

## **Oral Complications associated with Chemotherapy in Children's with Lymphoma**

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### **Abstract:**

**Background:** *Lymphoma is general term for a group of blood cancers that start in lymphatic system, which includes circulating lymphocytes, lymph nodes (also called lymphatic gland), spleen, tonsils, adenoids, payer patches, thymus, and bone marrow, as well as the channels (called lymphatic's or lymph vessels) that connect them, also which is a part of body's*

*immune system and helps filter out bacteria, viruses, and the other unwanted substance.*

**Objective :** *To assess oral complications & pain in children under chemotherapy treatment*

**Methods :** *A retrospective study, this included 70 lymphoma patients (Hodgkin's and Non Hodgkin's), for both sexes (50 male and 20 female), age between (6 – 15 years), all children receiving anti-neoplastic treatment in Oncology & Hematology Unit in Central Teaching Hospital & Children Teaching Hospital (medical city), during 1 year period start from 15th January 2011 to the 15th January 2012, the data were determine to each patient include demographic characteristics, clinical characteristics, hemogram diagnosis, assess pain by facial expression, main oral complications by (Oral Guide Assessment), also oral examination done for all patients by dentist by using dental instruments.*

**Results:** *Our study showed that (50%) of patients were age 15 years, family history was negative (71%), half patients were live in south of Iraq. Males more than females (71%). There was in table (1) significant different between age and gender of patients, painless enlargement of lymph node (50%)*

*was most common chief complaint in patients with lymphoma, duration of illness less than 6 months (72%), core biopsy was the most procedure use in diagnosis by physician (43%). Platelets counts below the normal range (thrombocytopenia), also most of patients had W.B.Cs counts of greater than normal range (leukocytosis) and Hb level was less than 8 g/dl presented in (50%), E.S,R more than 100 mm/1st hr west was (40%), (50%) from patients were presented with unbearable pain, main oral complications presented in painful speech, unable to swallow, mouth ulcerated, thick saliva, spontaneous gingival bleeding, generalized plaque or debris along gum line*

***Conclusions:*** *For this study males were more prevalent than females, enlargement in lymph node was the main chief complaint, also short duration for illness, pain was the most common complication, followed xerostomia, difficult in speech, unable to swallow, also thrombocytopenia lead to oral bleeding & leukocytosis lead to infection*

***Keywords :*** *Lymphoma, Pain, Oral Complications, Hematologic Diseases, Side Effect of Chemotherapy*

## Introduction

Lymphomas are a group of diseases caused by malignant lymphocytes that accumulate in lymph nodes and cause a characteristic feature of lymphadenopathy. Occasionally they may spill over in blood (leukemic phase) or infiltrate organs outside lymphoid tissue [1]. There are two major types of lymphoma, depending on the appearance of their cancerous (malignant) cells, these are known as Hodgkin's Lymphoma (HL), and Non Hodgkin's Lymphoma (NHL) together they are the third most common types of cancer in children [2,3,4]. Hodgkin's disease accounts for 5% of cancers in children and adolescent younger than 15 years in United States [4,6]. In Iraq NHL is 6th step, from comments ten cancer, No. of cases 719 cases, percent of total (5.50%), registered cases/105 population 2.24 [15]. Hodgkin lymphoma affects about 3 out of every 100,000 Americans [6, 7, and 8]. Hodgkin's lymphoma 50 cases per year present with non tender cervical supraclavicular lymphadenopathy, a minority have systemic symptoms history tends to be long, No. 70 cases per year present with cervical lower supraclavicular lymphadenopathy and / or disease in the abdominal hepatosplenomegaly or mediastinum [7, 9,10]. A diagnosis of NHL is usually made by examining a lymph node biopsy specimen, the examination includes tests called "immunophenotyping" and "cytogenetic analysis" it is important that all patients receive an accurate diagnosis and know their NHL subtype [18, 27]. Chemotherapy treatment for lymphoma varies widely depending on the type of lymphoma and stage of disease. Drug may be taken by pill or administered via injection, a lymphoma patient may only single drug or undergo regimen involving a combination of drugs. The use of chemotherapy in the management of cancer has increased the incidence of adverse effects, especially stomatitis, infection, taste alteration, mucositis, pain, loss of function and xerostomia. Therefore the oral complication of cancer chemotherapy divided into two main forms according to the origin, this includes direct effect: action of drug over mouth tissue – direct stomatotoxicity and mouth problem caused by change in other tissue

– indirect stomatotoxicity such as the bone marrow [2]. Treatment of pain and suffering should be a priority for all clinicians. Cancer pain is estimated to occur in 30% to 70% of patients with early-stage cancer and 60% to 95% with advanced cancer. Current research shows that cancer pain continues to be undertreated despite the viability of analgesics and established guidelines to maximize their effectiveness [23, 30]. Effective pain management in the inpatient oncology setting continues to be an important clinical issue, and patients do not receive all available pain treatment. They may be an important association between patients beliefs about pain and pain management and the pain management they receive [30]

## Methods

Benefits of research explain to all the parents and patients, collected data after the ethical approval was obtained from patients. Retrospective study have been carried out to achieve the aim of this study, 1 year period start from 15th January 2011 to the 15th 2012, 70 cases of lymphoma (50 males, 20 females) their age between 6 - 15 years, all patients diagnosed by physician, and their admission to receive anti-neoplastic treatment for Hodgkin's and Non-Hodgkin's Lymphoma in oncology and hematology unit, in central child teaching hospital & children teaching hospital (medical city), used questionnaire format was constructed particularly by the researchers the Construction was based on the extensive review of relevant literature and related studies, which included; demographic characteristics: age, gender, family history, address. Clinical characteristics: chief complaint, duration of illness, methods of diagnosis & hemogram diagnosis: platelet count, white blood cells count, Hb level, E.S.R (Erythrocytes Sedimentation Rate), also assess pain by use (facial expression)[13,23,30]. And main oral complications assess by used oral guide assessment[29]. Oral examination done carefully to all patients by dentist specialty oral medicine, examined by a single examiner, under standardized conditions; the oral cavity examined in an artificial light by using a

mouth mirror. Data were analyzed were using descriptive statistical including (frequency, percentage, mean of score & chi-Square test), in oral guide assessment average (cut-off point = 2) of all items are measured on 3 level of liker rating of scale (3,2 & 1)

### Results

The present study was carried out to assess the oral complications and pain in 70 lymphoma patients under chemotherapy treatment of both sex, 50(71%) were males and 20(29%) were female, the age of the entire sample present in 15 years 35(50%), in males 28(40%) and 7(10%) in females as the shown in table (1).

**Table 1: age and gender distribution for (70) patients with lymphoma**

Age group	No	%	Gender				C.S. P-value
			Males		Females		
			No	%	No	%	
6 – 8 yrs	10	14.3	6	8.5	4	6	X <sup>2</sup> = 2.595 df = 3 non-significant P≥0.05
9 – 11 yrs	15	21.4	10	14	5	7	
12 – 14 yrs	10	14.3	6	8.5	4	6	
15 yrs only	35	50	28	40	7	10	
<b>Total</b>	<b>100</b>	<b>100</b>	<b>50</b>	<b>71.4</b>	<b>20</b>	<b>28.6</b>	

Family history was negative in 50(71%) from patients, as show in table (2).

**Table 2: family history for (70) patients with lymphoma**

Categories	No	%
<b>Positive</b>	<b>20</b>	<b>28.6</b>
<b>Negative</b>	<b>50</b>	<b>71.4</b>
<b>Total</b>	<b>70</b>	<b>100</b>

35(50%) from patients were live south in Iraq, as show in table (3).

**Table 3: distribution of (70) patients with lymphoma**

Categories	No	%
Center	15	21.43
North	5	7.14
South	35	50
East	5	7.14
West	10	14.29
Total	70	100

In table (4), 28(40%) of 15 yrs males diagnosed N.H.L, also found significant differences between types of diagnosis with two variable (age & gender).

**Table 4: clinical diagnosis according age & gender distribution for (70) patients with lymphoma**

Clinical diagnosis	No	%	Age																Total
			6 – 8 yrs				9 – 11 yrs				12 – 14 yrs				15 yrs				
			M		F		M		F		M		F		M		F		
			No	%	No	%	No	%	No	%	No	%	No	%	No	%	No	%	
H.L	25	36	4	6	3	4	3	4	2	3	2	3	1	2	8	11	2	3	X <sup>2</sup> =34.721 df = 7 significant P≤.01
N.H.L	45	64	2	3	1	2	7	10	3	4	4	6	3	4	20	29	5	7	
Total	70	100	6	9	4	6	10	14	5	7	6	9	4	6	28	40	7	10	

M: Male, F: Female

In table (5), painless enlargement of lymph node as the major chief complaint present in 35(50%) patients.

**Table 5: chief complaint for (70) patients with lymphoma**

Categories	No	%
Pain less enlargement of lymph node	35	50
Fatigue	5	7.14
Poor appetite	5	7.14
Itching or hives	5	7.14
Unexplained fever	10	14.3
Night sweats	5	7.14
Weight loss	5	7.14
Total	70	100

Duration of illness less than 6 months, in 50(71.4%) patients, show in table (6).

**Table 6: duration of illness in (70) patients with lymphoma**

Duration of illness	No	%
Less than 6 months	50	71.4
More than 6 months	20	28.6
Total	70	100

Core biopsy the most common methods depended in diagnosis by physicians, in (42.9%), show in table (7).

**Table 7: methods of diagnosis for (70) patients with lymphoma**

Categories	No	%
Core biopsy	30	42.9
Blood tests	10	14.3
Biochemical tests	10	14.3
A computed tomography	5	7.1
Ultrasound	5	7.1
Bone marrow aspiration	10	14.3
Total	70	100

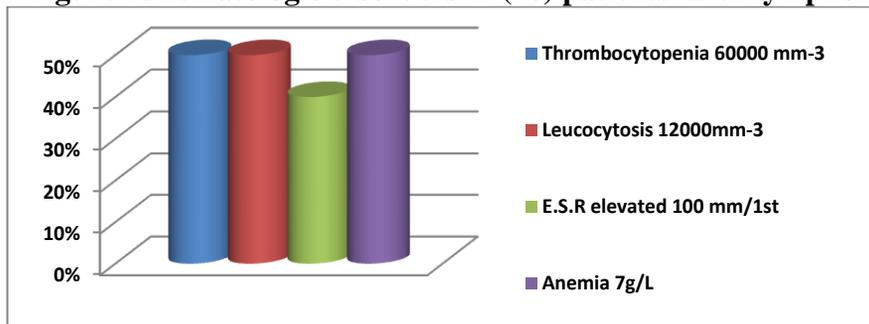
Assessment of oral complications average cut-off point of all items were measured on 3 level liker rating scale (3,2 & 1) this items which are more than cut-off point in items (A-2, B-1, C-2, D-2, F-1, G-1) were show in table (8).

**Table 8: main oral complications for (70) patients with lymphoma**

Category	Items	Always		Some time		Never		M.S	
		No	%	No	%	No	%		
A	Voice	1- Deep or rasp	10	14	0	0	0	0	0.42
		2- Difficult/painful speech	50	71	10	14	0	0	2.42
B	Swallow	1- Unable to swallow	40	57	20	29	0	0	2
		2- Painful	5	7	5	7	0	0	0.35
C	lips & angle of mouth	1- Ulcerated/with or without bleeding	40	57	10	14	0	0	2
		2- Dry/cracked	10	14	10	14	0	0	1
D	Tongue	1- Blistered	30	43	10	14	0	0	2
		2- Coated or loss of papillae	25	36	5	7	0	0	1
E	Saliva	1- Thick/ropy	40	57	30	43	0	0	3
F	Gingival mucous membrane	1- Ulceration (spontaneous bleeding)	30	43	30	43	0	0	2
		2- Candida infection suspected reddened coated or white patches	5	7	5	7	0	0	0.35
G	Oral cleansing compliance the teeth	1- Cleans but needs help	5	7	5	7	0	0	0.35

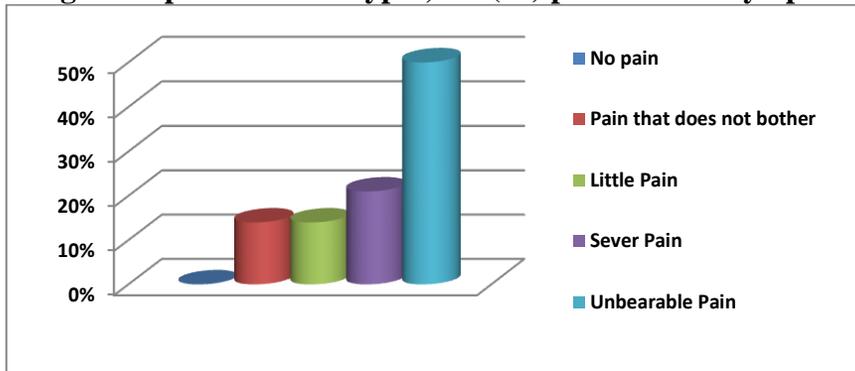
Hematologic disorders present in thrombocytopenia, leukocytosis, anemia in 35(50%) patients, while elevated in E.S.R in 28(40%), show in figure (1).

**Figure 1: hematologic disorders in (70) patients with lymphoma.**



Pain is the most common complications in patients with cancer, present in unbearable pain in 35(50%) patients, show in figure (2).

**Figure 2: pain assess & types, for (70) patients with lymphoma.**



## Discussion

Lymphomas are a diverse group of neoplasms affecting the lymphoreticular system. Lymphomas has been traditionally divided into Hodgkin's diseases and non Hodgkin's diseases. Hodgkin's diseases is characterized histological by presence of multi-nucleated Reed-Strenberg cells. All other neoplasms of the lymphoid system are referred to as Non- Hodgkin's lymphoma and are derived predominantly from the cells of B-lymphocyte series[1,3]. The malignant lymphomas, Hodgkin's diseases and non- Hodgkin's lymphoma, comprise approximately 5% to 6% of all malignancies and are the fifth most frequently occurring type of cancer in the United States. In 2007, an estimated 8260 new cases of HD and 81850 new cases of NHL where diagnosed in the United States[4].Several studies on chemotherapy were conducted including oral complications[6]. Hodgkin or Non-Hodgkin lymphoma, are types of cancer that effects the lymphatic system, this is highly sophisticated filtering system helps the body's immune system remove bacteria, viruses, and other unwanted substances[5,6]. This study was conducted with 70 Iraqi patients, all patients diagnosed with lymphoma by hematologist, oncologist, also under chemotherapy treatment[15]. In this study the age for patients with lymphoma 15 yrs in (50%), which agreed with (American Cancer Society 2004) that defined two peaks in the age

distribution that observed for this cancer type[7]. The first peak occurs in young adults between the ages of 15 yrs to 40 yrs, Non-Hodgkin lymphoma is slightly more common than Hodgkin disease in kids younger[2,4,7]. In this study male predominance has been observed for lymphoma patients in agreement with Devesa and fears, 1992 they stated that lymphoid cancers are more frequent in males than females throughout all age groups and across virtually all cancer registries in developed countries[8,9]. Incidence of NHL is increase 4% per yrs in males more than females, pre-adolescent peak followed by a nadir in incidence with gradual rise thereafter[2, 4, 8]. Family history was negative in (71%) patients, most lymphoma come from no inherited mutations in the genes of growing blood cells[5, 6]. (50%) patients were live south of Iraq, cancers were increase in south Iraq after war, also NHL in 4th step the commonest ten cancers in south of Iraq and although life style have been definitely linked to childhood lymphomas, kids who had received either radiation treatments or chemotherapy for other types of cancer seem have a higher risk of developing lymphoma late in life[6,7,15]. Chief complaint to half patients present painless enlargement of lymph node, this is the most common first symptoms of lymphoma in children (a condition known as swollen glands) located in the neck, above the collar bone, in the under arm area, or in the groin[11,13,16]. Duration of illness is short, less than 6 months in (71.14%)[16, 17, 18]. About (43%) from patients were diagnosed by core biopsy, which considered as an effective and safe procedure in diagnosis of patients with lymphoma with the possibility of determining the tumor subtype and subsequent specific treatment[19,20]. If the lymph node remains enlarged, the next step is biopsy (the removal and examination of tissue, cell or fluid from the body), and also very necessary for lymphomas to involve the bone marrow or structure within the chest or abdomen[4,7,20,23]. In hemogram diagnosis, 35(50%) from patients were present thrombocytopenia (dyscrasis), if the count falls below  $5 \times 10^9/l$  the patient will have a bleeding diathesis, the major causes of thrombocytopenia in lymphoma proliferative

disorders decreased marrow production[24,25]. (50%) from patients present leukocytosis, total circulating white blood cells as increase in cancers ( $> 11.0 \times 10^9/l$ )[3]. About (50%) from patients as anemic Hb level 7 g/dl, impaired red blood cells formation in bone marrow invasion & under toxins (cytotoxic treatment)[26,27]. E.S.R (Erythrocytes Sedimentation Rate) elevated in (50%) from patients, increase E.S.R clearly in malignancy cases & anemic patients[16,17,18]. Oral mucositis is a treatment limiting toxicity of cancer therapy which causes severe pain[29]. Type of pain, present unbearable pain in (40%) from patients, among the children unlike adults, the majority of cancer pain caused by procedures and treatments with far less stemming from the diseases itself[7,10,13,17]. The oral cavity is frequent site of therapy-related complications including mucositis, ulcerations, infections, bleeding, xerostomia[28]. Main oral complications present in table (9), painful/difficult speech, our study reported that the results related treatment & found that the oral complications is common in patients receiving chemotherapy to cancer[19,20,29]. unable to swallow, the study carried out that 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 result of mucositis of xerostomia[22,28,30]. Ulcerative with or without bleeding, among those problems, the most important one is the risk of infection, mucosal ulceration may become a portal entry for the invasion of pathogens that in turn may be life threatening[23,24,29]. Blistered, this is present because chemotherapy damage normal cells, inside of the mouth, tongue, throat become red, sore and ulcerated[25,26,30]. Thick/ropy saliva, 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[18,19,24]. ulceration gentle pressure, spontaneous bleeding, which is the usual causes of intra oral hemorrhage, hemorrhage

may present clinically as gingival bleeding or sub mucosal bleeding with hematoma formation[13,17,30]

### **Conclusions**

This study shows the main oral complications present in voice, unable to swallow, xerostomia, oral bleeding, ulcerated and blister in mouth and tongue, also unbearable pain.

### **Recommendations**

- 1- Encourage patients to continuous follow-up to doctor.
- 2- Provide booklet should be prepared for patients including the problems and side effects of chemotherapy.
- 3- Health education program for all patients in oncology unit is very necessary to determination or reduce risk
- 4- Nurse should carry on all nursing care & continuously follow up of patients
- 5- Nurse exigency responsible for nutrition program for patients

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## المشاكل الفموية المرتبطة بالعلاج الكيماوي في الأطفال بورم الغدد اللمفاوية

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### المستخلص:

**الخلفية:** ورم الغدد اللمفاوية مصطلح عام لمجموعة من أمراض سرطانات الدم والتي تبدأ في الجهاز اللمفاوي والذي يتضمن الخلايا اللمفاوية المتنقلة والعقد اللمفاوية والغدد اللمفاوية والطحال واللوزتين والزوائد الأنفية والغدد الزعترية ونخاع العظم بالإضافة إلى القنوات اللمفاوية المرتبطة معا والتي تربط أجزاء الجسم مع الجهاز المناعي وهذا بدوره يساعد في ترشيح الجسم من البكتريا والفيروسات والمواد غير المرغوب بها.

**الهدف:** تقييم المشاكل الفموية للأطفال والألم تحت العلاج الكيماوي

**الطرق:** دراسة ذات أثر رجعي تضمنت 70 مريض من حالات ورم الغدد اللمفاوية، (50 ذكر – 20 أنثى)، أعمارهم بين (6 – 15 سنة) جميع الأطفال أدخلوا لاستلام العلاج الكيماوي والمعالجة ضد أورام الغدد اللمفاوية في وحدة علم الأورام وأمراض الدم في مستشفى الطفل المركزي ومستشفى حماية الأطفال (مدينة الطب)، لفترة سنة واحدة وابتداء من 15 كانون الثاني 2011 إلى 15 كانون الثاني 2012. تضمنت البيانات لمتابعة المرضى الخصائص الشخصية والخصائص السريرية

وتشخيصات الدم وتقييم الألم بواسطة الوجوه ودليل التقييم ألفمي وأيضا تم فحص المرضى من قبل طبيب الأسنان بأدوات طب الأسنان.

**النتائج:** أظهرت دراستنا أن (50%) من المرضى كانت أعمارهم 15 سنة ومنهم (71%) لديهم تاريخ عائلي سلبي، (50%) من المرضى كانوا يسكنون جنوب العراق، نسبة الذكور أكثر من الإناث مايقارب (71%) إذ كان هناك اختلاف هام واضح بين الفئة العمرية وجنس العينة، تضخم العقد اللمفاوية غير المؤلم من أكثر المشاكل الرئيسية شيوعا بنسبة (50%)، الفترة المرضية كانت أقل من 6 شهور بنسبة (72%)، فحص عينة من الغدد اللمفاوية من أكثر الإجراءات اعتمادا في التشخيص من قبل الطبيب (43%). (50%) من المرضى كانت الصفائح الدموية تحت المستوى الطبيعي وأيضا مستوى الدم (الهيموكلوبين) أقل من الطبيعي وأيضا خلايا الدم البيضاء أعلى من الطبيعي، معدل ترسيب خلايا الدم الحمراء كان أعلى مستوى له (40%) من المرضى، (50%) من المرضى يعانون من ألم غير محتمل، وأكثر المشاكل شيوعا كانت ألم عند الكلام وعدم القدرة على البلع وتقرحات في الفم وقلة اللعاب ونزف اللثة التلقائي.

**الاستنتاجات:** أظهرت الدراسة إن الذكور أكثر الإناث وانتفاخ الغدد اللمفاوية من أكثر المشاكل الرئيسية لدى أكثر المرضى، مدة قصيرة للمرض وألم غير محتمل ولا يطاق، ومن أكثر المشاكل الفموية شيوعا جفاف الفم وصعوبة وألم في الكلام وعدم القدرة على البلع والنزف الدموي التلقائي نتيجة قلة الصفائح الدموية وزيادة الخلايا الدموية البيضاء يؤدي إلى العدوى أو الالتهاب

**الكلمات المفتاحية:** ورم الغدد اللمفاوية ، الألم ، المشاكل الفموية ، أمراض

الدم ، الآثار الجانبية للعلاج الكيماوي