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Follow up of Survivors of Childhood Acute Lymphoblastic Leukemia with Detection of Parental Psychiatric Disorders

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Abstract: *Objectives:* is to examine the late effects of cancer on parents of survivors of childhood acute lymphoblastic leukemia, with particular stress on posttraumatic symptoms. *Methods:* Fourty six children excluded from 60 children cured from acute lymphoblastic leukemia. They stopped therapy for at least 3 years. Remission of the 46 children was confirmed by thorough clinical examination as well as laboratory investigations including peripheral blood examination, bone marrow aspiration and C.S.F examination. Full medical history including onset, duration, severity and full detailed scheme of treatment were obtained. Special clinical files were done for all the studied cases with all their clinical and laboratory data. The parents of those children underwent the followings: General health questionnaire, ICD-10 symptoms checklist of mental disorder, rating scales for anxiety and depression, Post traumatic stress disorder assessment scale and the PCASEE questionnaire for quality of life. *Results:* 56% of the parents of cancer survivors suffered from psychiatric morbidity affective, financial and ego function subtests of the quality of life were significantly decreased in parents of acute lymphoblastic leukemia survivors than the controls. There was high significant elevation of the post traumatic stress symptoms in parents of acute lymphoblastic survivors than the controls. *Conclusion:* Though parents voiced relief at survival, they were anxious about relapse, together with concerns about meeting the long term psychological, medical, educational needs of the survivors. The need for long term follow up studies during different phases of treatment with and without psychological intervention is mandatory, which might improve the psychological outcome for both parents and children.

Key words: Childhood, acute lymphoblastic leukemia, parental psychiatric disorders.

INTRODUCTION

Hematological malignancies account for approximately 40% of childhood cancer (Gloeckler, 1999). Progress in the curative treatment of this group of cancers is one of the great medical success stories of the 20th century. There have been improvements in outcome for all major subtypes of pediatric leukemias and lymphomas, the most dramatic of which has been in acute lymphoblastic leukemia (ALL), the commonest childhood malignancy. At the time that the National Cancer Act of 1971 (Public law 92-218) made the "conquest of cancer a national crusade" (President Richard M. Nixon, December 23, 1971) fewer than 10% of children with ALL survived for 10 years after diagnosis. Survival rates for children diagnosed with ALL have increased steadily over ensuing eras and now exceed 80% (Kersey, 1997 and Pui and Evans, 1998).

Improvements in survival for childhood hematologic malignancies have been achieved as the result of serial clinical trials conducted by pediatric oncology cooperative groups and large single clinical research centers. Essential to these therapeutic advances has been the development of effective agents, along with combination chemotherapy and treatment phase-specific and central nervous system-directed regimens (Alan *et al.*, 2008).

Childhood acute lymphoblastic leukemia is a cancer of the blood and bone marrow. This type of cancer usually gets worse quickly if it is not treated. It is the most common type of cancer. The earlier acute lymphoblastic leukemia is detected, the more effective is the treatment. The aim is to induce a lasting remission defined as the absence of detectable cancer cells in the body (usually less than 5% blast cells in the

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bone marrow) Ashah *et al*. (2008). Acute lymphoblastic leukemia is subdivided into 4 types according to the presence of cell membrane markers (early pre B, pre B, T type and B type). Early pre. B is the most common and the one with best prognosis (95% of cases go into remission with therapy) followed by pre B and T types B type has the worst prognosis. The choice of treatment of All on the estimated clinical risk of relapse in the patient, which varies widely among the subtypes of ALL. Three of the most predictive factors are the age of the patient at the time of diagnosis, the initial leukocytic count and the speed of resonance to treatment (i.e. how rapidly the leukemic cells can be cleared from the bone marrow or peripheral blood. Age between 1-10 years and a leukocytic count < 50,000/UL are widely used to define average risk. Children > 10 years of age or who have initial leukocyte count > 50,000/UL are considered to be higher risk (Nelson, 2007).

Day after day the rate of survival of childhood cancer is increasing. But still, cancer alters children lives and their parents in myriad ways, beginning at diagnosis and continuing well beyond completion of therapy. Problems with growth, puberty, cardiac and intellectual disability are some examples of long term complications after cure of cancer (Pui *et al*., 2003). In Egypt, the 5 years relapse free survival in childhood acute lymphoblastic leukemia has reached 63.7% in the period of 1992-1997 in the Hematology/Oncology clinic, Children's hospital Ain Shams University (Khalifa *et al*., 1999). Empirical studies of the adjustment of parents of childhood cancer survivors report inconsistent results. Although some investigators report that parents cope well with the extreme stress that accompanies having a child with a serious illness, other researchers find that mothers of pediatric cancer survivors are at risk for a variety of psychosocial difficulties, including depression, anxiety, and marital discord (Alderfer, 2009).

This study investigates whether a sizable number of parents of children with serious illness meet all of the other criteria for PTSD. Such a finding would have implications for the diagnosis, treatment, and understanding of the effects of illness on family members of chronically ill children. The advantage of systematically assessing the prevalence of PTSD in this population is that, unlike more general approaches for assessing anxiety and depression, this method allows for specific questions about the impact of the illness and examines symptoms or reactions characteristically seen in persons affected by extreme stress (Nichole *et al*., 2009).

The aim of the present study is to examine the late effects of cancer on acute lymphoblastic leukemia survivors and their parents, with particular stress on posttraumatic symptoms.

Subjects and Methods:

Subjects:

This is a retrospective analysis of 60 pediatric patients with a documented diagnosis of ALL, treated at the hematology/ oncology clinic, Children Hospital, Ain Shams University. They stopped therapy for at least 3 years as confirmed by the pediatrician consultant investigator (group I). All patients were subjected to diagnostic work up which included history, clinical examination and laboratory evaluation including complete blood picture, blood chemistry, bone marrow analysis, CSF examination, chest X-ray, determination of leukemic cell markers (immunophenotyping) using flow cytometry. By the end of the 3 years, complete re-evaluation was again confirmed by clinical examination, CBC, bone marrow analysis, CSF examination and bilateral testicular biopsy. Complete remission is defined as normalization of hematological indices and bone marrow normocellularity with < 5% lymphoblasts. Special clinical files were done for all the studied cases including their accurate clinical examination excluding pallor, purpuric eruption hepatosplenomegaly generalized lymphoadenopathy, arthritis and bone pains as well as prolonged low grade fever and signs of increased intracranial tension. Remission was confirmed by laboratory investigations such as peripheral blood examination for demonstration of blast cells (< 2%), bone marrow aspiration where blast cells in bone marrow (< 5%) and C.S.F free of leukemic blast cells as well as chest x- ray which excluded mediastinal involvement.

The time of the study extended from the period of Jan. 2007 to December 2009. They were recruited from the Research Institute of Ophthalmology and National Research Center Pediatric Clinics as well as the Hematology/Oncology clinic, Children's hospital, Ain Shams University. They were compared to a comparison group of parents of healthy children, coming from the hospital workers, matching age, sex and socioeconomic status of parents of pediatric cancer survivors (group II).

The included parents of cancer survivors were fulfilling the following criteria:

1. Parents of children with acute lympoblastic leukemia.
2. Their children have stopped therapy for at least 3 years.
3. Parents don't have premorbid physical or psychiatric illness.

The exclusion criteria for the parents:

1. If their children are still on treatment.
2. Presence of chronic physical illness.

The healthy parents were fulfilling the following criteria:

1. Absence of chronic physical illness.
2. Absence of chronic physical illness to the children.

The exclusion criteria for the healthy parents are:

1. Presence of premorbid neuropsychiatry illness in the parents or their children.
2. Presence of chronic physical illness in the parents or their children.

Methods:

a) This study included 60 ALL patients. They were selected from the Pediatric Clinics of Research Institute of Ophthalmology and National Research Center as well as Heamatologic Clinic of Ain Shams University, Pediatric Hospital as well. The age of the studied group ranged from 2-10 years. There were 40 males and 20 females. Fourteen patients were excluded as the indications for remission were not fulfilled from whom there were 10 males and 4 females. The remaining 46 ALL patients fulfilled complete remission:

1. All signs and symptoms of leukemia disappeared.
2. There were no abnormal cells in the blood, bone marrow and C.S.F.
3. The percentage of blast cells in the bone marrow was less than 5%.
4. Blood platelet count returned to normal.
5. The diagnosis of ALL was based on morphologic, cytochemical, and immunophenotypic criteria. All patients had less than 3% blast cells positive for myeloperoxidase or Sudan black and were negative for nonspecific esterase according to French-American-British criteria (Bennett *et al*., 1976).

Immunophenotyping was performed by flow cytometry with a large panel of commercial monoclonal antibodies directed against the following surface and intracellular antigens: CD1a, CD3, CD4, CD5, CD7, CD10, CD13, CD14, CD15, CD19, CD20, CD24, CD33, CD34, CDw65, HLA DR, IgM, and terminal desoxyribonucleotidyl transferase. Threshold positivities were set at 20% for surface antigens and 10% for intracellular markers, according to the BFM family criteria (Van den Berg *et al.*, 1992 and Swerdlow *et al.*, 2008).

A complete remission occurred within the first four to six weeks. Forty six patients showed low disease levels within 7 to 14 days and needed less intensive treatment. The other fourteen excluded patients were patients with high disease levels after 14 days and to whom required more than four to six weeks to achieve remission and needed more aggressive treatment and they acquired relapse.

Immunophenotype:

The World Health Organization (WHO) classifies ALL as either "B lymphoblastic leukemia" or "T lymphoblastic leukemia." B lymphoblastic leukemia is subdivided by the presence or absence of specific recurrent genetic abnormalities (t[9;22]), MLL rearrangement, t(12;21), hyperdiploidy, hypodiploidy, t(5;14), and t(1;19).

Sampling:

For immunophenotypic analysis by flowcytometry, peripheral blood or bone marrow samples, drawn on heparin, were used. Fluorescent labeled monoclonal antibodies for CD1, CD2, CD3, CD4, CD5, CD7, CD8, CD10, CD13, CD19, CD22 and CD33 were used.

b) Both parents of healthy children or cured children from leukemia were subjected to the followings:

1) General Health Questionnaire (Goldberg, 1972):

This questionnaire was initially developed as a first screening instrument for psychiatric illness, in order to identify potential cases which could be later determined by the use of second stage instrument like the clinical interview. The questionnaire includes 28 items scored as (0-0-1-1).The threshold is seven in Egypt (Okasha *et al*., 1988).

2) Semistructured Psychiatric Interview According to ICD 10:

The subjects were interviewed guided by a psychiatric history taking sheet designed at the center of psychiatry, Ain Shams University. It includes detailed personal, family, medical and past history records. A detailed history of the present illness including mode of the onset, duration and course of illness, the principle and auxiliary symptoms were also obtained.

3) ICD-10 Symptoms Checklist of Mental Disorder:

The patients were diagnosed according the ICDS 10 research diagnostic criteria using the ICD 10 symptom checklist for mental disorder. This is Semistructured instrument tended for clinician to assess psychiatric disorders in the FO-F6 categories of the ICD 10.

4) Post Traumatic Stress Disorder Assessment Scale (El-Khawaga, 1994):

It was first administered in Kuwait after the Gulf war. It is a questionnaire composed of 30 questions. Each item on the posttraumatic assessment scale is scored from 0-4. It was assembled according to DSMIV and ICD 10 criteria. It tests flash backs, autonomic arousal, avoidance and hypervigilence. Each subtest can be used as a separate scale. After the subjects answer all questions of the questionnaire, he/she is asked to report the type of trauma one was exposed to, whether it occurred to them or was witnessing them.

5) Hamilton Anxiety Rating Scale (Fatin, 1994):

This scale was developed in the 1950 to assess anxiety both somatic and cognitive. There are 14 items each of which is rated 0-4 on an unanchored severity scale. A score of 14 or more has been suggested as the threshold for clinically significant anxiety.

6) Hamilton Checklist of Symptoms of Depressive Illness (Fatin, 1994):

The HAM-D was developed in the early 1960 to monitor the severity of major depression, with focus on the somatic symptomatology. It is a 17 items scale, scored from 0-4. A score of 10 has been suggested as threshold for clinically significant depressive symptoms.

7) The PCASEE Questionnaire for Quality of Life (Bech, 1998):

Quality of life is the subjective well-being. The subdimension of the quality includes physical, mental and social well-being. The PCASEE scale, is the quality of life questionnaire that measures P (physical problems), C (cognitive problems), A (affective problems), S (social problems), E (economic), and E (ego problems). Each subtest is put on separate column. The sum of each column is multiplied by 5 to give a percentage score, in which 100% means the best quality of life.

Statistical Analysis:

The results were analyzed using the statistical package version number six. The descriptive statistics were expressed as mean and standard deviation. The analytic statistic used the student's t-test.

Results:

A total of 60 patients within the pediatric age group were included in this study with a diagnosis of ALL. The clinic-pathological pictures are shown in Table (1). Forty six ALL children showed low disease levels within seven to 14 days and needed less intensive treatment, they were divided according to phenotype distribution into; Pre –B, C-ALL and T-ALL. The mean age, total leukocytic count (TLC) and the presence of hepatosplenomegaly (HSM), were comparable among the three groups and are shown in Table (2).

Table 1: Clinico-pathological features of pediatric ALL patients.

Parameter	ALL-children (n=60)
Total leucocytic count (TLC) Mean $\pm$ sd	60.5+42.1
Anemia: N (%)	50/60 (83%)
Purpura: N (%)	43/60 (71%)
Lymph Node Enlargment +HSM: N (%)	33/60 (55%)
Arthritis	19/60 (32 %)
Prolonged fever	16/60 (27%)

HSM: Hepatosplenomegaly

Table 2: Phenotypic distribution and clinic-pathological features of pediatric ALL patients.

Parameter	Age (Years)	Total Leucucytic Count	HSM
Pre-B	7.4+4.4	50.2+ 25.1	3/18 (16.6%)
C-ALL	8.1+2.3	80.0+60.1	9/20 (45%)
T-ALL(n=8)	8.0+ 5.9	70.9+57.2	4/8 (50%)

HSM: Hepatosplenomegaly

Post traumatic stress symptoms were assessed in parents of acute lymphoblastic leukemia survivors and the controls. There was high significant elevation of the post traumatic stress symptoms in parents of cancer survivors than the controls.

Table 3: Comparison between the posttraumatic stress symptoms in parents of acute lymphoblastic leukemia survivors and the controls.

Scale	Parents	Controls	T	P-value
Flash back	18.59 ± 10.09	5.0 ±6.9	5.1	< 0.001**
Autonomic arousal	13.55 ± 9.75	6.0 ±5.4	2.9	< 0.01**
Avoidance	20.55 ± 9.0	6.0 ± 6.4	5.5	< 0.001**
Hypervigilance	6.0 ± 4.23	3.55 ± 3.0	2.5	< 0.01**
PTS	59.0 ± 29.00	21.0 ± 20.0	4.9	< 0.001**

** = highly significant

Comparison between posttraumatic stress symptoms and the different psychological parameters, showed that both the posttraumatic stress total score, with the flash backs, autonomic arousal, and hypervigilance; were significantly positively correlated with the GHQ, depressive symptoms and anxiety symptoms. The posttraumatic stress total score, autonomic arousal and hypervigilance, was significantly positively correlated with increased duration of the illness. The avoidance and the flash back sub items of the scale did not correlate with the duration of the illness. The avoidance subscale correlated positively with the depressive symptoms and negatively with the quality of life. However, the posttraumatic stress symptoms assessments with its components were significantly negatively correlated with the quality of life. This is described in (Table 4).

Table 4: Relation between posttraumatic stress symptoms with the duration of treatment and different psychological parameters.

Parameters	Duration (4+3)	Ghq (67.1+2)	Hamilton depression (19.2+13)	Hamilton anxiety (13±11)	Quality of life (9±8)
Flash back (18.59 ±10.09)	0.0	0.6*	0.68*	0.73*	-0.7*
Autonomic arousal (59.2 ±29)	0.67*	0.88*	0.0*	0.84*	-0.87*
Avoidance (6.5 ±4.23)	0.37	0.0	0.48*	0.36	-0.42*
Hypervigilance (20.55 ± 9.6)	0.0*	0.0*	0.68*	0.79*	-0.73*
PTS (13.55 ±9.75)	0.58*	0.0*	0.2*	0.79*	-0.82*

Critical value: 0.4; *; Significant

Comparison between mothers and fathers of acute lymphoblastic leukemia survivors, regarding the different psychological parameters showed that, mothers had significantly high scores of general health questionnaire, depressive symptoms, anxiety symptoms, posttraumatic stress symptoms. The mothers also showed significantly lower scores on the quality of life. This is further illustrated in (Table 5).

Table 5: Shows comparison between fathers and mothers of pediatric acute lymphoblastic leukemia survivors.

Scale	Subjects	Mean +sd	"T"
GHO	Mother	11.9 + 7.3	
	Father	1.0 + 1.2	5.8***
Hamilton depression	Mother	16.4 ± 11.0	
	Father	1.4 ± 1.9	5.3***
Hamilton anxiety	Mother	23.7± 12.5	
	Father	4.4 ± 3.4	5.65***
QOL	Mother	60.4 ± 19.2	
	Father	86 ± 8.2	4.46***
Posttraumatic stress assessment	Mother	71. 8 ± 22.5	
	Father	25.6 ± 16.1	5.02***

*** very high significant

Using linear regression analysis, correlation between the education and the profession of parents of acute lymphoblastic leukemia survivors and different psychological parameters. There was significant negative correlation between the profession and the education of the parents with the GHQ, Ham-a, Ham-d and the post traumatic stress assessment. However, there was significant positive correlation between QOL and education of the parents. This is described in (Table 6).

Table 6: Correlation between the education and the profession of the parents with different psychological parameters.

Education	"R"	Profession	"R"
GHO	-0.53*	GHO	-0.5
Ham-d	-0.47*	Ham-d	-0.46
Ham-a	-0.44*	Ham-a	-0.44
QOL	-0.46*	QOL	-0.44
PTS	-0.52*	PTS	-0.54

R= ± 0.42

The forty six parents of cured acute lymphoblastic leukemia completed the questionnaire. They were compared to twenty healthy parents. They were matching regarding age, sex and education level, as described in (Table 7).

Table 7: Comparison between parents of acute lympholastic leukemia survivors and the controls regarding demographic variables.

Variable	Parents	Controls	Statistical value	P-value
Mean age (years)	40.3 ± 7	36 ± 8	T=0.09	>0.05
Sex (%):				
Male	26	27		
Female	74	72	X^ 2=0.13	>0.05
Education (%):				
Illiterate	54	54		
Read and write	6.25	4		
Primary	6.2	9		
Secondary	6.2	4		
Graduated	28	27	X^ 2=0.2	>0.05

According the general health questionnaire, 56% of the parents of acute lympholastic leukemia survivors suffered from psychiatric morbidity. Only13% of the controls suffered from psychiatric morbidity. Using the linear regression analysis test, showed that the proportion of psychiatric morbidity is increased in high significant manner with Z=3, and P<0.001. The types of psychiatric morbidity in the parents of cancer survivors were further illustrated in (Table 8).

Table 8: Different psychiatric morbidity in parents of acute lymphoblastic leukemia survivors.

Diagnosis	NO	%
F33 Single Depressive Disorder	10	21
F34 Persistent mood disorder	2	4.3
F41 Other anxiety disorders		
F41.1 Generalized anxiety disorder	8	17
F43 Reaction to severe stress, and adjustment disorder		
F43.1 Posttraumatic stress disorder	2	4.3
F43.2 Adjustment disorder	2	4.3
F45 Somatization disorder	2	4.3

The GHQ, the Hamilton anxiety, and the post traumatic symptoms assessment scores were high significantly elevated in the parent of acute lymphoblastic leukemia survivors group in comparison to the controls. The Hamilton depression scores were significantly decreased in parents of acute lymphoblastic leukemia survivors. The quality of life was highly significantly decreased in parents of acute lymphoblastic leukemia survivors. The data is described in (Table 9).

Table 9: Comparison between parents of acute lymphoblastic leukemia survivors and the controls regarding psychological parameters.

Scale	Parents	Controls	T	P-value
GHQ	9 ± 8	4.2 ± 4	2.49	< 0.001*
Ham-a	19.2 ± 13	8.4 ± 8	3.18	< 0.001*
Ham-d	13 ± 1.1	7.4 ± 6	1.98	< 0.05*

* = significant; ** = high significance; GHQ: general health questionnaire; Ham-a: Hamilton anxiety scale; Ham-d: Hamilton depressive symptoms.

Different components of the quality of life that include: physical, cognitive, affective, social, ego function and financial were compared between the parents' of acute lympholastic leukemia survivors and the controls. Affective, financial and ego function subtests of the quality of life were significantly decreased in parents of cancer survivors than the controls.

The physical, cognitive and the affective components of the quality of life did not differ significantly between parents of acute lymphoblastic leukemia survivors and controls. Moreover the total score of the quality

of life questionnaire was significantly decreased in parents of acute lymphoblastic leukemia survivors than the controls. This is illustrated in (Table 10).

Table 10: Comparison between quality of life and its sub items in parents of acute lymphoblastic leukemia survivors and the controls.

Scale	Parents	Controls	T	P-value
Physical	66.5 ± 26	69.55 ± 18.89	0.45	> 0.05
Cognitive	81.7 ± 24	82.70 ± 12.00	0.17	> 0.05
Affective	57.8 ± 34.37	73.18 ± 18.80	1.87	< 0.05*
Social	78.0 ± 21.8	86.80 ± 14.60	1.55	> 0.05
Financial	58.2 ± 23.48	80.90 ± 16.88	3.73	< 0.001**
Ego function	60.4 ± 28.6	85.90 ± 10.98	3.97	< 0.001**
QOL	67.1 ± 2.0	79.08 ± 10.00	2.6	< 0.001**

* = significant; ** = highly significant; QOL= quality of life.

Discussion:

The first step in the research was to confirm that the 46 children were cured of from acute lymphoblastic leukemia and were in the remission stage by thorough clinical examination as well as confirmation by laboratory investigation including peripheral blood examination, bone marrow aspiration, C.S.F and chest x-ray. By clinical examination there was no pallor, no purpuric eruption no lymph node enlargement, no hepatosplenomegaly, no arthritis nor low grade fever. By peripheral blood examination blast cells < 2 and by bone marrow aspiration blast cells < 5 and C.S.F free of leukemic blast cells.

Table (1) shows the clinical presentation of cases at the beginning of consultation where 83% of cases presented with anemia, 71% with purpura, 55% with lymph node enlargment plus hepatosplenomegaly, 32% with arthritis and 27% with prolonged fever.

Impact of survival on parents was an important area of research. Though parents voiced relief at survival, they were anxious about relapse, together with concerns about meeting the long term psychological, medical, educational needs of the survivors. Effects of co-morbidity in this stage is potentially traumatic e.g. hepatitis and infertility (Stiller *et al*., 2007).

As a life time post traumatic stress disorder in 55% of the parents as evidenced by the post traumatic stress assessment scale (Table 3). The post traumatic stress assessment total score, and its sub-items flash back, autonomic arousal, hypervigilence and avoidance were highly significantly elevated in the parents of cancer survivors in comparison to the controls. There are many aspects of childhood cancer and its treatment that can be considered as trauma to the parents. The diagnosis itself is shocking and inevitably one of the most difficult stressor a family can face. Hospitalization of the child and watching the children of others with same diagnosis dying can remain as traumatic memories (Ozono *et al.*, 2007).

Coyne *et al.* (2007) found that 40% of the mothers and 35% of the fathers of pediatric cancer survivors suffered from severe level of posttraumatic symptoms. Childhood cancer survivors are at increased risk for medical difficulties, ongoing medical care is essential. Yet for the parent with posttraumatic symptoms, clinics and medical personnel can be a powerful reminder of the cancer experience. Moreover, parents usually play an important role in shaping child experience and overall family function. Therefore, long-term implications for children understanding the illness and overall adjustment, while parents experience posttraumatic symptoms are potentially harmful (Kazak, 2004).

These posttraumatic stress symptoms were significantly positively correlated with worsening the psychological outcome regarding both depression and anxiety. Also, it was significantly negatively correlated with the quality of life (Table 4). The avoidance subscale of the posttraumatic stress assessment scale was significantly positively correlated with depressive symptoms. This may resemble the model of learned helplessness, introduced by Soligman (1975).

Mothers of acute lymphoblastic leukemia survivors were at high risk of psychiatric co-morbidity than the fathers of the same group (Table 5). This finding was found across the GHQ, Hamilton anxiety, Hamilton depression, posttraumatic symptoms and quality of life (Table 4). Usually the mothers are more intimately related to their children. In addition they are more prone biologically for depression and anxiety in the face of life events (Kendler *et al.*, 1995).

Lower education level represents a risk factor for parental psychological maladjustment (Table 6). Parents with lower education level are more likely to have poor information about the disease. Dealing with the unknown is most frightening, Parents of high level of education can express their worries more readily to the clinician; this sort of ventilation may bring psychological comfort to the parents (Speechly and Noh, 1999). This may also point to the value of educational intervention about the disease to improve their psychiatric outcome.

In this present study around 56% of parents of the survivors had psychiatric comorbidity. This high psychiatric co-morbidity is evidenced by both diagnosis according to research diagnostic criteria (Table 7) and high scores on the general health questionnaire (Table 8). The most common psychiatric co-morbidity encountered in the parents of survivors was depressive disorder in about 25% of parents (Table 8) comparable to the finding of Hersov (1998) who reported nearly similar findings. Those parents are exposed to chronic stress. Their sibs have received 2-3 years. Some of the children encountered relapse during chemotherapy or immediately after discontinuation of treatment. This chronic stress can virtually play a role in the development of depression in such population (Compeland *et al*., 2007).

The high prevalence of depressive disorder is further supported by high depressive symptoms on the Hamilton depression scale (Table 9). Seventeen percent of the parents suffered from generalized anxiety disorder (Table 8) the parents were anxious about relapse, together with anticipated loss of bringing up a healthy child. Many of the children, although cured from cancer, yet they still suffered from late complication of treatment like infertility, osteoporosis, and liver affection (Pui *et al.*, 2003).

This is further more documented by presence of high anxiety symptoms in parents of cancer survivors as evidenced by Hamilton anxiety scale (Table 9). Current posttraumatic stress disorder was found in 4.6% of the sample (Table 8).

The results generally support the hypothesis that diagnosis and treatment for childhood cancer may have significant long term effects which are manifest in symptoms of post traumatic stress for parents of childhood cancer survivors.

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