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Frequency of Steroid Induced Diabetes in Young Patients Treated Pre B-Cell Acute Lymphoblastic Leukemia

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ABSTRACT

Introduction: It has been noted in the literature that while there is information on the prevalence of steroid-induced diabetes, there is little information on its severity or rate. There is no proof for the local populace either. Therefore, the goal of this research is to ascertain if the level of concern is high or low among local community members who have pre-B-cell acute lymphoblastic leukemia. **Materials & Methods:** Total 100 patients between the ages of 18 and 50, both male and female, who were diagnosed with pre-B-cell acute lymphoblastic leukemia and who were receiving oral or intravenous steroids of any kind for a minimum of months were included. We excluded patients with unstable glucose levels due to another known co-morbidity and chronic diabetes. Steroid-induced diabetes is defined as blood glucose levels that are randomly higher than or equal to 200 mg/dl on two separate occasions after starting steroidal medication for more than three months. Patients with diabetes brought on by steroids were treated according to conventional procedure. **Results:** The study's participants ranged in age from 18 to 50, with a mean age of 31.11 ± 6.51 years. Seventy-eight (78.0%) of the patients were between the ages of 18 and 35. With a male to female ratio of 1.4:1, 58 (58.0%) of the 100 patients were men and 42 (42.0%) were women. In our study, 40 (40.0%) of the young patients receiving treatment for pre-B-cell acute lymphoblastic leukemia also developed hyperglycemia brought on by steroids. **Conclusion:** Our research revealed a relatively high incidence of steroid-induced diabetes in young children receiving treatment for pre-B-cell acute lymphoblastic leukemia.

INTRODUCTION

The most common cancer in children is acute lymphoblastic leukemia, an aggressive white blood cell malignancy that begins in the bone marrow and spreads quickly.[1,2] About 400–450 new instances of acute lymphoblastic leukemia are recorded each year in the UK, making it the most common pediatric cancer. It accounts for 80% of juvenile leukemias and about 25% of all childhood cancers. Acute lymphoblastic leukemia has seen significant improvements in treatment and prognosis over the past few decades, and in most cases, the once-fatal illness is now treatable.[3]

Steroids are frequently included in chemotherapy regimens for the treatment of lymphoid cancers, including acute lymphoblastic leukemia.[4] Steroid use is associated with a multitude of negative consequences that can be broadly divided into three groups, despite their effectiveness: Impaired eyesight, mood swings, immunological response changes, fluid retention with oedema, and the emergence of steroid-induced hyperglycemia are some of the early side effects. Insanity, glaucoma, cataract formation, and avascular necrosis are all summed up by unique side effects. More subtly detrimental effects that affect the endocrine system and result in bone disease, obesity, dyslipidemia, and adrenal suppression.[5] Steroid medications have the highest risk of causing hyperglycemia and overt diabetes mellitus because they impair the pancreas's ability to produce and secrete insulin, increase hepatic gluconeogenesis, decrease peripheral insulin sensitivity, and cause insulin resistance in adipose tissue and lipid metabolism.[6] Drug-induced diabetes mellitus, which can impact the prognosis of acute lymphoblastic leukemia and raise the risk of infections such cellulitis, bacteremia, fungemia, and febrile neutropenia, can be brought on by corticosteroids used to treat the disease.[7] Diabetes brought on by steroids in patients with pre-B-cell acute lymphocytic leukemia is not well documented in the literature. According to estimates, 47.9% of cases (n=70/146) may have it.[8]

This work is justified by the desire to ascertain the incidence of steroid-induced diabetes in young patients with pre-B-cell acute lymphoblastic leukemia. Although the occurrence of steroid-induced diabetes has been documented in the literature, little is known about its severity or rate. The local population also has no proof. Determining whether the degree of problem is high or low among local community people with pre-B-cell acute lymphoblastic leukemia is the aim of this study. This will help us improve our processes and ultimately use the study's findings in a local setting.

MATERIALS AND METHODS

The Shaukat Khanum Memorial Cancer Hospital & Research Center at Lahore's Department of Medicine conducted this descriptive cross-sectional study between May and October of 2024. After being approved by the institutional ethical review committee, 100 patients who satisfied the inclusion criteria were selected via non-probability sequential sampling. The informed consent of each patient will be sought. The WHO calculator is used to determine the sample size of 100 cases with a 95% confidence level, 10% margin of error, and the percentage of patients with pre-B-cell acute lymphocytic leukemia who had steroid-induced diabetes, or 47.9%.[8] Patients between the ages of 18 and 50, both male and female, who were diagnosed with pre-B-cell acute lymphoblastic leukemia (bone marrow aspirate and biopsy containing B-cell lymphoblasts; immature white blood cells >20% in bone marrow sample) and who were receiving oral or intravenous steroids of any kind for a minimum of months were included. We excluded patients with unstable glucose levels due to another known co-morbidity and chronic diabetes.

Age, gender, BMI, length of leukemia from diagnosis, history of smoking (>5 pack years), drunkenness (>20 ml daily), hypertension (BP≥140/90 mmHg), anemia (hb<10 g/dl), and prescribed steroids (type, dosage, route of delivery, and recommended duration) were recorded. The hospital's laboratory was used for blood collection and testing. Steroid-induced diabetes is defined as blood glucose levels that are randomly higher than or equal to 200 mg/dl on two separate occasions after starting steroidal medication for more than three months. Patients with diabetes brought on by steroids were treated according to conventional procedure. Performa was used to record all of the data (attached).

SPSS was used to enter and evaluate the data. The mean and standard deviation of numerical data such as age, BMI, leukemia duration, recommended dosage, and blood glucose level were computed. The frequency and percentage of categorical factors, such as gender, history of smoking, drunkenness, hypertension, anemia, steroid prescription, and steroid-induced diabetes, were displayed. Age, gender, BMI, length of leukemia, history of smoking, alcoholism, hypertension, anemia, prescribed steroids, and recommended dosage were all taken into consideration when stratifying the data. Using the chi-square test, the prevalence of steroid-induced diabetes was compared across stratified groups. A significance level of 0.05 was used to P-values.

RESULTS

The study's participants ranged in age from 18 to 50, with a mean age of 31.11 ± 6.51 years. Seventy-eight (78.0%) of the patients were between the ages of 18 and 35. With a male to female ratio of 1.4:1, 58 (58.0%) of the 100 patients were men and 42 (42.0%) were women. In our study, the average length of illness was 23.11 ± 5.20 weeks. A mean BMI of 27.61 ± 3.04 kg/m2 was recorded. Table 1 displays the patient distribution based on confounding variables.

40 (40.0%) of the young patients treated for pre-B-cell acute lymphoblastic leukemia in our study had steroid-induced diabetes (Figure 1). Steroid-induced diabetes stratification by age, gender, BMI, length of leukemia, history of smoking, drinking, high blood pressure, anemia, and steroid prescription.

Table 1

Distribution of Variables (n=100)

Variables		Frequency	%age
Age (years)	18-35	78	78.0
	36-50	22	22.0
Gender	Male	58	58.0
	Female	42	42.0
Duration (weeks)	≤24	60	60.0
	>25	40	40.0
BMI (kg/m^2)	≤30	77	77.0
	>30	23	23.0
Anemia	Yes	48	48.0
	No	52	52.0
Hypertension	Yes	64	64.0
	No	36	36.0
Smoking	Yes	28	28.0
	No	72	72.0
Drug prescribed	Prednisolone	38	38.0
	Dexamethasone	62	62.0

Figure 1

Frequency of Steroid Induced Diabetes in Young Patients Treated Pre B-Cell Acute Lymphoblastic Leukemia (n=100).

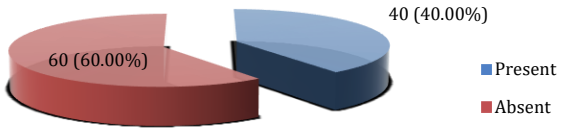

Table 2
Stratification of Steroid Induced Diabetes with respect to Age, Gender, BMI, Duration of Leukemia, History of Smoking, Alcoholism, Hypertension, Anemia and Steroid Prescribed.

Variables		Present (n=40)	Absent (n=60)	P-value
Age (years)	30-50	33 (42.31%)	45 (57.69%)	0.375
	51-70	07 (31.82%)	15 (68.18%)	
Gender	Male	22 (37.93%)	36 (62.07%)	0.619
	Female	18 (42.86%)	24 (57.14%)	
Duration (weeks)	≤24	20 (33.33%)	40 (66.67%)	0.096
	>25	20 (50.0%)	20 (50.0%)	
BMI (kg/m²)	≤30	33 (42.86%)	44 (57.14%)	0.286
	>30	07 (30.43%)	16 (69.57%)	
Anemia	Yes	20 (41.67%)	28 (58.33%)	0.744
	No	20 (38.46%)	32 (51.54%)	
HTN	Yes	25 (39.06%)	39 (60.94%)	0.799
	No	15 (41.67%)	21 (58.33%)	
Smoking	Yes	09 (32.14%)	19 (67.86%)	0.317
	No	31 (68.89%)	41 (31.11%)	
Drug prescribed	Prednisolone	17 (44.74%)	21 (55.26%)	0.449
	Dexamethasone	23 (37.70%)	39 (62.30%)	

DISCUSSION

Steroids are frequently included in chemotherapy regimens for the treatment of lymphoid cancers, including acute lymphoblastic leukemia (ALL).[9] During the treatment of lymphoid cancers, hyperglycemia is common because it occurs frequently during steroid therapy. Several studies found that the odds ratio for getting new-onset diabetes following glucocorticoid medication varied from 1.36 to 2.31. Exaggerated hepatic glucose production, increased insulin resistance, and decreased insulin secretion are common causes of steroid-induced diabetes (SID). An elevated risk of infection, extended hospital stays, and even higher fatality rates can make it more difficult.[10]

40 (40.0%) of the young patients treated for pre-B-cell acute lymphoblastic leukemia in our study had steroid-induced diabetes. A study of people with diabetes who were diagnosed between 2003 and 2004 found that oral glucocorticoid treatment was responsible for 2% of GIH.[11] Similar results were found in a study that employed the same glucose threshold (≥200 mg/dL) to detect new cases of GIH in dermatology patients who were steroid-naive and undergoing systemic glucocorticoid therapy.[12] In a recent retrospective study, 2,424 inpatients during a 4-year period had an overall incidence of GIH of 34%.[13]

In line with the findings of several earlier research[14,15], a 32% incidence of GIH was found in a meta-analysis of more than 35,000 participants from 13 studies in non-diabetic patients who took glucocorticoids for at least one month.[16] GIH prevalence was 10% (OR, 2.1) according to another recent meta-analysis that combined data from 118 randomized controlled trials. Severe hyperglycemia, which is defined as needing treatment, having recently been diagnosed with diabetes, or withdrawing from the research because it was recorded as a major adverse event, was 5%.[17]

The incidence of SID was 8.8% in rheumatoid arthritis patients who were given a low dose of prednisone (often 7.5 mg) (Panthakalam et al.[18]). However, no one experienced SID in four randomized controlled trials when patients received 5–10 mg of prednisone for two years.[19,20,21]

Even a single dose of GS can affect the regulation of blood sugar levels. Typically, it is linked to elevated postprandial glucose levels that do not affect fasting glucose levels. Interestingly, regardless of a previous history of diabetes mellitus, the likelihood of acquiring SID or SIH is dependent on the length of treatment. A 60% decrease in insulin sensitivity was noted in patients who received 30 mg of prednisone daily for just 7 days. Nonetheless, See KC et al. reported that individuals receiving a dose equal to 5 mg of prednisone alone for a maximum of 6 months were at risk of developing diabetes.[22]

Over the course of the historical evaluation of pediatric literature, studies have revealed the occurrence of hyperglycemia among pediatric ALL cases more frequently, despite the lack of evidence to differentiate between the two GCs' hyperglycemic capacities. This rise might be the result of more people using dexamethasone instead of prednisone. In the CCG-11922 research, for instance, individuals who got dexamethasone were far more likely than those who received prednisone to experience reversible grade 3 or 4 hyperglycemia (5% vs. 1.5%; P =.001).[23] According to a literature review, prevalence in pediatric literature varies greatly, ranging from 11% to 56% depending on the study.[24] Although the prevalence of hyperglycemia in people with ALL has been reported to be 37%, there have been fewer investigations on this topic.[24,25]

The only risk factor for GC-induced hyperglycemia that has been shown to be statistically significant is age. This has been attributed to puberty in the pediatric population, when growth hormone and sex hormones spike, leading to increased insulin resistance and, consequently, altered glucose metabolism. Older age, notably age >60 years, has also been linked to an increased risk of inducing hyperglycemia in the adult population.[26] Other possible risk variables, such as BMI (obesity), Trisomy 21, and the type of asparaginase used concurrently, have all been shown to have varying statistical significance in the literature.[24]

Hyperglycemia-related complications in ALL can take many different forms. Issues including hyperglycemic hyperosmolar state and diabetic ketoacidosis (DKA) have been reported in adults with ALL, despite the fact that they have not been fully studied in the juvenile population.[27] It has been proposed that the degree of hyperglycemia and the risk of infection have a dose-response relationship, and that hyperglycemia is significantly associated with a higher risk of viral, bacterial, and fungal infections in addition to febrile neutropenia.[24,28]

CONCLUSION

Our research revealed a relatively high incidence of steroid-induced diabetes in young children receiving treatment for pre-B-cell acute lymphoblastic leukemia. SID

is linked to worse disease outcomes and more therapy-related problems in patients with pre-B-cell acute lymphoblastic leukemia. Therefore, we advise patients with lymphoid cancers undergoing induction therapy to have their glycemic status closely monitored

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