MUCOCUTANEOUS MANIFESTATIONS ASSOCIATED WITH PEDIATRIC MALIGNANCIES

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ABSTRACT

Background*: Skin lesions may help clinicians to diagnose and evaluate pediatric malignancies. However chemotherapy and radiotherapy have major role to fight cancer, they also have destructive side effect on skin and mucous membranes.*

Aim of Study*: to be aware of their side effects on skin apparatus and to clarify initial skin lesions that may precede appearance of neoplasm.*

Methods: *In this Prospective study, 199 patients diagnosed as malignancies in Pediatric oncology department at Nasser Institute Hospital and Benha University Hospitals during the period from November 2017 to May 2018. Complete clinical history was taken, systemic and local examination was carried for all the patients. Detailed dermatological examination was performed at initial presentation and when any mucocutaneous sign appeared. Biopsies taken when needed. Imaging of all positive signs to evaluate and follow up.*

Results: *122 males (61.31%) compared to 77 females (38.69%). Hematological malignancies constitute 103(51.75%) and Non-Hematological 96 case (48.25%). The most prevalent sign was chemotherapy induced alopecia which found in 145(72.86%). Infections were the second in 23 cases (60.53%). Drug reaction, echymosis, radio-related dermatitis and oral mucositis found in 8(21.05%), 3(7.89%), 1(2.63%) and 6(15.79%) patients respectively. Some specific skin lesions precede the systemic appearance of the malignancies. Leukemia Cutis and Histiocytosis were encountered in our study in 1(2.63%) and 5(13.16%) respectively.*

Conclusion: *Alopecia found in 72.86%, Langerhans Cell Histiocytosis may presented with skin lesions initially, Neutropenic patients have higher risk to skin lesions.*

INTRODUCTION

During the last decades of the 20th century and early in the current millennium, the incidence of cancer among children has increased and has assumed relatively greater importance in pediatric practice [1]. In Western countries, cancer-related deaths are the second most common cause of death (20%) following traumatic injuries (21%). [1]

Diagnosis of skin, mucosae, hair and nail manifestations in malignant diseases are often challenging because of life threatening drug reactions, opportunistic infections or skin involvement of primary processes. Description of morphology, configuration and distribution of lesions are important in order to differentiate self-healing eruptions from serious side effects of chemotherapy, such as acral erythema and intertriginous eruption. [2]

The identification of the reaction pattern associated with the trigger drug and of the possible dose limiting toxicity is of extreme importance to the assistant physician, as well as the differential diagnosis with infectious processes and specific manifestations of the neoplasm. Most reactions can be reverted with dose reduction or with an increase of the interval between doses. Some toxic effects can be successfully treated or prevented. Medication administered before the chemotherapeutic treatment can prevent hypersensitivity reactions. The use of oral antiseptic solutions is useful in the control of mucositis. [3]

Systemic malignancies can present with a variety of cutaneous manifestations. Given that accurate, prompt diagnosis of malignancy can have tremendous prognostic significance, it is imperative that clinicians are familiar with features of skin lesions that may be seen in this setting.[4] Leukemia Cutis result from infiltrations of skin by neoplastic leukocytes or their precursors. Leukemia Cutis can be seen in both congenital and childhood leukemias including Acute lymphoblastic leukemia (ALL), acute myelogenous leukemia (AML), chronic lymphoblastic leukemias(CLL) and chronic myelogenous leukemia (CML). The presence of Leukemia Cutis tends to be associated with a high tumor burden and a poor prognosis. [4]

A wide range of cutaneous side effects can be observed in pediatric oncology patients undergoing chemotherapeutic agents. It is important for

oncologist and dermatologist to recognize and evaluate cutaneous side effect of chemotherapy. [5]

Neutropenia is common in pediatric malignancies so infection was commonly found. Mucous membrane and skin are most common portals for microorganism in these patients 44% of all neutropenic patients developed skin lesions. [6]

PATIENT AND METHODS

This prospective follow up study was conducted on 199 subjects in Pediatric Oncology Department at Nasser Institute Hospital in Cairo and Benha University Hospitals. During period from November 2017 to May 2018.

Ethical considerations:

- Approval of the local ethical committee in the pediatrics department, college and university were obtained before the study.
- Written parent consent for the study was obtained before the study.
- The author's declared no potential conflict of interest with respect to the research and publication of this article.
- All the data of the patients and results of the study are confidential & the patient has the right to keep it.
- The authors received no financial support for the research & publications of the article.

Inclusion criteria:

- All patients aged below 18 years old.
- Patient who diagnosed as malignancies both solid and hematological.
- Patients who received both chemotherapy and patients who received both chemotherapy and radiotherapy.

Exclusion criteria:

- Any patient above 18 years old.
- Patients who have skin rash and they have no malignancies.
- Patients who received radiotherapy only.

All the studied patients were subjected to the following:

● Medical History:

- Age of presentation, gender, diagnosis, relation of skin lesion to presentation, regimen of treatment, itchy, painful or asymptomatic skin lesion.

● Physical Examination:

- General clinical examination: to detect any possible skin lesion.

- Local dermatological examination to determine type, site, shape and number of lesions.

● **Imaging skin lesions and full description.**

● **Investigations:**

- Complete blood picture.
- Skin biopsies whenever indicated.

RESULTS

Table (1): Demographic data of the studied patients

Variable (no.=199)		No.	%
• Sex	Female	77	38.69
	Male	122	61.31
		Mean ±SD	Range
• Age (years)		9.56±5.88	0.15-18

Table (1) shows that male predominance in the study with mean age 9.56±5.88 years and male to female ratio about (1.58:1).

Table (2): Classification of study group according to diagnosis

	No.	%
Haematological	103	51.76
Non-Hematological	96	48.24
Total	199	100.0

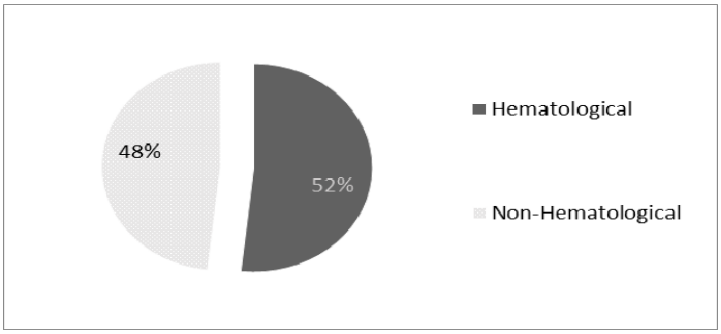

Fig (1): Classification of study group according to their oncological diagnosis

Table (2) and Figure (1) show that hematological cases formed 52% of study group and non-hematological group formed 48%.

Table (3): Diagnosis of patients included in the study

	Diagnosis (no.=199)	**No.**	**%**
Hematological	Leukemias	85	42.71
	Lymphoma	18	9.04
Non-Hematological	Brain tumour	11	5.53
	Colon	1	0.5
	Endometrial sarcoma	1	0.5
	Ewing sarcoma	11	5.53
	Germ cell tumour	4	2.01
	Hemophagocytic lymphohistiocytosis	30	15.07
	Langerhans Cell Histiocytosis	2	1.0
	Neuroblastoma	9	4.52
	Non Rhabdomyosarcoma	1	0.5
	Osteosarcoma	16	8.04
	Retinoblastoma	1	0.5
	Rhabdomyosarcoma	7	3.52
	Willm's tumour	2	1.0

Table (3) shows that leukemias were the most common (42.7%) followed by Hemophagocytic Lymphohistiocytosis (15.07%) in the studied group.

Table (4): Protocols of chemotherapy used in the study

Chemotherapy received (no.=199)	No.	%
ABVD Protocol	3	1.5
AML Protocol	10	5.02
Anaplastic Lymph protocol	1	0.5
Choroid Protocol	1	0.5
EURAMOS Protocol	16	8.04
Ependymoma Protocol	2	1.0
Ewing Sarcoma Protocol	8	4.02
FLAG-M	2	1.0
Folfox protocol	1	0.5
HLH Protocol	30	15.07
ICE Protocol	9	4.52
LCH Protocol	2	1.0
LGG protocol	3	1.5
LMB Protocol	4	2.01
MB Protocol	5	2.51
NB Hr Protocol	8	4.02
Non Rms protocol	2	1.0
PEB Protocol	4	2.01
Palliative VP 16	2	1.0
RICE	1	0.5
RMS Protocol	6	3.01
Re-induction	12	6.03
Retinoblastoma Protocol	1	0.5
Total XV	63	31.66
Not started	2	1.0
Willm's protocol	1	0.5

This table (4) shows the different combined regimens of chemotherapy that used in the treatment of patients in the study. Total XV protocol was the most common protocol used in 63 patients (31.66%) followed by HLH protocol in 30 (15.07%).

Table (5): Incidence of alopecia in the study group

Variable (no.=199)		No.	%
Alopecia	**No**	54	27.14
	Yes	145	72.86

Alopecia found in 145 patients (72.86%) and it was the commonest lesion in the study.

Table (6): Classification of skin lesions according to etiology

Category of skin lesions (no.=48)		No.	%
Specific malignancies	Histiocytosis	5	13.16
	Leukemia cutis	1	2.63
Non-specific causes	**Infection**		
	Bacterial	13	34.21
	Fungal	5	13.16
	Viral	5	13.16
	Total	23	60.53
	Drug reaction	9	23.68
	Echymosis	3	7.89
	Radio-related	1	2.63
	Oral mucositis	6	15.79

Table (6) describes the classification of skin lesions according to the etiology in the study group. Specific malignancies as leukemia cutis and histiocytosis found in 6 patients (15.7%) and non-specific causes found in 42 patients (84.3%) ten of them were repeated.

Table (7): Skin lesions found in the study group

Type of skin lesions (no.=38)	No.	%
Beau line	3	7.89
Hair follicle infection	1	2.63
Hairy tongue	1	2.63
Herpes simplex	2	5.26
Angular stomatitis	2	5.26
Histiocytosis	4	10.53
Lupus erythromatosis	1	2.63
Oral mucositis	6	15.79
Abscess	4	10.53
Echymosis	3	7.89
Radio-dermatitis	1	2.63
Scalp crustation (tinea capitis)	1	2.63
Acni-form	1	2.63
Bed sores	1	2.63
Canula site infection	1	2.63
Hand and foot syndrome	1	2.63
Herpes zoster	3	7.89
Leukemia cutis	1	2.63
Maculopapular rash	4	10.53
Multiple boil	2	5.26
Pyoderma	1	2.63
Napkin dermatitis	1	2.63
Orbital cellulitis	1	2.63
Perichondritis	1	2.63
Ulcer	1	2.63

Table (7) shows that there were 48 skin lesions (Alopecia not included) found in the study group. So, skin lesions found about 19%. Oral mucositis found in 6 patients(15.79%) followed by abscess and maculopapular rash each in 4 patients (10.53%) then Beau line, Herpes Zoster and echymosis each in 3 patients (7.89%).

Table (8): Comparison between the two group (Hematological and Non- Hematological) according to many variables

Variable		Haematological (no.=103)		Non-Hematological (no.=96)		Chi-square test	P
		No.	%	No.	%		
Sex	Female	29	28.16	48	50.0	9.99	0.002 (S)
	Male	74	71.84	48	50.0		
Age (years)	Mean ±SD; (range)	9.77±5.57; (1-18)		9.34±6.21; (0.15-18)		MW= 0.70	0.48
Skin lesion	No	81	78.64	80	83.33	0.71	0.40
	Yes	22	21.36	16	16.67		
Repeated skin lesion (no.=38)	No	16	72.73	12	75.0	FET	1.00
	Yes	6	27.27	4	25.0		
Skin lesion is the first presentation (no.=38)	No	22	100.0	11	68.75	FET	0.009 (S)
	Yes	0	0.0	5	31.25		
Alopecia	No	8	8.08	47	54.65	47.78	<0.001 (HS)
	Yes	91	91.92	39	45.35		

This table (8) shows the two groups of patients with Hematological and Non-Hematological malignancies, that males were predominant in hematological group with (74.84%) but no sex difference in the non-hematological group with significant P value (0.002). Also, skin lesions appeared at first presentation was statistically significant in non-hematological group with P value (0.009). Alopecia was highly significant P value (<0.001) in Hematological group with 91.9%. Other variables were with no significant. So, Group 1 (Hematological) was in higher risk with percentage 21.3% to develop skin lesion more than Group 2 (Non-Hematological) with percentage 16.6%.

Table (9): Relation between skin lesions and complete blood picture in study groups

CBC in patients with skin lesion (no.=38)	No.	%
Leucocytosis (TLC more than 15.000)	3	7.89
Neutropenia (TLC less than 1500)	16	42.11
Pancytopenia	4	10.53
Thrombocytopenia (Platelet count less than 50.000)	1	2.63
Normal	14	36.84

Neutropenic patients have higher risk to develop skin lesions more than others with 42.1% followed by normal CBC with 36.84%.

Table (10): Relation between skin lesions and diagnosis of malignancy

Diagnosis (no.=199)		No skin lesion --Ve (no.=161)		Skin lesion + VE (no.=38)		z-test	P
		No.	%	No.	%		
Hematological	Leukemias	64	39.75	21	55.26	1.74	0.08
	Lymphoma	15	9.32	3	7.89	0.27	0.78
Non-Hematological	Brain tumor	11	6.83	0	0.0	1.66	0.10
	Colon	1	0.62	0	0.0	0.49	0.63
	Endometrial sarcoma	1	0.62	0	0.0	0.49	0.63
	Ewing sarcoma	10	6.21	1	2.63	0.87	0.38
	Germ cell tumor	4	2.48	0	0.0	0.98	0.33
	Hemophagocytic Lymphohistiocytosis	21	13.04	9	23.68	1.65	0.10
	Langerhans Cell Histiocytosis	0	0.0	2	5.26	2.92	0.003 (S)
	Neuroblastoma	8	5.06	1	2.63	0.63	0.53
	Non RMS	1	0.62	0	0.0	0.49	0.63
	Osteosarcoma	16	10.13	0	0.0	2.03	0.04 (S)
	Retinoblastoma	1	0.62	0	0.0	0.49	0.63
	Rhabdomyosarcoma	7	4.43	0	0.0	1.31	0.19
	Willm's tumor	2	1.27	0	0.0	0.69	0.49

Table (10) summarize the relation between skin lesions and malignancies; Langerhans Cell Histiocytosis and Osteosarcoma showed statistical significance regarding appearance of skin

lesions with P values (0.003 and 0.04 respectively).

DISCUSSION

This study conducted on 199 patients who diagnosed as pediatric malignancies both hematological and non-hematological. Many patients developed skin lesions either on the onset of disease, during the treatment or follow up.

We aimed in the study to make pediatric oncologist aware of possible mucocutaneous lesions that may be specific or non-specific to malignancies. Some lesions need to start chemotherapy urgently and other lesions need only to reassure the child and their parents.

The study included 199 patients, 122 were males (61.31%) and 77 were females (38.69%) with male: female ratio (1.58:1). Males were predominant (61.31%) which is comparable with **Yeole et al.** (61.2%), **Cardoza-Torres et al.** (61.5%) [7, 8] and **Rajashekar et al.** (65.1%). [1] (Table 1)

We grouped patients into two groups according to their oncological diagnosis; Hematological malignancies and non-hematological malignancies. 103 children (51.76%) with hematological malignancies showed male predominance with male to female ratio (2.55:1) with mean age 9.77±5.57 Years. While, Non hematological patients were 96 (48.24%) with male to female ratio (1:1) and mean age 9.34± 6.21. (Table 2)

The most prevalent diagnosis is acute lymphoblastic leukemia ALL in 67 cases which represent (65.07%) of hematological malignancies and (33.66%) of total malignancies. This percentage is lower than **Rajashekar et al.** (60.3%) [1] and **Cardoza-Torres et al.** (78.4%) [8] It may be explained by our larger study group and various diagnosis compared to both studies. (Table 3)

Hematological group of patients were more vulnerable to develop skin lesions more than non-hematological group as they showed 22 (21.36%)skin manifestations compared to 16 (16.67%) respectively. (Table 8)

Chemotherapy induced alopecia was the commonest adverse effect of chemotherapy in the study. It was found in 145 patients (72.86%). It is nearly similar to **Cardoza-Torres et al.** (74.3%) [8] and higher than **Rajashekar et al.** (68.3%) [1],

Trueb et al. (65%) [9] and **Kamil et al.** (64.3%) [10]. Alopecia was more associated with cytotoxic therapy e.g. Anthracyclines, Cytrabine and High dose of Methotrexate , we are nearly in concordant with **Ralph M.** results. [11] (Table 5)

Anthracyclines showed complete alopecia in our study and also Ralph M. concordant. Methotrexate, Cisplatin and Cytrabine differed in the two studies as it showed complete alopecia in our study and it was rare in Ralph M. study. [11]

Regarding combined regimens; TOTAL -XV, EURAMOS and AML protocols were statistically highly cytotoxic. But HLH protocol and LCH protocol showed low incidence. No available results to compare regarding pediatric combined protocols.

According to the etiology of skin lesions we found one case of Leukemia Cutis presented in our study as initial presentation of acute myeloid leukemia case. This was in agreement with **Wright TS** that Leukemia Cutis is more common with AML cases. Our twelve cases of AML showed one case (8.33%) compared to 10% in **Wright TS** study. [4] (Table 6)

Histiocytosis class I (Langerhans Cell Histiocytosis) and class IIb (Hemophagocytic Lymphohistiocytosis) appeared to be highly significant to develop skin lesions; LCH patients developed skin rash at initial presentation with 100% percentage and significant p value (0.009%) we agreed with **Wright TS** but we have higher incidence mostly due to LCH found in two cases only. [4] (Table 6)

Wright TS found Lymphoma cutis (0.5%), Neuroblastoma (3%) and sarcomas (1%) but we did not find any of them in our study due to their rarity. [4]

Infections were aggressive and not responding to routine antibiotics, twenty three (60.53%) infectious manifestations found in our study which represented the second common lesion after alopecia. It was lower than **Bailey et al.** reported 85% [12], and **Rajashekar et al.** 88.8% [1] and higher than **Cardoza-Torres et al.** 56.6%. [8] (Table 6)

We found bacterial infections in 13 patients (56.52%) which were higher than **Rajashekar et al.** (14.33%) [1], **Cardoza-Torres et al.** (15.6%) [8], and in agreement with **Bailey et al.** (5-60%) [12]. It may be due to loose infection control in the unit. (Table 6)

Viral infections in 5 patients (21.73%) which are comparable to

Cardoza-Torres et al. (19.6%) [8] and **Bailey et al.** (10%) [12] but much lower than **Rajashekar et al.** (42.85%) [1]. (Table 6)

Fungal infections found in 5 patients (21.73%) which is slightly agree with **Rajashekar et al.** (23.4%) [1] But higher than Bailey **et al.** (5-10%) [12] and **Cardoza-Torres et al.** (5.8%) [8]. (Table 6)

So, Bacterial infection was predominant in our study, the same as **Bailey et al.** [12] but viral infections was predominant in **Rajashekar et al.** [1] and **Cardoza-Torres et al.** [8]

Many drug reactions found in the study including nail changes, skin rashes, hand and foot syndrome. Nail changes occurred due to cytotoxic effects of chemotherapy on nail apparatus as Beau's and Mee's lines. Beau's lines found in 7.89% and all of them received AML protocol that contains High Dose Cytrabine. It was lower than **Cardoza-Torres et al.** (15.6%) [8] and **Rajashekar et al.** (11.31%) [1] results. Mee's lines detected once via **Rajashekar et al.** [1] but no cases in our and **Cardoza-Torres et al**. studies. [8] Skin rashes found in 8 patients (4%) compared to Ceylan et al. (3.2%). [5] (Table 7)

Palmar and plantar erythrodysesthesia (Hand and Foot syndrome) found in patients who received AML protocol with percentage 2.6% it is much lower than **Zhang B.** (18%) but we are in common regard the chemotherapeutic agent which develop the lesion; Cytrabine. [13] (Table 7)

In our study, all cases that developed oral mucositis were acute leukemias and this agree with **Ramon G et al., 2017**. Six patients developed oral mucositis with (15.79%) percentage. [14] It was much lesser than previous results. But nearly similar to **Rajashekar et al.** That present in 8 cases (12.7%) [1] And lesser than **Cardoza-Torres et al.** (23.1%) [5] and **Ramon G et al.** (73.33%). [14] All of them were males but without statistical importance. (Table 7)

Rajashekar et al. found Echymosis in 12.7% of patients with malignancies and we found it in 7.89% of total number of skin lesions [1]. **Ceylan et al.** found higher percentage with 21%. [5] (Table 7)

Radiotherapy is out of our duties as we are concerned with chemotherapy mainly. So, percentage of Radio-dermatitis was low (2.63%) it was nearly

comparable with **Cardoza-Torres et al.** (1.5%). [8] (Table 6)

Statistical analysis showed that neutropenic patients were in high risk to develop skin lesions. 16 patients (42.11%) with neutropenia developed skin lesions and 14 patients (36, 84%) with normal blood picture developed lesions. This was in agreement with **(Wananukul S et al. 2005)** [6] (Table.9)

CONCLUSION

- Pediatric malignancies may be presented with mucocutaneous lesions as first presentation. So, skin examination may lead to diagnosis.

- One hundred percent of Langerhans cell histiocytosis patients in the study presented by skin manifestation initially followed by systemic involvement.

- Neutropenic patients at higher risk to develop mucocutaneous lesions more than patients with normal total leucocytic count.

- Alopecia was the most common mucocutaneous lesion that cause psychological distress among this group.

- Infections were nearly to be predominant in the study group and may delay the treatment of cancer and even loss of them. Bacterial were predominant.

- Hematological malignancies patients were more vulnerable to suffer from skin lesions than non-hematological.

RECOMMENDATIONS

- Pediatrician should be aware of possible alarming skin lesions that may precede systemic appearance of malignancies.

- Pediatrician should recognize side effect of chemotherapeutic agents and radiotherapy to make it avoidable as much as possible.

- Hold awareness courses to pediatricians aimed to clarify specific mucocutaneous signs of malignancies that may appear as initial marker which precede the malignancies.

- Further studies with large number of patients with mucocutaneous involvement in children with malignancies.

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الأعراض الجلديه المصاحبه للأمراض السرطانيه في الأطفال

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تعد الأورام السرطانية أحد أهم الأمراض المؤديه للوفاة في الأطفال. و تنقسم تلك الأمراض إلى نوعين رئيسيين : أمراض الدم السرطانيه والأورام السرطانية الصلبه.

و تعتبر أمراض الدم الخبيثة) الليوكيميا) الأكثر إنتشارا بنسبة 30 بالمائة ويليها أورام المخ بنسبة 26 بالمائة و الأورام بالغدد الليمفاوية بنسبة 8 بالمائة الأورام بالعقد العصبيه بنسبة 6 بالمائة و أورام الكلى بنسبة 5 بالمائة و أورام العظام بنسبة 3 بالمائة و غيرهم.

ظهور الأعراض الجلدية المصاحبة للاورام السرطانية في الأطفال الذين تم تشخيصهم بالمرض أو الخاضعين للفحوصات قد يكون ذو أهمية كبيرة لتحديد المرض و بدء العلاج.

العديد من الأعراض الجلدية يمكن ملاحظتها بالأطفال المصابين بالأورام الخبيثة و قد تكون تلك الأعراض أولية مع بداية المرض و ترسب خلاياه بطبقات الجلد أو ثانوية و جانبيه أثناء العلاج الكيميائي و الإشعاعي و أثناء فترات المتابعة.

هدف الرسالة: توضيح و تقسيم الأعراض الجانبية المصاحبة للأمراض السرطانيه في الأطفال و جعل طبيب أورام الأطفال على دراية بها و معرفة كيفية التعامل معها.

ضمت الدراسة كل المرضى:

- الذين لا تتجاوز أعمارهم ال 18 عام.
- المصابين بالأمراض السرطانيه بالدم و الأورام السرطانية الصلبه.

- ضمت الدراسة 199 طفل مريض يتلقون العلاج بوحدة أورام الأطفال بمستشفى معهد ناصر و مستشفى بنها الجامعي.
- متوسط عمر المرضي : 9 سنوات
- تلقى العلاج الكيميائي 197 طفل و تلقى العلاج الإشعاعي 38 طفل. و لم يتلقى طفلين أي علاج.

أسفرت الدراسات الإحصائية عن :

- ظهرت الأعراض الجلدية كعّرض أولي في تسعة أطفال بنسبة 23 بالمائة من مجمل الأعراض الجلدية.
- سقوط الشعر المرتبط بالعلاج الكيميائي حدث بنسبة 72 بالمائة من مجمل المرضى و هو أهم عرض جلدي و أكثرهم على الإطلاق.
- المقارنة بين المرضى الذين أصيبوا بالأعراض الجلدية و المرضى الغير المصابين أوضحت إحصائيا أهمية وجود الأعراض الجلدية الأولية في بداية المرض. ولم تظهر أي أهمية للعمر و الجنس.
- أمراض الدم السرطانية أظهرت تكرارا للأعراض الجلدية بشكل أكبر من الأورام الصلبة و ظهر ذلك في ستة حالات بنسبة 60 بالمائة.
- تم تقسيم الأعراض الجلدية لمجموعتين: أولية و ثانوية.
- الأعراض الجلدية الأولية الخاصة بالمرض و التي كان سببها ترسب الخلايا السرطانية بطبقات الجلد وجدت في 15 بالمائة من مجمل الأعراض الجلدية.
- الأعراض الجلدية الثانوية ضمت الإصابات المعدية و الأعراض الجانبية للعلاجات الكيميائية و الكدمات الدموية و الأعراض المصاحبة للعلاج الإشعاعي و إلتهاب الأغشية المخاطية الفموية.
- يعد الأطفال المصابين بالأمراض السرطانية الأكثر عرضة للعدوى و مثلت الأعراض الجلدية الناتجة عن عدوي (بكتيرية- فيروسية – فطرية) 60 بالمائة.

- الأعراض الجلدية الناتجة عن العلاجات الكيميائية و التدعيمية تواجدت بنسبة 21 بالمائة.

- الكدمات الدموية بنسبة 3 بالمائة.

- الأعراض المصاحبة للعلاج الإشعاعي تمثلت بنسبة 2 بالمائة.

- التهابات الأغشية المخاطية الفموية وجدت بنسبة 6 بالمائة.

- تم ملاحظة ظهور الأعراض الجلديه عند 16 طفل أثناء إنخفاض عدد كرات الدم البيضاء لديهم.

- ظهر إحصائيا بشكل واضح أهمية وجود العرض الجلدي منذ بداية التاريخ المرضي.

- أظهرت المقارنات الإحصائية علاقة واضحة بين ظهور الأعراض الجلدية و التشخيص المرضي، و ظهر ذلك جليا في مرض الخلايا الآكلة لانجرهانس و سرطان العظام.

- ظهرت علاقة بين الأعراض الجلدية و بروتوكولات العلاج الكيميائية خاصة مع بروتوكول سرطان الدم الميلودي و الخلاية الآكلة لانجرهانس و الخلايا الآكلة اللمفية.

نستنبط من هذه الدراسه:

- تمثل الأعراض الجلديه المصاحبه للأمراض السرطانيه أحد أهم الصعوبات التي تواجه أطباء الأطفال أثناء مرحلة التشخييص و العلاج.

- سقوط الشعر المصاحب للعلاج الكيميائي مثل 72% من الأعراض الجلديه التي واجهت الأطفال المصابين بالسرطان.

- الإنخفاض الشديد في كرات الدم البيضاء المناعية ساعد كثيرا في ظهور الأعراض الجلدية لدي الأطفال المصابين خاصه الأعراض الجلديه الناتجه عن عدوى.

- كان للعلاجات الكيميائية أثار جانيه علي الجلد و الأغشيه الفمويه و الأظافر و أدت الى أثار نفسيه سيئه لدي الأطفال الذين يتبقون العلاج

و أخيرا نوصي بـــ:

- ضرورة توعية أطباء الأطفال بالأعراض الجلدية المنذره بإحتماليه الأصابه بالأورام الخبيثه و التي قد تسبق ظهور الأعراض العامه.

- يجب على أطباء الأطفال معرفه الأثار الجانيه للعلاجات الكيميائيه و العلاجات الإشعاعيه و محاولة تفاديها قدر الإمكان.

- عقد الدورات التدريبيه و اللقاءات العلميه التي تهدف لزيادة الوعي و التعريف بالأعراض الجلديه الأوليه التي من الممكن أن تساعد في تشخيص المرض في مراحله المبكره و بدء العلاج.

- عمل أبحاث مستقبليه تشمل عدد كبير من الأطفال المصابين بالسرطان مع وجود علامات جلدية و التعريف بالأثار الجانيه أثناء مراحل العلاج.