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Effect of the Cancer Pain on the Neurocognitive Function in Children undergoing chemotherapy

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Abstract:
Background: Pediatric cancer and its treatment may influence physical, psycho social and neurocognitive functions of childhood cancer survivors (CCS). The present study **aimed** to identify cancer pain and its effect on the functional ability and neurocognitive function among children receiving chemotherapy **Adescriptivedesign** was used to conduct this study.The study was conducted on 60 children receiving chemotherapy at Pediatric oncology departement at Zagazig University children Hospital. **Fourtools** were used in the study: The first tool : Structured interview sheet. The second tool :Mcgill pain scale. The third tool: FACT-Cog scale. The **results** that most of the studied children had negative impact on quality of life. It was found that there was highly statistically significant ($p<0.01$) relation between total pain score, total physical function score and total score of neuro-cognitive function of studied children. Therefore it was **concluded** that children suffering from cancer pain and receiving chemotherapy had negativeimpact on functional ability & neurocognitive function due to cancer treatment and chemotherapy side effects. It was **recommended** that developing educational program to family members about early interventions to improve cancer treatment and decrease negative side effects of functional disability& neurocognitive impairment is mandatory.

Keywords: cancer, chemotherapy, functional ability, neurocognitive function

Introduction:

GlobalBurdenofDisease (**2017**) revealed that childhood cancer is a main cause of global disease burden, particularly in resource-limited settings. It is becoming a public health problem in low- and middle-income countries (LMICs), due to the large numbers of children with cancer (84% of global estimates), high mortality rates and limited resources. Although 5-year survival now exceed 80% in high-income countries (HICs), these improvements poorly translate to LMICs.

Pediatric pain can be divided into three major categories, i.e.:somatic, visceral and neuropathic. Somatic pain is caused by tissue injury or inflammation. When involving skin and superficial structures, somatic pain is sharp and well-localized. Visceral pain is caused by inflammation or injury of internal organs (viscera), usually poorly localized or referred to

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distant locations. Finally, neuropathic pain is caused by injury, inflammation, or dysfunction of the peripheral or central nervous systems(**Zeltzeret al**., **2015**)

As childhood cancer survival rates continue to improve, there is a growing need to reduce treatment-related complications , including social, academic, and physical functioning. A prevalent and serious long-term consequence of childhood cancer treatment is impaired physical function with limited ability to perform daily tasks, impaired self-perception , and reduced capacity to fully participate in social activities, including school. These disabilities are associated with poor health (**Wilsonetal** ., **2018**).

Phillipsetal.,(**2021**) stated that neurocognitive impairment in survivors of pediatric cancer is often preceded by physiologic events or changes in biomarkers that may help us to understand underlying mechanisms. Children exposed to cranial irradiation and/or intrathecal chemotherapy are at elevated risk for leukoencephalopathy or seizures that often emerge during or shortly after therapy. Typically, leukoencephalopathy will persist into long-term follow-up and seizures may be recurrent, both associated with impaired neurocognitive outcomes. Serious infections during therapy are also associated with neurocognitive impairment in long-term survivors.

Chemotherapy aggravates the cognitive-educational outcomes of children. So, the neurocognitive impairments in childhood Acute lymphoblastic leukemia (ALL) survivors following treatment was significantly affected. chemotherapy- and/or radiotherapy-induced neuroimaging changes underlying cognitive function of children are explored, adolescents and young adults whose intelligence was measured with different scales dependent on participants' ages(**Zhouetal**., **2020**).

Howlader,(**2016**) stated that treatment for childhood cancer has advanced such that more than 80% of newly diagnosed children are expected to become long-term survivors. Improved survival has led to the recognition of many potential late effects of therapy, including impaired neurocognitive function, mental health, and health-related quality of life (HRQOL).

Significance of the study:

Studies reveal that upward of 50% of pediatric cancer out patients reported under treated pain. Studies have documented numerous adverse outcomes of unmanaged pain in children with cancer include: declines in quality of life, difficulty in, increase pain sensitivity, as well as procedural distress, restriction of social activities and development of emotional and behavioral problems.

Cancer-related cognitive changes and impairment also have been documented in children with non-central nervous system cancer prior to exposure to treatment interventions. Several studies have identified cognitive impairment in newly diagnosed children with cancer across several cognitive domains, including verbal memory, learning, language, visual spatial skills, executive and psychomotor functions.

Aim of the study

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The study aimed to identify cancer pain and its effect on the functional ability and neurocognitive function in children treated at the Zagazig University Hospital.

Research Question:

1- What is the effect of cancer pain on the functional ability among children with cancer?

2-What is the effect of cancer pain on the neurocognitive function among children with cancer?

Researchdesign: A descriptive design was used to conduct this study.

Setting: The current study was conducted at Pediatric oncology departement at ZagazigUniversity Hospitals.

Subjects: The subjects of this study were conducted on sample of 60 children (school and adolescent stages), with cancer pain at Pediatric oncology departement at Zagazig University Hospitals..

Tools of data collection:

Three tools were used to collect the necessary data.

ToolI: **Structuredinterviewquestionnaire** was developed by the investigator which was used to collect data about children such as:

A- Personal characteristics of studied children as age, sex, birth, order……etc

B-Personal characteristics of parents as age, educational level and occupation.

Medical history of the disease as past and present complain and onset of the disease……etc

Tool II: Mcgill pain scale

A- Mcgill pain scale was developed by **Melzack**(**2005**). This scale allows individuals to give a good description of the quality and intensity of pain that they are experiencing. It includes 20 items. The MCgill scale indicates overall pain intensity and includes 4 levels: none (0), mild (1), moderate(2) and(3) severe(Fischer, 2010).

ToolII : FACT-Cog scale

FACT-Cog scalewas adopted by DavidCella(2016). It was used to assess neurocognitive function. This scale consists of 37 items and includes the following:

-perceived Impairments(20 items).

-Impact On Quality Of Life(4 items)

-Comments From Others(4 items)

-Perceived Cognitive Abilities (9 items)

The items were answered by 0= Never, 1= sometimes, 2= always. The total score which was interpreted as good was less than 50%,fair was more than than 50% - 75% and bad was more than 75%.

Administrative Design and Ethical Consideration:

An official permission for data collection in Zagazig University Hospitals was obtained from the hospital administrative personnel by the submission of a formal letter from the Dean of the faculty of Nursing Zagazig Universityto the responsible authorities of Pediatric Oncology Departement at Zagazig University Hospital to obtain their permission for data collection.

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explaining the aim of the study in order to obtain permission and help. At the interview, each subject was informed about the purpose, benefits of the study, and Children were informed that their participation is voluntary and they have right to withdraw from the study at any time without given any reason. In addition, confidentiality, and anonymity of the subjects were assured through coding of all data. The researcher assured that the data collected will be confidential and would be used only to improve their knowledge and practice for the purpose of the study.

Ethical considerations:

All ethical issues were taken into consideration during all phases of the study:

- The research approval was obtained from ethical committee before starting study.
- The researcher maintained an anonymity and confidentiality of the subject.
-The inclusion of subjects in the study was totally voluntary.
- The aim of this study was explained to every child before participation and oral consent was obtained from parent.
-Children were notified that they can withdraw at any stage of the research; also they were assured that the information obtained during the study will be confidential and used for the research purpose only.

C. Pilot study:

It was carried on 10%of the children of cancer pain to test clarity and applicability of the tools. It was included in the total sample since no modifications were done in the tools.

D. Field work:

Data were collected within a period of six months from the beginning of february2020 to end of August 2020. The data were collected at three days per week (Sunday, Tuesday and Thursday) from 9:00 am to 1:00 pm. Each child was interviewed individually, the researcher started with introducing herself and explaining the aim of the study for the selected child and obtaining their oral consent assured that date collected was confidential and would be used only to achieve the purpose of the study. The questionnaires were read, explained and the choices were recorded by the researcher. The time consumed to answer each sheet ranged from 20–30 minutes.

Statistical Design:

Data entry and statistical analysis were done by the SPSS version 23. Data were presented by frequency tables with percentages for qualitative variables and means and standard deviations for quantitative variables. The chi-square test was used to find the significant association between the demographic and clinical data and the outcome measures. Multiple linear regressions (step-wise) were also used to characterize the relationship between children's demographic and clinical details with the outcome measures. Cronbach alpha coefficient was calculated to assess the reliability of the scales through their internal consistency.

Results:

Personal characteristics of the studied children were found that 35% of children's ages were

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from 8 to 11 years, 40% were from 11 to 14 years with mean age of 12.4±2.6 years. Also, 56.7% were male compared to 43.3 % were female. Those who ranked the first birth order constituted 20%, the second 38.3% and the third 31.7%. It is revealed from the same table that 71.7% were from rural area compared to 28.3% were from urban in table(1).

Medical history of the studied children was revealed that the disease onset was sudden in 68.3% of the studied children, while 31.7% were gradual,also regarding disease duration, 95% ranged from 1 to less than 5 years. Only 21.7% had others diseases such as infection (61.5%), allergy (23.1%) and immune deficiency (15.4%). It was also found that only 28.3% was hospitalized.Table(2)

Total pain score of the studied children was found that 63.3% and 26.7% had mild and moderate pain scores respectively compared to 10% had no pain in table(4)

Regarding total scores of neuro cognitive function and its domains among the studied children. It was revealed that 93.3% of children had good score regarding total score of neuro-cognitive function compared to 6.7% had fair score. About perceived impairments and comments from others, 96.7% and 100% of children had good scores respectively. However, 63.3% of children had poor score as regard to impact on quality of life.Table(5)

Relation between personal characteristics of the studied children and total pain score was showed in table (13). It was revealed that there was statistically significant ($p<0.05$) relation between birth order, crowding index, family income and total pain score.Table(6)

Relation between medical history of the studied children and total score of neuro-cognitive function is illustrated. It was found that there was no statistically significant relation between medical history of the studied children and total score of neuro-cognitive function.Table(7)

It was clarified the relation between total pain score, total physical function score and total score of neuro-cognitive function of studied children. It was found that there was statistically significant ($p<0.01$) relation between total pain score, total physical function score and total score of neuro-cognitive function of studied children. Where, higher percentage of children with good score of neuro-cognitive function had mild pain and good physical function score.

Discussion:

The present study revealed that 35% of children's ages were from 8 to 11 years, 40% were from 11 to 14 years with mean age of 12.4±2.6 years. Also, 56.7% were male compared to 43.3 % were female. Reasons for sex differences are not fully understood but probably largely reflect differences in exposure to environmental risk factors and endogenous hormones, as well as complex interactions between these influences and also due to incidence rate(Klein , 2016). This result was in agreement with the **Stinsonetal** .,(**2013**) about The Construct validity and reliability of a real-time multidimensional smartphone app to assess pain in children and adolescents with cancer in Canada which revealed that the mean age of the 92 participants in

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the study was 13.1 years (SD = 2.9; range: 8-18 years), and the sample was even in terms of sex distribution (female: 48.9%; male: 51.1%).

Concerning medical history, The present study revealed that nearly children and adolescent with cancer had family history. Family history did not predict the presence of an underlying predisposition syndrome in most Knowledge. As their presence may influence clinical management by directing the antineoplastic protocols used during the treatment. Enabling presymptomatic genetic testing of relatives, Guiding family-planning measures and Facilitating measures for cancer prevention and surveillance.**Knapkeetal**, (**2012**) agreed in a study about Germline Mutations in Predisposition Genes in Pediatric Cancer with the present study in which germline mutations in cancer-predisposing genes were identified in 8.5% of the children and adolescents with cancer who participated in this study.

Regarding Distribution of pain among children,The present result stated that 46.7% of children were undergoing chemotherapy protocol more than 3times per month as the outcome is better when applied in high doses and smaller intervals to prevent recurrence. With that 47.8% of participants were in the weekly chemotherapy protocol, that is with short intervals between sessions in order to reduce the risk of worsening.This result was in the same line with **Raphael** (**2016**), stated in study about " Pain evaluation in patients under chemotherapy " were in the weekly chemotherapy protocol The antineoplastic protocols used during the treatment have varied purposes, such as cure and supportive care.

According Total pain score of the studied children.**AL-Qaaydehetal**.,(**2018**) mentioned in study about "Symptoms in Children Receiving Treatment for Cancer—Part II: Pain, Sadness, and Symptom Clusters" that The prevalence of pain varied from 28% to 62% across studies and pain tended to be of moderate or greater severity and moderate or greater distress when it was reported. This result was in the same side with the present study. It was found that total pain score of the studied children was 63.3% and 26.7% had mild and moderate pain scores respectively. As all mild pains were medicated with stronger analgesia than necessary to control pain and moderate pain was the one following the most WHO recommendations.**Madietal**., (**2018**) stated in the last - mentioned study that the most frequent locations of severe pain were the abdomen, lower back, forehead, and upper chest. Approximately half of children who reported severe pain often described the pain they experienced during breakthrough episodes "sharp" or "shooting". This result was in the same side with the present study. About 51.7% 0f children had sharp pain this may be due to excess administer of analegesics.

The present result showed distribution of perceived impairments of neuro cognitive function and revealed that 95% of the studied children had good score in relation to forming thoughts, concentrating, finding way to a familiar place, remembering place of things like keys and remembering new information like phone numbers. Regarding recalling the name of an object while talking to someone, finding the right word(s) to express himself, remembering

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names of people soon after being introduced and keeping track of what he is doing, 96.7% of studied children had good scores. As most of children had short –time hospital stay and newly-diagnosed with cancer and less chemotherapy side effects existed. This result was in the opposite line with (**Rencken**, **2011**) in study about Occupational Performance in Children Aged 6 to 13 Years with Cancer at Iran university in which the central nervous system (CNS) of children with cancer is affected by the disease and its complications and causes learning deficits, attention-deficit/hyperactivity disorder, and occupational as well as educational deficits. Neurological deficits of children with cancer include learning deficits, poor attention and memory and executive function deficit. Such children usually have problems in academic performance, concentration, self-regulation, compliance with the environment, and learning abilities.

The present study revealed that 53.3%, 70%, 73.3% and 60% had fair scores in relation to ability to concentrate, bring to mind words while talking to someone, remember things, like keys or wallet and remember to do things respectively. Additionally, 55%, 50% and 55% had good scores regarding ability to pay attention, having a sharp mind and ability to keep track of what doing, even if being interrupted respectively. Due to cancer complications, side effects of its treatment, and hospital stay may cause cognitive, emotional, and physical changes, which affect the welfare of children with cancer. This result was in the same line with the study about Cognitive Impairment in Survivors of Pediatric Acute Lymphoblastic Leukemia Treated With Chemotherapy Only which revealed that relevant neurocognitive studies published in the past two decades in survivors of ALL treated with chemotherapy-only regimens have consistently highlighted difficulties in areas of attention, fine motor skill, processing speed, mathematics, and executive functions (**Lofstadetal**.,**2019**).

Distribution of impact on quality of life of neuro cognitive function **Amidietal**.,(**2017**) stated that cognitive difficulties have a negative impact on QoL (autonomy, return to work, social relationships, and self-confidence) in the context of long-term cancer care, there is a growing demand from patients for Cancer – Related Cognitive Impairment (CRCI) management. This has led to studies implementing cognitive rehabilitation in cancer patients. This result was in the same line with the present result which revealed that 46.7% and 56.7% had poor scores regarding being upset about these problems and his ability to work is interfered by these problems respectively. Furthermore, 51.7% of studied children had poor score in relation to his ability to do things he enjoys is interfered by these problems.

The present study illustrates total scores of neuro cognitive function and its domains among the studied children. It was revealed that 93.3% of children had good score regarding total score of neuro-cognitive function compared to 6.7% had fair score. The study results are in agreement with **Pengetal**., (**2020**) in study about Neurocognitive and Behavioral Outcomes of Chinese Survivors of Childhood Lymphoblastic Leukemia in which ALL survivors were shown to exhibit deficits in neurocognitive domains . A minority of survivors

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(4.0% to 36.2%) demonstrated moderate impairment on performance-based cognitive assessments across the domains of attention, executive function, motor processing speed and memory.

Relation between characteristics of the studied children and total pain score was showed in the present study. It was revealed that there was statistically significant ($p<0.05$) relation between birth order, crowding index, family income and total pain score. As low income of the family possibly have led to lack of awareness, reluctance to seek medical advice, and to attend to hospital on time, that not only would contribute to advanced disease stages at diagnosis but also to poor compliance to treatment and abandonment that would lead to treatment failure & more disease-related pain. This result was in agreement with **Mohamed**(**2016**) in which there was statistically significant ($p<0.05$) relation between family income and total pain score.

Also, **Recklitisetal** .,(**2019**) mentioned in study about Pain in long-term survivors of childhood cancer: A systematic review of the current state of knowledge and a call to action from the Children's Oncology Group that biologic factors explored in relation to pain included age and sex. Data supporting age at the time of study were inconsistent: study indicated that pain was negatively associated with age, and other studies indicated that pain was positively associated with age. There was conflicting evidence that age at diagnosis was related to pain, with 3 studies indicating that younger age was significantly related to increased reports of pain, and 1 study demonstrating no association between age at diagnosis and pain.

Relation between personal history of the studied children and total score of neuro-cognitive function **Schuitemaetal** .,(**2015**) mentioned in study about Neurocognitive Outcomes and Interventions in Long-Term Survivors of Childhood Cancer that Acute lymphoblastic leukemia (ALL) was historically treated with CNS prophylaxis, resulting in neurocognitive impairment, although impact can be exacerbated by younger age at diagnosis, female sex, and longer time since diagnosis. Elevated rates of severe impairment are reported in intelligence, attention, memory, processing speed, and executive function after chemotherapy-only treatment.This result was not in the same line with the present result in which there is no significant ($p>0.05$) relation between personal characteristics of the studied children and total score of neuro-cognitive function as neuro-cognitive impairment may occur at any age and with any sex and with different pattern.

Patelet al.,(**2017**) stated in study Factors Associated with Overall Pain Intensity that while prospectively assessing cognitive functioning in patients with acute lymphoblastic leukemia (ALL) using computerized battery compared to same age peers along with the baseline cerebral spinal fluid (CSF) markers being within expected normal ranges.This result was in the same line with the present result in which there is no significant ($p>0.05$) relation between personal characteristics of the studied children and total score of neuro-cognitive function.

Relation between medical history and total score of neuro-cognitive function indicate

Espyetal.,(**2001**) mentioned in study about A narrative review of risk factors and interventions for cancer-related cognitive impairment at china that 25% and 33% of children have cognitive

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impairment due to the chemotherapy. Boys shows better performance than girls in the aspect of cognitive function , and children who have the chemotherapy at younger ages have the worse performance. As the higher dose of chemotherapy, the severer cognitive deficits when the child grow up. In contrast, It was found that there was no statistically significant relation between medical history of the studied children and total score of neuro-cognitive function. As health problems contribute to neurocognitive impairment in survivors occur with or without exposure to neurotoxic therapies. We conclude this review with a discussion of literature supporting specific interventions that may be beneficial in the treatment of survivors who already experience neurocognitive impairment, as well as in the prevention of impairment manifestation.

Relation between total pain score, total physical function score and total score of neuro-cognitive function of studied children

The present result found that there was statistically highly significant ($p<0.01$) relation between total pain score, total physical function score and total score of neuro-cognitive function of studied children. Where, higher percentage of children with good score of neuro-cognitive function had mild pain and good physical function score.

Gauntlett et **al**., (**2007**), showed in study about Pain and its Impact on the Functional Ability in Children Treated at the Children's Cancer Center of Lebanon(Functional Disability Inventory) FDI scores correlated significantly with procedure-related pain,cancer-related pain, and pain duration. Similar findings have been re-ported in previous studies . Greater pain intensity is re-lated to poor functioning. A moderate significant correla-tion was found between FDI and duration of pain children at theCCCL; the longer the duration of participants' pain, the higher the levelof functional disability.

WorldHealthOrganization (WHO) (**2001**) revealed in study about Childhood Cancer and Functional Impacts Across the Care Continuum in Washington that the effects of cancer and its treatment manifest as impairments in body structures and functions (including psychological functions), with resulting activity limitations and restrictions on participation.

Notably, the impact of childhood cancer is not limited to physical or cognitive functions but also includes psychosocial and emotional functions. Moreover, these areas of function interact such that impairments in one area (e.g., physical) may precipitate or exacerbate impairments in one or more of the others (cognitive, psychosocial, and/or emotional).

Panwalaetal., (**2019**) stated in study about "Treatment and Long-Term Sequelae in Childhood Brain Tumors" that Some studies have hypothesized that females are at higher risk for cognitive deficits than males and reported that female survivors were more affected when compared to males in terms of the living skills, domain of adaptive functioning as well as of processing speed. Those deficits can negatively impact on daily living skills.

CONCLUSION

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In the light of the present study, it was concluded that more than half of children with cancer had pain that negatively impact on functional ability & neurocognitive function due to cancer itself and chemotherapy side effects. In addition, there is a statistical significant relationship between pain of the studied children, functional ability and neurocognitive function. Cognitive impairment can affect daily functioning, quality of life.

Recommandation

In the light of the findings of the present study , the following recommendations are suggested

1-Presence of psychologist and social worker in oncology unit is mandatory to encourage children to express their own feelings and concerns about the effects of chemotherapy on their physical appearance.

2- Presence of cognitive rehabilitation, occupational therapy, instruction in coping strategies, behavioral modification and mindfulness practices is mandatory to manage distress, pain, sleep disturbances ,fatigue and self-reported quality of life.

3- Presence of physical therapists helps children with cancer to participate in daily activities , exercise assisting children with cancer to reconstruct new life style.

4- Educational program should be developed to family members about cancer , chemotherapy and possible side effects.

5- Identifying neurocognitive impairments and react with early interventions to improve cancer treatment and decrease negative side effects eg functional disability& neurocognitive impairment.

6- Develop a training program to children with cancer to help them to cope with body image changes to improve their self- esteem.

7- Guidance of children undergoing chemotherapy about cancer, chemotherapy, it's major side effects, proper nutrition and body image.

Future research

- Developing longitudinal studies to evaluate children at all stages of chemotherapy (by the beginning, the middle, and by the end of chemotherapy).
- Future research should focus on evaluating the measurement properties of methods in pediatric cancer populations and children with other chronic diseases.
-To expand existing knowledge about leukemia patients to other diagnoses, cancer types like neuroblastoma, retinoblastoma, renal tumors, or soft tissue sarcoma should be tested for physical performance limitations to evaluate their special needs.
-The inclusion of exercise programs also promotes their skills and abilities &enhances their self –esteem.
- Concerning social support &psychosocial guidance could be developed in the future to reduce psychological stress and improve sef –confidence of children and adolescents withcancer

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Table (1): Personal Characteristics of The studied Children (n=60).

Characteristics	N	(%)
Age (year)		
8-11	21	35.0
11-14	24	40.0
14-18	15	25.0
Mean ± SD 12.4±2.6		
Gender		
Male	34	56.7
Female	26	43.3
Residence		
Rural	43	71.7
Urban	17	28.3
Birth order		
The first	12	20.0
The second	23	38.3
The third	19	31.7
More	6	10.0
Educational level		
Primary	27	45.0
Preparatory	18	30.0
Secondary	15	25.0

Table (2): The medical history of the studied children (n=60):

Medical history	No.	(%)
Disease onset		
Sudden	41	68.3
Gradual	19	31.7
Disease duration		
1- years	57	95.0
5-10 years	3	5.0
Presence of other diseases		
No	47	78.3
Yes	13	21.7
If yes what (n=13)		
Infection	8	61.5
Allergy	3	23.1
immune deficiency	2	15.4
Family history		

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No	57	95.0
Yes	3	5.0
If yes who (n=3)		
1st degree	2	66.7
2nd degree	1	33.3
Hospitalization		
No	43	71.7
Yes	17	28.3
If yes how many times (n=17)		
3- times	14	82.4
5-10 times	3	17.6
Causes of hospitalization*		
Fever	11	18.3
Anorexia	4	6.7
Weight change	6	10.0
Other causes(**anemia,allergy,infection,and immune deficiency**	4	6.7
No. of chemotherapy sessions per month		
<2	20	33.3
2-3	12	20.0
>3	28	46.7

*: multiple choice

**: other causes (acute anemia, allergy, infection and immune deficiency).

Table (3): Total Pain Score of The Studied Children (n=60).

Items	No pain		Mild pain		Moderate pain	
	No.	%	No.	%	No.	%
Total pain score	6	10.0	38	63.3	16	26.7

Table (4): Total scores of Neuro Cognitive Function and Its Domains among the Studied Children (n=60).

Items	Good		Fair		Poor		Mean ±SD
	No.	%	No.	%	No.	%	
Total score of neuro-cognitive function	56	93.3	4	6.7	0	0.0	0.43±0.14
Perceived impairments	58	96.7	2	3.3	0	0.0	0.12±0.193

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Comments from others	60	100.0	0	0.0	0	0.0	0.02±0.1
Perceived cognitive abilities	17	28.3	32	53.3	11	18.3	0.89±0.47
Impact on quality of life	10	16.7	12	20.0	38	63.3	1.34±0.59

Table (5): Relation between personal characteristics of the studied children and the total pain score.

Personal characteristics		**Total pain score**						χ^2	**P-value**
		No pain (n=6)		**Mild pain (n=38)**		**Moderate pain (n=16)**			
		No.	**%**	**No.**	**%**	**No.**	**%**		
1-Child age in years	8-11	1	16.7	16	42.1	4	25.0	4.171	0.383 NS
	11-14	4	66.7	14	36.8	6	37.5		
	14-18	1	16.7	8	21.1	6	37.5		
2- Sex	Male	3	50.0	22	57.9	9	56.2	0.133	0.936 NS
	Female	3	50.0	16	42.1	7	43.8		
3- Birth order	The first	0	0.0	9	23.7	3	18.8	13.975	0.030*
	The second	1	16.7	15	39.5	7	43.8		
	The Third	2	33.3	11	28.9	6	37.5		
	More	3	50.0	3	7.9	0	0.0		
4-Residence	Rural	5	83.3	26	68.4	12	75.0	0.687	0.709 NS
	Urban	1	16.7	12	31.6	4	25.0		
5- Educational Level	Primary	1	16.7	19	50.0	7	43.8	8.715	0.069 NS
	Preparatory	4	66.7	12	31.6	2	12.5		
	Secondary	1	16.7	7	18.4	7	43.8		
6- Crowding index	≤2	2	33.3	32	84.2	12	75.0	7.532	0.023*
	>2	4	66.7	6	15.8	4	25.0		
7-Family income	Sufficient and save	1	16.7	0	0.0	0	0.0	11.627	0.02*
	sufficient	2	33.3	5	13.2	4	25.0		
	Insufficient	3	50.0	33	86.8	12	75.0		

NS: Non significant (p>0.05)
*: statistically significant (p<0.05)

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Table (6): Relation between medical history of the studied children and the total score of neuro-cognitive function.

Medical history		Total score of neuro-cognitive function				χ^2	P-value
		Good (n=56)		Fair (n=4)			
		No.	%	No.	%		
Disease duration	1- years	54	96.4	3	75.0	3.609	0.057 NS
	5-10 years	2	3.6	1	25.0		
Presence of other diseases	No	44	78.6	3	75.0	0.028	0.867 NS
	Yes	12	21.4	1	25.0		
Hospitalization	No	41	73.2	2	50.0	0.991	0.320 NS
	Yes	15	26.8	2	50.0		
No. of chemotherapy sessions per month	<2	19	33.9	1	25.0	0.153	0.926 NS
	2-3	11	19.6	1	25.0		
	>3	26	46.4	2	50.0		

NS: Non significant (p>0.05)

Table (7): Relation between total pain score, total physical function score and the total score of neuro-cognitive function of studied children (n=60).

Item		Total score of neuro-cognitive function				χ^2	P-value
		Good (n= 56)		Fair (n=4)			
		No.	%	No.	%		
Total pain score	**No pain**	6	10.7	0	0.0	11.786	**0**.003**
	Mild pain	38	67.9	0	0.0		
	Moderate pain	12	21.4	4	100.0		
Total physical function score	**Good**	35	62.5	0	0.0	12.86	**0**.002**
	Fair	11	19.6	4	100.0		
	Bad	10	17.9	0	0.0		

**: statistically highly significant (p<0.01)

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