

Phototherapy in Cutaneous T-cell lymphoma dermatology department - Tripoli central hospital (2008-2020)

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Abstract:

Background: Primary cutaneous lymphomas (PCL) are non-Hodgkin lymphomas presenting in the skin with no evidence of extracutaneous disease at the time of diagnosis. There are several skin directed as well as systemic treatments for these lymphomas with effectiveness limited to reducing symptoms only. Phototherapy is one of the key treatments of cutaneous T-cell lymphoma (CTCL).

The objective of the study was to evaluate the effectiveness of phototherapy in treating patients with early stage Cutaneous T-cell lymphomas.

Methods: A case series study of total 87 patients registered in lymphoma clinic at Tripoli Central Hospital in a period of thirteen years.

Results: The study included 87 patients diagnosed as PCL, 44 males (50.57%) & 43 females (49.43%) with ♂ : ♀ of 1: 0.98. Their age ranged from 9 yrs to 82 yrs, with the mean age of 41.97±16.2 yrs. The most age group affected was between 21 to 40 years of age, from all patients 79.31% were skin type IV. Mycosis fungoides was the most common type of PCL in our patients (87.35%), most of them (39.08%) presented with the disease duration more than 5 years before diagnosis. The most common complaint was pruritus in (57.47%) of patients and (79.74%) were having skin lesions scattered all over the body. Most of the patients were treated with NB-UVB (92.2%) while (5.2%) were treated with systemic PUVA, with complete response to treatment in (53.2%) of them, (59.7%) of the cases were regular during treatment and (74.0%) completed their treatment without complications. The mean number of sessions of NB-UVB in patients with complete response was 40 sessions with the mean cumulative dose of 53.12 J/cm²

While the mean number of sessions of systemic PUVA in patients with complete response was 83 sessions with the mean cumulative dose of 599.32 J/cm².

Conclusion: Phototherapy is an effective and well-tolerated treatment for early stage MF and its response depends on adherence to the treatment.

Keywords: Cutaneous lymphomas, Mycosis fungoides, Phototherapy, NB-UVB

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I. Introduction :

Primary cutaneous lymphomas (PCLs) are defined as non-Hodgkin lymphomas presenting in the skin with no evidence of extra cutaneous disease at the time of diagnosis with an estimated annual incidence of 1/100 000 in Western countries^[1] and men are more involved than women (1.6:1 to 2.0:1). They typically afflict adults with a median age of 55 to 60 years^[2]. After gastrointestinal lymphomas, PCLs are the second most common group of extranodal non-Hodgkin lymphomas^[3]. PCL include a heterogeneous group of cutaneous T-cell lymphomas (CTCLs) and cutaneous B-cell lymphoma (CBCLs)^[4]. cutaneous T-cell lymphomas (CTCL) represent the majority of CL accounting for approximately 65% to 75% of all CL^[5]. Mycosis fungoides (MF) and Sezary syndrome (SS) are the classic types of CTCL^[6], MF is the most common type and accounts for 60% of CTCLs^[7] and almost 50% of all primary cutaneous lymphomas^[8]. Clinically, MF presents in its classic form with erythematous patches, which may evolve to infiltrated plaques. In a subset of patients, large and often ulcerated tumors develop on preexisting plaques^[9]. Folliculotropic MF (FMF) is a distinct variant of MF accounting for approximately 10% of all MF cases^[10]. The diagnosis and classification of PCLs should always be based on a combination of clinical, histological, immunophenotypical and genetic data^[11]. Since early aggressive chemotherapy is associated with considerable side effects but does not improve survival, a stage adapted conservative therapeutic approach is recommended for MF and its variants^[12].

Aim of the study:

Our aim was to evaluate the effectiveness and safety of phototherapy in the treatment of early stage cutaneous T-cell lymphoma.

II. Objectives:

- To evaluate the effectiveness of phototherapy by finding the relation between clinical improvement, the number of sessions and cumulative dose.
- To determine the safety (number of patients developed side effects) of phototherapy in the treatment of early stage cutaneous T-cell lymphoma.
- To evaluate the compliance of patients to our treatment.

III. Methodology :

study design was a case series study

Study place: lymphoma clinic in dermatological department ,Tripoli central hospital

Study period: from January 2008 to Mars 2021

Study tool & population: all medical record of patients attending the clinic for diagnosis,treatment follow up. the inclusion criteria was all patients diagnosed clinically as Cutaneous lymphoma , confirmed by histopathological examination. Immunohistological examination was asked only in some patients where diagnosis was not confirmed.

Data management and analysis : data was drawn from medical records of patients included : age and gender of patients ,skin type, diagnosis, the main complain, duration of disease at time of diagnosis, clinical presentation, type of treatments, number of sessions & cumulative dose of phototherapy, complications of the treatment . The data collected was analyzed with SPSS version 20 , descriptive statistics; Frequency, means, standard deviation were used .

Ethical approval from head of dermatology department in the central hospital.

For phototherapy Waldmann UV 7001 K cabinets with both UNB and UVA fluorescence lamps are used for total body treatments and Waldmann UV 181 AL , Waldmann UV 200 Al with UVA fluorescent lamps are used as Hand-foot units. All treatments were given three times per week. The starting doses were determined by the patient's skin type . The treatment dose was increased by 10 % of the previous dose if there was no erythema. Dose increment was done every third session. For systemic PUVA patients were given 8-methoxy psoralen tab (0.6 mg per Kg body weight) then exposed to UVA during the second hour after tablet ingestion. All patients wore UV-blocking goggles or UV-blocking masks during treatment, and in males genitalia was covered from UV exposure. The patients are followed up regularly for evaluation of clinical response and development of any side effects and managed accordingly. When the clearance of the skin lesions is 90% or higher it is considered complete response, when it is less than 25% (after receiving adequate treatments; which are ≥ 12 sessions it is considered therapy failure.

IV. Results :

This study included 87 patients diagnosed as PCL , 44 males (50.57%) & 43 females (49.43%) with ♂ : ♀ of 1: 0.98. Their age ranged from 9 yrs to 82 yrs, with the mean age of 41.97 ± 16.2 yrs (figure-1). The most common age group affected was between 21 to 40 years of age; (table-1) shows details of the epidemiological characters of included patients, from all patients 69 (79.31%) were skin type IV followed by 10 patients (11.49%) with skin type III (figure-2). Fifty patients (57.47%) presented with pruritus while 34 patients (39.08%) presented with asymptomatic skin lesions (figure-3) At the time of diagnosis 34 patients (39.08%) were having the skin problem for more than 5 years (figure-4). Mycosis fungoides was the most common type of PCL with 77 patients (88.51%) having MF , presenting with only erythematous scaly patches in 27 patients (31.03%) followed by patches and plaques in 18 patients (20.69%) & hypopigmented patches in 18 patients (20.69%) , 8 patients (9.20%) were having plaques only, 2 patients (2.30%) presented with erythroderma, one patient (1.15%) had follicular papules, one patient (1.15%) had tumors, one patient (1.15%) presented with ichthyosis and one patient (1.15%) with pagetoid reticulosis presentin as ulcerating plaque on the leg (fiure-5). Apart from MF we had 5 patients with lymphomatoid papulosis (5.75%), one patient (1.15%) with Extranodal NK/T-cell lymphoma, nasal type and 4 patients (4.60%) with parapsoriasis (figure-5). Regarding distribution of the lesions 67 patients (76.74%) were having skin lesions scattered all over the body, (figure-6) shows distribution patterns in all patients. The diagnosis was confirmed with histopathological examination in 70 (90.9%) of MF patients & it was suspicious in 7 patients(9.1%) . According to TNM staging for MF cases; 51patients (66.6%) were in stage IB followed by 18 patients (23.4%) in stage IA while 5 patients (6.5%) in stage IIB, 2 patients (2.6%) in stage III and one patient (1.3%) in stage IIA (table-2). Most of the patients; 70 patient (90.9%) were treated with NB-UVB alone, one patient (1.3%) received systemic retinoid with UB-UVB (Re-UVB) while 2 patients (2.6%) received systemic PUVA only and patients (2.6%) received systemic PUVA with systemic retinoid (Re-PUVA) (table-2) complete clinical response to phototherapy

treatment was achieved in 41 (53.2%) of the the cases , 11 patients (14.3%) showed partial response and 4 patients (5.2%) had no response to treatment (table-2). From the MF patients who received phototherapy 57 patients (74.0%) completed their treatment without any complications while 14 patients (18.2%) had erythema during treatment & 4 patients (5.2%) had itching (table-2). During treatment 46 (59.7%) of the cases were regular, 6 patients (7.8%) were coming irregularly, 4 Patients (5.2%) showed therapy failure and 18patients (23.4%) dropped out during treatment (table-2). The mean number of sessions of NB-UVB in patients who had complete clinical response was 40 sessions with the mean cumulative dose of 53.12 J/cm² while the mean number of sessions of systemic PUVA in patients with complete response was 83 sessions with the mean cumulative dose of 599.32 J/cm² Other treatments given to our patients alone or with phototherapy were local steroids& tacrolimus, systemic steroids, methotrexate, chemotherapy, total skin electorn beam & systemic retinoids (figure-7) .

V. Discussion :

we present in this study the analysis of 87 Libyan patients with PCL how were registered in our lymphoma clinic in a period of twelve years, the sex ratio was nearly equal with male: female ratio of 1:0.98 which is different from the ratio recorded by De Luca DA et al ^[10] in Argentinian patients with a female predominance of 2.75:1. Most of the studies we revised included adult patients while we have included all registered patients in our clinic with age ranged from 9 to 82 years; the mean age of our patients was 41.97±16.2 yrs (figure-1) which is younger less than the mean ages registered by De Luca DA et al^[10] (60.8 years) & by B. Pattamadilok et al^[11] (52 years). The most common skin type in our patients was skin type IV (79.31%) which is the most common skin type in Libya in general followed by skin type III (11.49%) (figure-2). Although pruritus was recorded as a common symptom that affect the life quality of CTCL patients by many authors like A. Wright et al^[13] ere (88%) of his patients had itching only (57.47%) of our patients had pruritus while a good percentage of them (39.08%) had asymptomatic lesions (figure-3). At time of diagnosis (39.08%) of our patients gave history of having the disease for more than 5 years (figure-4) which is going with the duration of the disease reported by many author like Quaglino Pet al^[14] Mycosis fungoides was the most common type of PCL with 77 patients (88.51%) having MF as reported by most of the studies like that by K. Bisherwal et al^[15] , they presented with only erythematous scaly patches in 27 patients (31.03%) followed by patches and plaques in 18 patients (20.69%) & hypopigmented patches in 18 patients (20.69%) , 8 patients (9.20%) were having plaques only, 2 patients (2.30%) presented with erythroderma, one patient (1.15%) had follicular papules, one patient (1.15%) had tumors, one patient (1.15%) presented with ichthyosis and one patient (1.15%) with pagetoid reticulosis presenting as ulcerating plaque on the leg (fiure-5). Apart from MF we had 5 patients with lymphomatoid papulosis (5.75%), one patient (1.15%) with Extranodal NK/T-cell lymphoma, nasal type and 4 patients (4.60%) with parapsoriasis (figure-5), among the 77 MF patients (66.6%) were in stage IB followed by stage IA (23.4%) near to that reported by B. Pattamadilok et al. Most of our patients were treated with NB-UVB (90.9 %) & only (2.6%) were treated with systemic PUVA which is done in many studies like that by B. Pattamadilok et al^[16] were (80%) of their patients were treated with NB-UVB & (20%) were treated with systemic PUVA. From the 77 MF patient 56 completed their treatment either with complete response only in (53%), partial response (14.3%) or no response (5.2%) and this was because (23.4%) of the patients were dropped out by themselves & didn't complete their treatment (Table-2) as we compared our results with other studies in literature we found that De Luka et al^[17] reported complete response rate of (66%) which is near to our result while P. Rattankaemakorn et al^[18] reported a much higher rate of complete response in (93.5%) of their patients. No complications was recorded in (74%) of the patients while (18.2%) of them had mild erythema & (5.2%) had pruritus unlike the results of a study done byK. Phan et al^[19] were only (13.9%) of their patients had erythema during treatment & only (2.1%) of the patients had pruritus. We have compared the mean number of sessions & cumulative dose of our patients who had complete response to treatment with NB-UVB with those of De Luka et al^[17] were our results was 40 sessions & 39 sessions for their patients, but the mean cumulative dose for our patients was 53.12 J/cm² while they recorded mean cumulative dose of only 28.7 J/cm² and this can be explained by the smaller size of their population study (18 patients) compared to our size (77 patients) as well as the skin type of the study population were most of our patients were skin type IV.

VI. Conclusion &Recommendations:

- Phototherapy is an effective and well-tolerated treatment for early stage MF and its response depends on adherence to the treatment.
- comparing our study with previous studies in literature NB-UVB remains the safest and most widely used in treating early stage MF.
- larger sized multicenter studies with long term follow up are required to assess the duration of remission after each treatment course & evaluate the prognosis after treatment with phototherapy.

Limitation of study: it is a retrospective study ; based on single center experience.

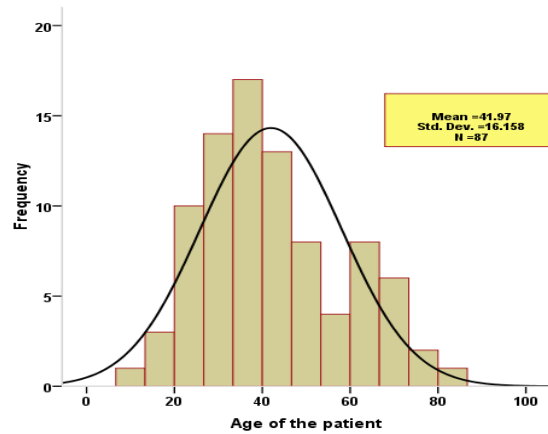


Fig-1: Histogram showing distribution of the patients according to the age

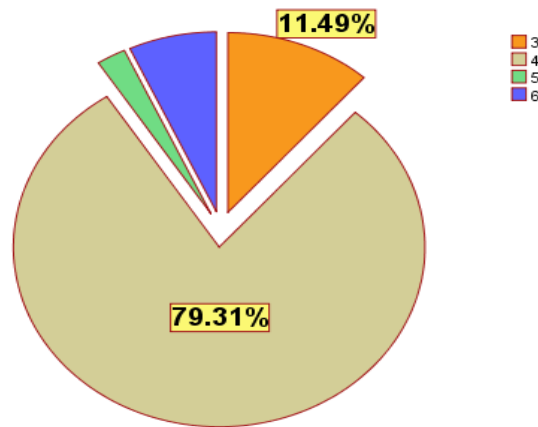


Fig-2: distribution of the patients according to their skin type

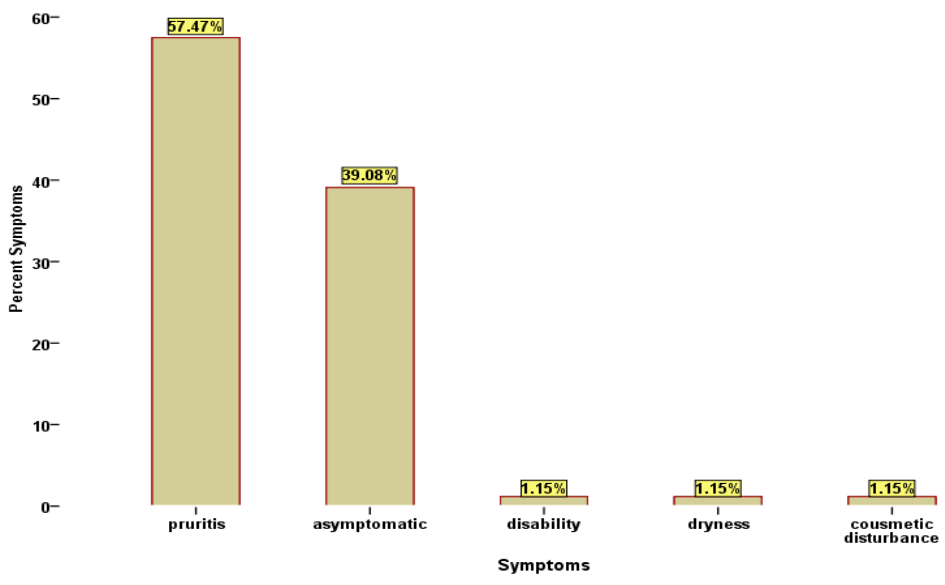


Fig-3 : distribution of the patients according to the presenting symptoms

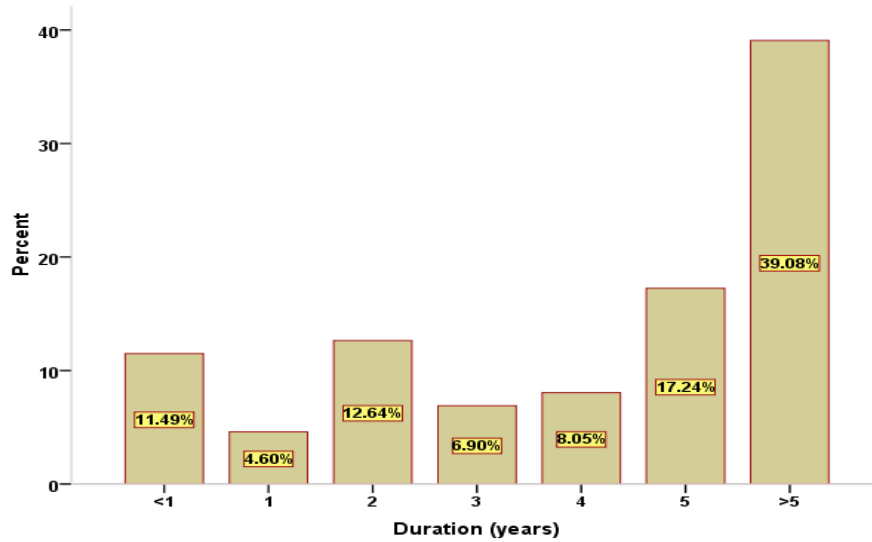


Fig- 4 : distribution of the patients according to duration of disease at time of diagnosis

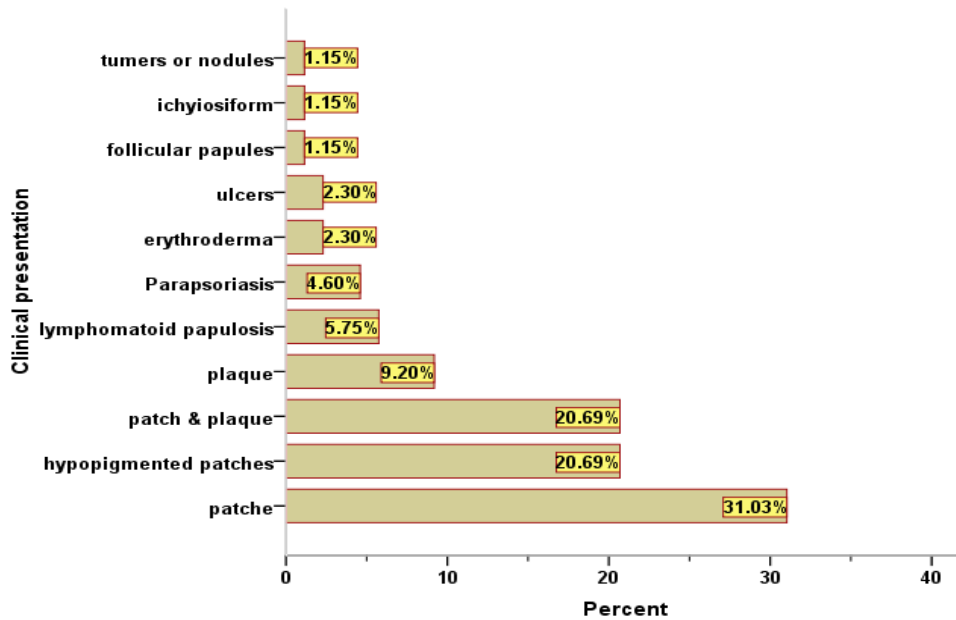


Fig- 5 : distribution of the patients according to the clinical presentation

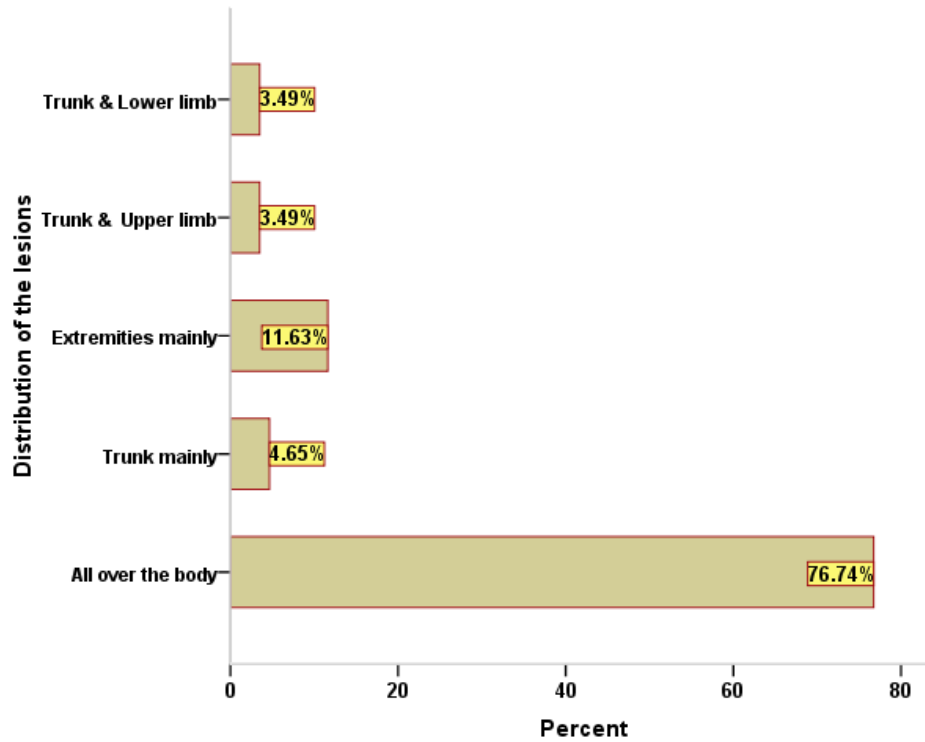


Fig- 6 : distribution of the patients according to the distribution of the lesions

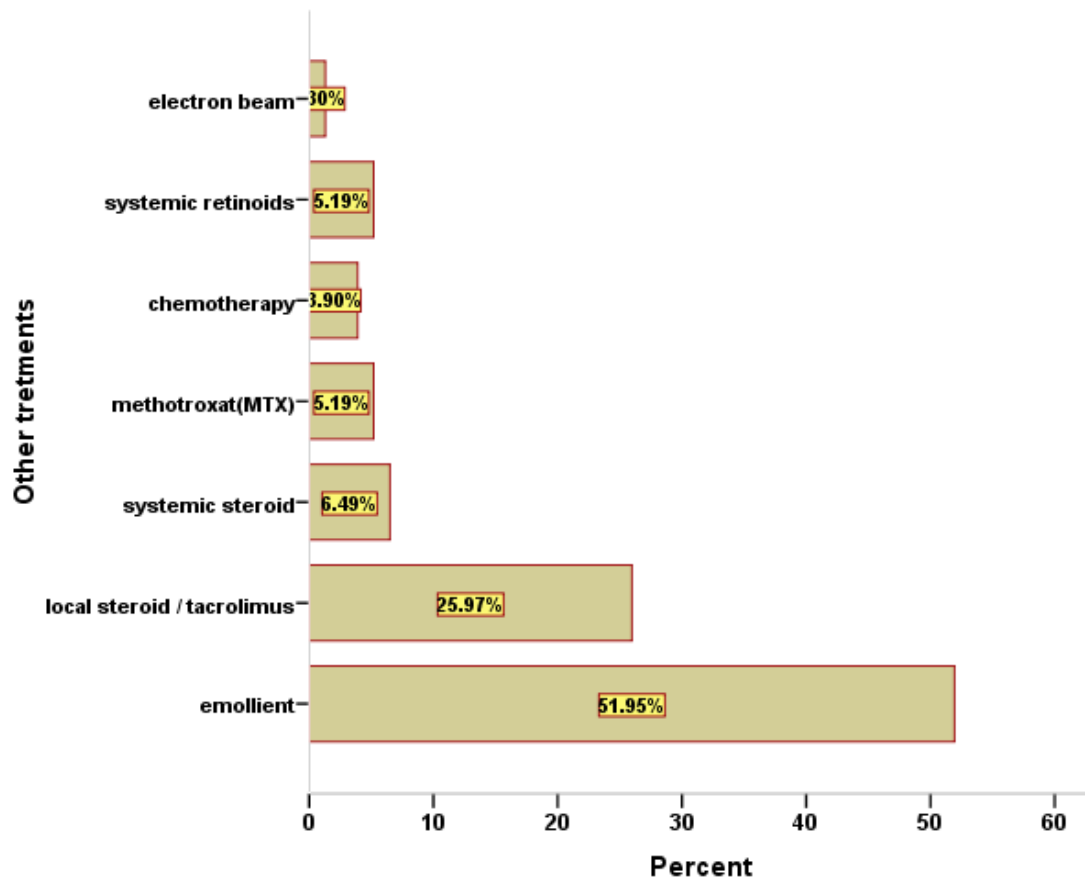


Fig- 7 : distribution of the patients according to other treatments received

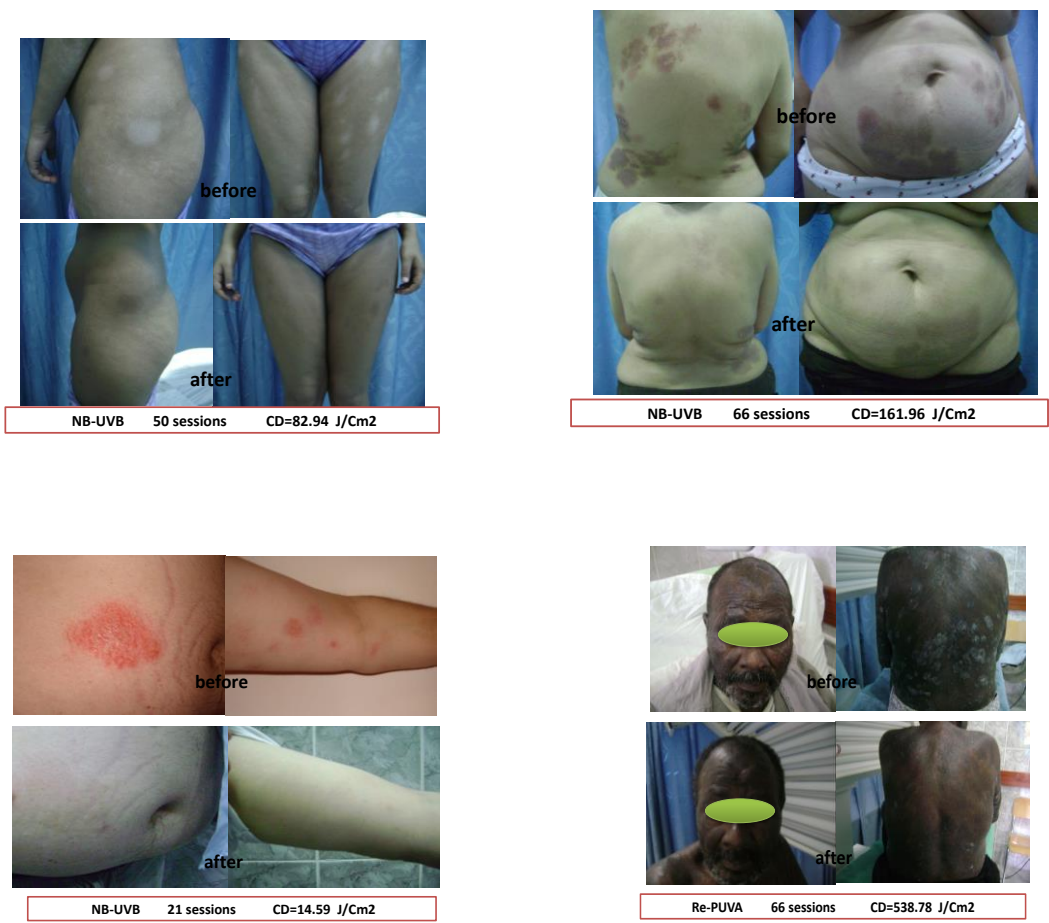
Table-1 : Epidemiological characters of our lymphoma clinic patients (TCH) :

character		N _e	Percent
Age group:	<10 – 20 yrs	4	4.6 %
	21 – 40 yrs	45	51.7 %
	41 – 60 yrs	23	26.4 %
	61 – 80 yrs	14	16.6 %
	> 80 yrs	1	1.1 %
Gender:	Male	44	50.6 %
	Female	43	49.4 %
Marital state:	single	25	28.7 %
	married	60	69.0 %
	divorced	1	1.1 %
	widow	1	1.1 %
Residency :	inside Tripoli	56 %	64.4 %
	outside Tripoli	31 %	35.6 %
Occupation :	student	11	12.8 %
	house wife	21	24.4 %
	employed	34	39.5 %
	free Job	12	14.0 %
	retired	9	9.3 %
Total		87	100 %

Table- 2 : MF patients treated with phototherapy :

character		N _e	Percent
Histopathological diagnosis :	confirmed	70	90.9 %
	suspecious	7	9.1 %
Staging (TNM) :	stage IA	18	23.4 %
	stage IB	51	66.6 %
	stage IIA	1	1.3 %
	stage IIB	5	6.5 %
	stage III	2	2.6 %
Type of phototherapy :	NB-UVB	72	93.5 %
	PUVA	2	2.6 %
	Re-PUVA	2	2.6 %
	Re-UVB	1	1.3 %
Clinical response :	complete response	41	53.2 %
	partial response	11	14.3 %
	no response	4	5.2 %
	drop out	18	23.4 %
	still on treatment	3	3.9 %
Complications of therapy :	erythema	14	18.2 %
	itching	4	5.2 %
	no complications	57	74.0 %
Follow up :	regular	46	59.7 %
	irrigular	6	7.8 %
	therapy failure	4	5.2 %

drop out	18	23.4 %
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