors of infection in DKA patients and found leukocytosis is a more accurate predicator for DKA severity rather than infection (11). In a case report conducted by Kayshyma et al (1993), leukemoid reaction (increased leukocytes over $25 * 10^5$ without leukemia) occurred in patients with DKA absences of infection (12).

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In several studies, leukocytosis in DKA has been attributed to various factors. many of researcher believed lack of insulin can stimulate production of Neutrophil in bone marrow (13) , upon insulin administration and fluid therapy induced to decrease leukocyte count. after 120 hours (9). furthermore, secretion of adrenaline, cortisol and inflammatory mediators can lead to increase of leukocytes amount (14). In another study, it evaluated correlation Granulocyte Colony Stimulating Factor (GCSF) level and leukocytosis in DKA that results showed no relationship both of them. (13).

In general, leukocytosis in DKA can linked to different factors such as infections, insulin deficiency, dehydration and stress hormones secretion. At first, medical team should determine infection with take a history, physical examinations and laboratory tests. These results can be useful for make a proper decision about antibiotic initiation. Therefore, decision for antibiotic initiation based on leukocytosis as a sign of infection isn't reliable.

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