

Oral manifestation of leukemic children under chemotherapy

الإعراض الفموية لأطفال سرطان الدم تحت العلاج الكيميائي

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الخلاصة

خلفية البحث: يشير المصطلح إلى اللوكيميا سرطان خلايا الدم البيضاء (وتسمى أيضا الكريات البيض أو الكريات البيضاء). عندما يكون الطفل مصاب بسرطان الدم، يتم إنتاج أعداد كبيرة من خلايا الدم البيضاء غير الطبيعية في نخاع العظام. هذه الخلايا غير طبيعية تنتج، لكنها لا يمكن أن تؤدي دورها الصحيح تجاه حماية الجسم ضد المرض لأنهم معيبة. ومعظم الأطفال المصابين بسرطان الألم الشديد

الهدف: تقييم حالة الفم في الأطفال الذين يعانون من سرطان الدم تحت العلاج الكيميائي وعلاقته مدة الاستشفاء المريض.
المنهجية: وعشرون مريض مشخص بسرطان الدم الليمفاوي الحاد (ALL)، تم جمعها من مستشفى حماية / مدينة الطب، ومستشفى الطفل المركزي التعليمي / () 25 يناير 2009 25 يناير 2010، على الاستبيان لك المعلومات الديموغرافية و السريرية والمظاهر الفموية الرئيسي.

النتائج: تراوحت عينات المرضى أعمارهم بين (5-16) سنة، و الذين تتراوح أعمارهم بين 55 مريضا فقط (43) (10-8) مريضا (58.5) 40 مريضا (31) كانوا يعيشون في جنوب العراق . واهم الشكوى كانت تورم العقد الليمفاوية في 40 مريضا (31)؛ مدة المرض هو أقل من 6 أشهر في 65 مريضا (51)؛ المرضى الذين يبقون في المستشفى أكثر 15 يوما كانت 90 مريضا (70.8) ذي استندت التشخيص على الخزعة الأساسية و خزعة نخاع العظم كانت أكثر الوسائل التشخيصية 40 مريضا (31)، في حوالي نصف المرضى أظهرت اختبارات الدم نقص في الصفيحات والكريات الدم البيضاء وارتفاع في كريات الدم الحمراء ومعدل الترسيب و فقر الدم. أهم الفموية هي: جفاف الفم؛ والتهاب / مع أو بدون نزيف من الشفتين؛ تقرح مع ضغط خفيف، ألم الحنجرة وصعوبة البلع والتكلم.
الاستنتاجات: في هذه الدراسة يمكننا أن نستنتج أن الفموية الرئيسية لمريض سرطان الدم هو تقرح مع ضغط خفيف؛ جفاف الفم والتهاب / مع أو بدون نزيف الشفتين، الحنجرة و غير قادر على البلع الرئيسية.

التوصيات: الباحثين للمصابين بسرطان الدم يتم التركيز عليه ير الملطفة مثل علاج الألم، و

Abstract

Background: The term leukemia refers to cancers of the white blood cells (also called leukocytes or WBCs). When a child has leukemia, large numbers of abnormal white blood cells are produced in the bone marrow. These abnormal white cells crowd the bone marrow and flood the bloodstream, but they cannot perform their proper role of protecting the body against disease because they are defective. Most of the children with cancer will be at risk for significant pain at some time during the course of illness.

Objective: To assess the oral manifestation in children with leukemia under chemotherapy treatment and its relation to the duration of patient's hospitalization.

Patients and methods: One hundred twenty seven patients diagnosed Acute Lymphocytic Leukemia (ALL), collected from Children Welfare Teaching Hospital /Medical City, Central Child Teaching Hospital/Baghdad (hematology & oncology unit) from 25th January 2009 to 25th January 2010, the questionnaire including demographic & clinical information, main oral manifestations.

Results: Patients samples ranged in age from (5 – 16) years, only 55 patients (43%) were aged from (8-10) years; 75patients (58.5%) were males;40 patients (31%) were living in south of Iraq. Swollen&palpable lymph node were the main chief complaints in 40 patients (31%); duration of disease is Less than 6 months, in 65 patients (51%); patients who stay in hospital more than 15 days were 90(70.8%); patients who their diagnosis were based on core biopsy & bone marrow biopsy were the most diagnostic methods in 40 (31%); in about half of the patients hematological tests showed that Thrombocytopenia &leucocytosis, elevated in erythrocytes sedimentation rate and anemia. Main oral manifestations presented were: ulceration gentle pressure, spontaneous bleeding, dry mouth, ulcerated/with or without bleeding of lips, laryngeal pain, unable to swallow and difficult/painful speech and mucositis.

Conclusions: In this study we can conclude that the main oral manifestations in patient with leukemia were ulceration after gentle pressure; spontaneous bleeding; dry mouth; ulcerated/with or without bleeding of lips, laryngeal pain; unable to swallow and difficult/painful speech, and the duration of hospitalizations were related to the manifestations of patients and their chief complaints; diagnostic procedure and their therapy.

Recommendation: the oral manifestations of patient with leukemia are focusing on them through a palliative measures such as the treatment of pain, and nutritional support and maintenance of good oral hygiene.

Keywords: Leukemia, oral manifestations, chemotherapy.

INTRODUCTION:

The etiology of childhood leukemia remains incompletely understood. It is concerning, therefore, that studies from different parts of the world have indicated an increase in recent decades in the incidence of childhood leukemia⁽¹⁾. Neoplasia is the second leading cause of death by disease in the world, and about 70% of patients undergo antineoplastic chemotherapy during the treatment so, ALL is a type of cancer of the blood and bone marrow – the spongy tissue inside bones where blood cells are made, the word “acute” in acute lymphocytic leukemia comes from the fact that the disease progresses rapidly and affects immature blood cells, rather than mature ones, the “lymphocytic” in acute leukemia refers to the white blood cells called lymphocytes, which ALL affects, Acute lymphocytic leukemia is also as acute lymphoblastic leukemia and acute childhood leukemia⁽¹⁾. Leukemia, the most common childhood cancers, account for about one third of pediatric malignancies, Acute lymphoblastic leukemia (ALL) represents about 75% of all cases in children and has a peak incidence at age 4 years⁽²⁾. The overall annual incidence of leukemia in white children is 43.7 per million populations and in black children, 24.3 per million children age 0 to 14 years^(1, 2). The clinical features of leukemia are similar, because all involve severe disruption of bone marrow function, specific clinical and laboratory features differ, however, and there is marked variability in responses to therapy and in prognosis^(2, 3). Childhood ALL was the first from disseminated cancer shown to be curable with chemotherapy and irradiation^(3,4). If too many lymphoblasts (a certain type of WBC) are produced, a child will develop acute lymphoblastic, or lymphoid leukemia (ALL), this is the most common type of leukemia, affecting nearly 60% of kids with this cancer of the blood cells, kids ages 2 to 8 are more likely to be affected, but all age groups can develop ALL⁽⁵⁾. ALL presentation is usually with bone marrow failure although generalized lymphadenopathy and splenomegaly are common.⁽⁶⁾ Prognosis of 70% is within 5-years survival in children with good prognostic indices W.B.C: $< 10 \times 10^9/l$, age from 2 – 10 year, cell markers: common ALL Ag, remission, early (within 4 weeks).^(5,6) Most leukemia are caused by specific gene mutations, deletion or translocation, ALL manifests as a neoplastic proliferation of lymphoblast.⁽⁷⁾ Incidence 48/million population/y, males more than females, usual age range: 2-10 years, with a peak at 3-4 years, accounts for 85% of childhood leukemia⁽⁸⁾. In Iraq leukemia in 3rd step from the commonest ten cancers by site, No, cases 960, males 555 cases, females 405 cases, percent of total 6.77%, registered cases/ 10^5 population 3.01⁽⁹⁾. The causes of ALL is not known, however, certain risk factors might increase a child's chance of developing it, in most cases, however, neither parents nor children have control over the factors that trigger leukemia, current studies are investigating the possibility that some environmental factors may predispose a child to develop the disease, for example, parental radiation exposure (such X-Rays) may trigger ALL in a developing fetus^(8,10). About two thirds of children with ALL have had signs and symptoms of their diseases for less than 4 week at the time of diagnosis, progressive bone marrow failure leads to pallor, bleeding, petechial, and fever-the features that usually promote diagnostic studies⁽¹¹⁾. On initial examination, most patients are pale, and about 50% have petechial or mucous membrane bleeding, about 25% have fever, which is may be falsely ascribed to an upper respiratory infection or otitis media, lymphadenopathy is occasionally prominent; splenomegaly is found in about 60% of patients, where is hepatomegaly is less common, 25% of patients presents significant bone pain and arthralgia's caused by leukemic infiltration of the perichondria bone or joint or by leukemic expansion of the marrow cavity^(10, 11). On initial examination, most patients have anemia, although only about 25% have hemoglobin levels below 6g/dl, most patients also have thrombocytopenia (platelets counts greater than $100,000/mm^3$), half of patients had WBC counts less than $10,000/mm^3$, and about 20% had counts greater than $50,000/mm^3$,

bone marrow biopsy provides the needed material for study, core biopsy of lymph node⁽⁹⁾ contemporary treatment of ALL is based on the clinical risk, although there is no universal definition of risk groups, in general patients with standard or average risk of relapse are between the ages (1- 10) year, have a WBC count under 100,000/mm³, the bone marrow is the most common site of relapse, although any site can be affected, in most center bone marrow is examined at infrequent intervals to confirm continued remission⁽¹²⁾. Accurate assessment is essential for appropriate & successful management of pain in children with cancer.⁽¹³⁾ Some other studies focused on estimating prevalence have included assessment of the intensity & source pain. Using of comprehensive approach to pain assessment will help attain the goals for caring for children with pain, these goals are to enhance the child's comfort, promote recovery when possibly & improve functional status, & prevent detrimental effects from unrelieved pain⁽¹⁴⁾. Typically assessments of pain involve unstructured observation^(4,15). These observations are causal rather than systematic & the reliability, validity of such observations is unknown⁽¹⁶⁾. The temperament, level & type of activity, & interactions for verbal children, irritability & agitations for preverbal children & pain (undefined) muscle spasms, immobility for terminally ill children who had communication skills all are an example⁽¹⁷⁾.

OBJECTIVES:

To assess the oral manifestation of leukemic children under chemotherapy treatment and its relation to the duration of patient's hospitalization.

PATIENTS AND METHODS:

A descriptive quantitative purposive "non-probability" study was done on one hundred twenty seven patients who were diagnosed as ALL, their age were between 5 – 16 years old. The data collected from Children Welfare Teaching Hospital /Medical City and Central Child Teaching Hospital/Baghdad (hematology & oncology unit) from 25th January 2009 to 25th January 2010, In patients who receiving chemotherapy treatment. Methods of data collections based on demographic characteristics like age, sex, address; clinical characteristics (some take from chart) chief complaint, duration of illness, duration of hospitalization, methods of diagnosis; hematological parameters at diagnosis, the final diagnosis of leukemia was based on the clinical laboratory criteria which applied to all patients were platelets counts $>60.000\text{mm}^{-3}$ (thrombocytopenia), white blood cells counts (W.B.Cs counts) $>12,000\text{mm}^{-3}$ (leucocytosis), erythrocytes sedimentations rate (E.S.R) was elevated above 100mm/1st hr west, Hb level less than 8g/dl (anemia); Main oral manifestations were recorded. Oral examination was done to all patients under light by used sterile dental instrument after taking approvals by the parents. Data were analyzed by using descriptive statistical including (frequency, percentage, mean of score). The reliability was determine of questionnaire (0.894), and main oral manifestation items were measured by 3 Likert rating scale (Always = 3, Sometime = 2, Never = 1) and cut-off point=2

RESULTS:

The study involved one hundred twenty seven patients diagnosed (ALL), admitted to receiving chemotherapy in oncology & hematology unit.

Table (1) age and gender distribution of patients with ALL

Age	No.	%	Males		Females	
			F	%	F	%
5 – 7	20	16	10	8	10	8
8 – 10	55	43	35	27.5	20	16
11 – 13	30	23.5	18	14	12	9.5
14 – 16	22	17.5	12	9.5	10	8
Total	127	100	75	58.5	52	41.5

This table shows that patients samples ranged from (5 – 16) years, only 55 patients (43%) from age (8-10) years and according to sex the study showed 75 patients (58.5%) were male.

Table (2) address of patients with ALL

Categories	No.	%
Center	25	20
North	25	20
East	18	14
West	19	15
South	40	31
Total	127	100

This table shows that most of patients (31%) were lived in south of Iraq.

Table (3) chief complaint of patients with ALL

Categories	No.	%
Swollen lymph node	40	31
Fatigue and weakness	15	12
Recurrent infection	12	9
Easy bruising	10	8
Bone and joint pain	30	24
Abdominal pain	20	16
Total	127	100

This table shows that most common chief complaint was (31%) swollen lymph node, while (24%) bone and joint pain.

Table (4) duration of disease of patients with ALL

Categories	No.	%
Less than 6 months	65	51
More than 6 months	57	49
Total	127	100

This table shows that (51%) of patient was less than 6 months duration of illness

Table (5) duration in hospitalization

Categories	No.	%
Less than 15 days	37	29.1
More than 15 days	90	70.8
Total	127	99.9

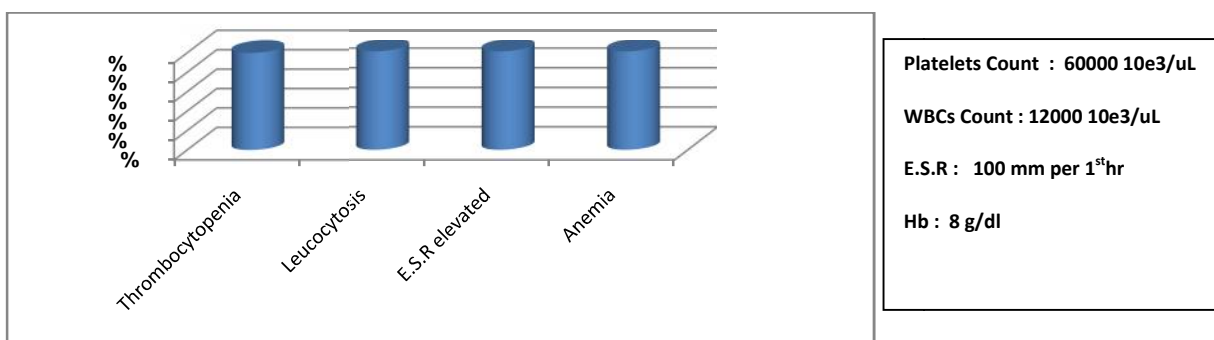
This table shows that only 90 patients (70.8%) were hospitalized more than 15 days

Table (6) methods of diagnosis of patients with ALL

Categories	No.	%
Core biopsy lymph node	40	31
Blood tests	20	16
Biochemical tests	15	12
Ultra sound abdomen	12	9
Bone marrow biopsy	40	31
Total	127	100

The main methods or procedures used for diagnosis were core biopsy & bone marrow biopsy in 40 patients (31%) for each method.

Figure (1) hematology disorders of patients with ALL



The results of Figure show that the hematological investigations were done for all patients, about (51%) presented with thrombocytopenia, White blood cells counts (leucocytosis). From patients present 12000mm⁻³, Erythrocyte Sedimentation Rate (E.S.R), E.S.R elevated in malignancy diseases, were 100 mm/1sthr west, Hemoglobin level record less than 8 g/dl .

Oral manifestations	Always		Sometime		Never		M.S
	NO.	%	NO.	%	NO.	%	
Mucositis	80	62.9	30	23.6	17	13.3	2.4
Unable to swallow	80	62.9	30	23.6	17	13.3	2.4
Laryngeal pain and Difficult/painful speech	80	62.9	30	23.6	17	13.3	2.4
Ulcerated/with or without bleeding of lips	90	70.8	20	15.7	17	13.3	2.5
Tongue Blistered	40	31.4	45	35.4	42	33.07	1.9
Change in the taste	40	31.4	45	35.4	42	33.07	1.9
Dry mouth	90	70.8	17	13.3	20	15.7	2.5
Candida infection suspected reddened coated or white patches in Gingival mucosa membrane	40	31.4	45	35.4	42	33.07	1.9
Ulceration gentle pressure, spontaneous bleeding	127	100	0	0	0	0	3

Table (7) oral manifestations of patients with ALL

Main oral manifestations presented in (table 7) were the major following items: ulceration gentle pressure, spontaneous bleeding, dry mouth, ulcerated/with or without bleeding of lips, laryngeal pain, unable to swallow and difficult/painful speech and mucositis.

DISCUSSION:

Leukemia is characterized by uncontrolled production of immature white blood cells, causing a series of clinical and oral manifestations, which are important in disease diagnosis. Acute leukemia develop quickly and need to be treated urgently. Early detection of leukemia is very important because it provides a favorable prognosis. For a child with ALL, the treatment period will be around two years for girls and three years for boys^(1,4). Studies from various countries have found an increasing incidence of childhood leukemia in recent decades^(18,19). In this study the majority of patients (43%) occur at the age between (8 – 10) years and this will be agree with other studies which recorded that the usual age range from 2-10 years, and this aged riskily more than others groups with a peak at 3-4 years⁽²⁰⁻²³⁾. According to sex this study showed that incidence occur at males more than females (58%), this supported by other studies⁽²⁴⁾. Also this study showed that (31%) from patients lived in south of Iraq, life style factors have been definitely linked to childhood leukemia, kids who have received either radiation treatments or chemotherapy for other types of cancer seem to have a higher risk of developing leukemia late in life, In Iraq leukemia in 3rd step from the commonest ten cancers by site, so, it is true that the number of cancer registered cases of childhood leukemia related to the socioeconomic measure. However, its approved that, strictly, these factors are not 'known to influence childhood leukemia risk', but are known to be associated with it; the explanation is unknown. Under-diagnosis in poorer communities may have contributed to socioeconomic variation in recorded childhood acute lymphoblastic leukemia incidence. Implications for clinical practice and epidemiological studies should be considered⁽²⁵⁾. About the oral manifestation treatment with chemotherapy can affect the neoplastic tissues or cells that multiply quickly, such as cancer cells as well as normal tissues specially the rapid growth cells so, chemotherapy causes damage to fast-growing normal cells, including cells of the oral tissues. including mucositis, our results also showed about 63% of our patients had sever mucositis. Mucositis is a specific problems for the effects and appearance in mucous membrane epithelial for mouth and the incidence and severity of mucositis have been related to the degree of the preexisting mucosal diseases, oral hygiene and nature of therapy^(17,18). Many studies recorded that mucositis typically appears 7 to 10 days after initiation of high-dose cancer therapy. Clinicians should be alert to the potential for increased toxicity with escalating dose or treatment duration in clinical trials that demonstrate gastrointestinal mucosal toxicity. High-dose chemotherapy, such as that used in the treatment of leukemia⁽²⁶⁾. Many studies carried out that the cytotoxic effects of chemotherapeutic agents on the oral mucosa which predispose the patient to pain, difficulty in mastication, and dysphasia caused by atrophy of the mucosa which leads to mucositis and ulceration, also xerostomia^(18,20).

Management of oral complications of cancer therapy includes identification of high-risk populations, patient education, initiation of pretreatment interventions, and timely management of lesions. Assessment of oral status and stabilization of oral disease before cancer therapy are critical to overall patient care. Care should be both preventive and therapeutic to minimize risk for oral and associated systemic complications⁽²⁷⁾. The platelet count may also be affected by disease and by the chemotherapy whose patients are receiving and they may become thrombocytopenic (a reduction in the number of platelets circulating in the blood). When platelet count is very low tissues can bruise and bleed more easily. During this time it is helpful to avoid sharp objects in the mouth such as chop bones or potato chips as these can cut the gums. Using a soft toothbrush also helps to protect gums. Oral cavity is a frequent site of therapy-related complications including ulcerations; infections; bleeding and xerostomia⁽²⁸⁾. Other oral manifestations were inability to swallow and laryngeal pain which result from the cytotoxic effects of chemotherapeutic agents on the oral mucosa predispose the patient to pain, difficulty in mastication, and dysphasia caused by atrophy of the mucosa which leads to mucositis and ulceration, also as a result of mucositis & xerostomia^(29,30). Ulcerated/with or without bleeding lips, among those problems, the most important one was the risk of infection because mucosal ulceration may become a portal entry for the invasion of pathogens that in turn may be life threatening⁽³¹⁾. Dry mouth, salivary gland dysfunction present in a shift highly carcinogenic microorganism seen with some chemotherapeutic agents and radiation therapy that incorporates the salivary glands in radiation field. Ulceration due to gentle pressure and spontaneous bleeding was, a result from chemotherapeutic agents may which secondarily induce thrombocytopenia, which is the usual cause of intra oral hemorrhage and hemorrhage may present clinically as gingival bleeding or sub mucosal bleeding with hematoma formation⁽³⁰⁾.

Poor oral health has been associated with increased incidence and severity of oral complications in cancer patients, hence the adoption of an aggressive approach to stabilizing oral care before treatment. Primary preventive measures such as appropriate nutritional intake, effective oral hygiene practices, and early detection of oral lesions are important pretreatment interventions⁽²⁹⁻³¹⁾. Chief complaint present in lymphatic system was swollen lymph nodes, ALL presentation is usually with bone marrow failure although generalized lymphadenopathy, this is the most common first symptoms of malignancy in children (a condition known as swollen glands) located in the neck, above the collar bone, in the underarm area, or in the groin. In this study the main ALL presentation was bone marrow failure. Diagnosis of ALL in this study was based on both core biopsy & bone marrow aspiration, About two thirds of children with ALL have had signs and symptoms of their diseases for less than 4 weeks at the time of diagnosis, progressive bone marrow failure leads to pallor, bleeding, petechial, and fever-the features that usually promote diagnostic studies⁽³²⁾. Bone marrow samples are obtained from a bone marrow aspiration and biopsy – 2 tests that are usually done at the same time. The samples are usually taken from the back of the pelvic (hip) bones, but in some cases they may be taken from the front of the pelvic bones^(4,5,13,14). On initial examination, most patients have anemia, although only about 25% have hemoglobin levels below 6g/dl, most patients also thrombocytopenia platelets counts greater than 100,000/mm³, half patients WBC counts more than

12,000/mm³, and about 20% have counts greater than 50,000/mm³, & elevated in E.S.R, bone marrow biopsy provides the needed material for study, core biopsy of lymph node^(9,33). In this study, all patients feeling unbearable pain , among the children unlike adults, the majority of cancer pain caused by procedures and treatments with far less stemming from the diseases itself. stay in hospitalization related with manifestation, when increase stay in hospital long time increase oral complications specialty under chemotherapy treatment, pain and the major complications for patients in oncology unit. Duration of the disease has been reckoned from the onset of the first sign or symptoms attributable to the disease. Obviously this is not a precise measure of the duration of the pathological process, since there is no way of knowing how long hematological changes might have existed before symptoms occurred. Duration from time of definitely established diagnosis is unsatisfactory, since many of the patients had symptoms obviously due to leukemia for many weeks preceding the time of first blood studies, in this study 51% of patients showed their symptoms and did their first test for final diagnosis before 6months^(34,35).

CONCLUSIONS:

In this study we can conclude that the main oral manifestations in patient with leukemia were ulceration gentle pressure, spontaneous bleeding, dry mouth, ulcerated/with or without bleeding of lips, laryngeal pain, unable to swallow and difficult/painful speech and mucositis and the duration of hospitalizations were related to the manifestations of patients and their chief complaints; diagnostic procedure and their therapy.

RECOMMENDATIONS:

The research recommended that, the oral manifestations of patient with leukemia are focusing on them through a palliative measures such as the treatment of pain, and nutritional support and follow-up oral health.

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