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Research Article

The Impact of Body Mass Index and Diabetes Mellitus on Patients with Acute Myeloid Leukemia

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Abstract:

Background: The incidence of obesity and diabetes mellitus (DM) is increasing worldwide and are associated with an adverse health outcome.

Aim: To evaluate the impact of obesity and DM on overall survival (OS) of adult patients with AML.

Methods: A retrospective data from AML patients between (2002-2011). Body mass index (BMI) of < 18.5 defined as underweight, 25-30 was defined as overweight, and >30 as obesity. DM patients had Hemoglobin A1C ≥ 6.5 or fasting blood sugar ≥126 mg/dL.

Results: A Total of 187 patients with median age of 70 years, 98 were men. Median BMI was 28.7. 34 patients (18%) had normal BMI, 10 (5%) were underweight, 59 (32%) were overweight, and 84 (45%) were obese. 26 patients (14%) had DM and 161 patients (86%) were not Diabetic,

Median OS was 23 weeks; with 46 weeks in normal BMI, 30 weeks in overweight, 14 weeks in obese, and 15 weeks in underweight (p=0.32). According to DM subgroups; median OS was 22 weeks in non-diabetic patients and 37 weeks in diabetic patients (p =0.42).

Conclusions: Obesity and DM did not show statistically significant association with OS in AML patients. Larger prospective studies are needed to understand this relationship better.

Keywords: AML; Body Mass Index; Diabetes Mellitus

Introduction: AML is considered to be the second most common type of leukemia in adult, with an estimated 10,430 deaths from AML [1]. It has marked heterogeneity in both response to therapy and survival [2]. Some prognostic factors have been described for AML including age, performance status, karyotype, and other factors related to patient and tumor characteristics. Some of these factors affect the response to treatment, prognosis and overall survival in AML patients. These factors predict the likelihood of attaining a complete remission and subsequent disease-free survival. Morbid obesity and diabetes have been studied as potential risk factors for the development of many hematologic malignancies including AML [3].

The prevalence of obesity is 35% of adult population in United States [4] with estimated annual medical cost was $147 billion in 2008 U.S dollars. With estimated $1,429 higher medical cost for obese versus normal weight patient [5]. Obesity is a known risk factor for certain disease including heart disease, DM II and certain malignancies including endometrial, breast and colon cancer. Higher incidences of chemotherapy toxicity and overall worse prognosis have been reported in obese pediatric patients with AML [6].

According to national diabetes, statistics reports 2014 that estimate 9.3 of United States population have diabetes and 27.8 of diabetics are undiagnosed. Additionally, diabetic patients diagnosed with AML have multiple complications related to infection, organ failure, and chemotherapy side effects. Additionally, epidemiological studies in children have shown significant correlations in incidence between AML and DM [7]. Also, many studies found a strong association between DM II and hematological malignancies [8,9]. Giving the high prevalence of DM and obesity in United States and the growing evidence of their negative effect on health and quality of life. In addition to the lack of studies evaluating the effect of DM and obesity on AML patients. The aim of the current study is to assess the impact of obesity and DM status on overall survival of adult patients with AML.

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Materials and Methods: A retrospective chart review study of AML patients treated at Akron General Medical Center, Akron, Ohio from January 2002 till December 2011.After obtaining IRB approval, we were able to identify187 patients according to World Health Organization (WHO) classification criteria of AML [10]. Inclusion criteria are all patient diagnosed with AML/high-risk MDS diagnosed in our hospital. Patient demographics, diagnosis types/subtypes, treatment, cytogenetic were recorded, and overall survival (OS) was calculated.

BMI of <18.5 was defined as underweight, 18.5-24.9 as normal weight, 25-30 as overweight, and >30 was defined as obese. Fasting blood glucose and Hemoglobin A1c were measured, Diabetic patients identified based on Hemoglobin A1C ≥ 6.5 or fasting blood sugar ≥126 mg/dL. Non-diabetics had a normal fasting blood sugar or Hemoglobin A1C <6.5.Fischer's and Wilcoxon tests were used to comparing between groups, Cox proportional hazards and logistic regression for associations for OS/RFS and CR, Kaplan-Meier test for OS and RFS estimates via JMP software V9.0.

Continuous variables in comparison groups are described using mean, standard deviation, medians, and interquartile ranges (IQR). Categorical variables in comparison groups were defined using percentages. A Cox Regression model was analyzed to account for survival over time, adjusted for BMI and for DM status while controlling for patient age at diagnosis and Complex cytogenetics.

Results: One hundred eighty-seven patients were identified in our study population with AML or high-risk MDS. The median age was 70 years. 98 (52%) were male. 46 patients had moderate to severe Bone marrow fibrosis and complex cytogenetics, and eight patients had trisomy 8.

The majority of AML patients were treated with 7+ three induction protocols. There were only 15 patients with the diagnosis of high-risk MDS according to the International Prognostic Scoring System criteria. These patients were treated with seven þ 3 or hypomethylating agents such as azacitidine or decitabine.

Median BMI was 28.7 (range 14.8-51.4). 34 patients (18%) had normal BMI, 10 (5%) were underweight, 59 (32%) were overweight, and 84 (45%) were obese. 161 patients (86%) were not Diabetic, 26 patients (14%) had DM (2 patients underweight, 5 had normal weight, four patients were overweight, and 15 patients were obese).

Overall Median OS in our study populations was 23 weeks. AML patients normal BMI had OS of 46 weeks' versus 30 weeks in overweight, 14 weeks in obese, and 15 weeks in underweight. Non-diabetics patients with AML had OS of 22 weeks versus 37 weeks for diabetic patients Even though median survival in weeks was lower in obese and underweight pts, Median OS and RFS were not significant in univariate or across BMI subgroups or DM status.

In univariate analysis, no correlation was found between survival in weeks and BMI (p=0.32) or DM status (p=0.42). In a multivariate model controlling for age and risk of mortality, no significant correlation was found between survival and DM status or BMI.

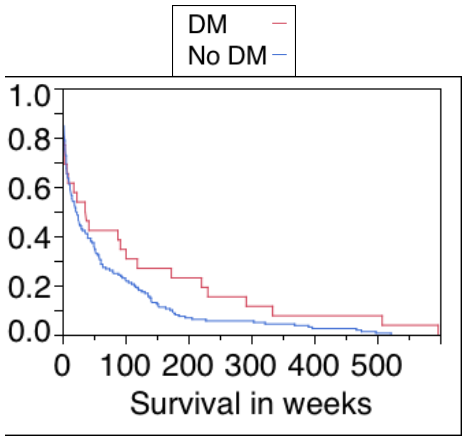

Figure 1a: Overall Survival in Patients with AML According to Diabetes Mellitus Status

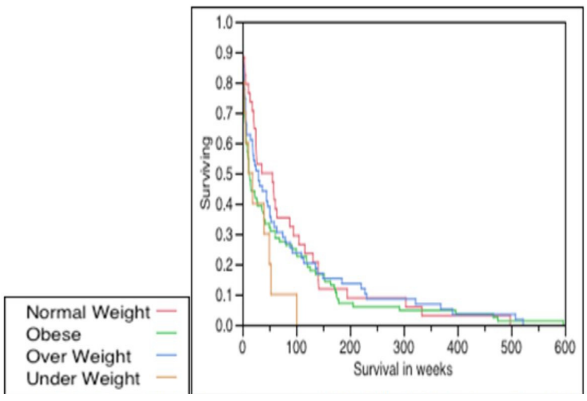

Figure 1.b: Overall Survival in Patients with AML According to BMI Classification

	Patients Characteristics	Significance
Mean Age (years)	70.0 ± 13.0	≤.001
Gender male (n)	98 (52%)	
% Trisomy 8 (n/N)	8 (4.6)	0.459
% Complex Cytogenics (n/N)	30 (17.3%)	0.269
% Osteopenia/Osteoporosis (n/N)	31 (17.9%)	0.76
Mean BMI (kg/m2) • Underweight • Normal weight • Overweight • Obese	29.0 ± 8.1 10 (5%) 34 (18%) 59 (32%) 84 (45%)	0.834
Chronic Kidney disease	41	0.121
% High level of bone marrow fibrosis	46 (26.5%)	0.71
Diabetes Mellitus	26(15 male)	0.42

Table 1: Characteristics of Patients Diagnosed with Acute Myeloid Leukemia Based on Survival

Discussion: Over the past decade, there have been climactic advances in understanding the cytogenetic and molecular genetics underlying the pathogenesis of acute myeloid leukemia (AML) [11].It is becoming increasingly apparent that AML prognosis is highly heterogeneous [12]. Therefore, defining different prognostic factors can provide significant information and establishing their respective relationships to other pre-treatment characteristics that impact the outcome. The association between obesity, diabetes mellitus and AML is not [13]. Recently, there were an increasing number of epidemiologic trials that indicated obesity and diabetes mellitus as potential risk factors for developing a variety of cancers [14-16].

In our retrospective analysis, the results showed that the median survival was lower in obese and underweight patients. However, these results weren't statistically significant. Also, there was no significant correlation between classifying the patients according to their diabetes mellitus status and overall survival.

As obesity becoming an increasing matter of concern worldwide, especially in the United States, the first finding in our study concentrates on the effect of BMI on AML survival. Previous studies suggested that abnormal BMI might be a risk factor for poor outcome in different malignancies [17]. Most of these observed associations were limited to specific types of cancers, such as liver and pancreatic cancer but not in adult AML [18,19]. Our study is considered one of the first few studies that correlate the different patterns of BMI with survival and outcome in AML patients. The second finding in our study regarded the correlation between DM and AML outcome. A recent meta-analysis study showed that diabetic patients have a 20 percent increased risk of developing blood cancers, such as non-Hodgkin lymphoma, leukemia, and myeloma [3]. However, this study did not identify a specific explanation for such association. One of the pharmacokinetic effects of DM can be explained by insulin resistance and higher glucose levels which fuel tumor growth [20,21].Another explanation could be insulin-like growth factor 1 (IGF-1) that acts as a promoter of tumor cell growth and differentiation, and has been associated with increased risk of several cancers such as colorectal, breast and prostate cancer [22,23].In fact, the possible mechanisms by which diabetes mellitus increases the risk of blood cancer are not only limited to insulin and IGF-1, and there may be additional mechanisms that need to be studied further.

The main limitation of our study is the retrospective nature, small sample size that limited the sub-analysis and missing some patient data. The lack of statistically significant results could be related to the small sample size. Giving the prevalence of obesity and DM in the United States, further research in larger prospective studies is crucial to find a possible correlation between survival in AM and obesity or DM status.

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