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Assessment of Neurocognitive Functions in Children Treated for Cancer

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ABSTRACT

Background: About eight percent of adults and children who receive a cancer diagnosis today are projected to live at least 5 years thanks to advancements in pediatric cancer therapy over the last several decades. More than half a million people will have survived childhood cancer by 2020, according to current estimates.

Objective: To evaluate the association between childhood cancer, antineoplastic treatment and neurocognitive dysfunction.

Patients and Methods: In the Pediatrics Department of the Faculty of Medicine at Zagazig University, a case control study was undertaken on 25 cancer patients who had completed their treatment and on 25 healthy children between August 2020 and July 2021. Children of both sexes, aged 5-15, were enrolled in the study.

Results: In terms of full and performance intelligence quotient (IQ) scale, there was statistically significant difference between the groups (much higher in the control group), but the verbal scale did not differ statistically between the groups. Regarding verbal IQ, there was no statistically significant difference between the groups examined. However, there were no significant differences in IQ subtests for information, vocabulary, arithmetic, comprehension, picture completion, mazes or block design between groups. Control group was significantly higher as regard similarity and geometric design.

Conclusions: Neurocognitive function is affected in cancer survivors of children as there is statistically significant difference between the studied groups regarding full, and performance IQ scale (significantly higher in control group) but verbal scale was not statistically different between the groups.

Keywords: Cancer, Neurocognitive functions, Survivors,

INTRODUCTION

There are many different types of childhood cancer, and each one has its own etiology, treatment, prognosis, and treatment options. There is also a risk of long-term hazardous side effects from chemotherapy, radiation, and other treatments. In the last 50 years, significant progress has been made in diagnostics, pharmacology, therapy combinations, and methods for children cancer, resulting in increased survival and decreased mortality rates for this disease. The five-year survival rate for children with cancer has increased from 30% in the 1960s to over 80% in most high-income nations. It's important to note, however, that these advancements do not benefit all children equally, and the prognosis varies depending on the type of cancer, age at which it first manifests itself clinically, anatomical site, and stage of the disease (in solid tumours). Furthermore, survival rates differ significantly based on geographic region and even within regions. The percentage of pediatric cancer patients who survive into adulthood is rising. Increased attention and worries regarding cancer treatment exposures at a young age resulting in late effects have accompanied this rising population, which has prompted a surge in interest in survivorship research. Surviving children's cancer puts survivors at risk for a wide range of physical and mental health issues, including depression, anxiety, suicidality, and suicidal ideation, as well as other social and economic effects [(1)].

Neurocognitive impairments are common among childhood cancer survivors. It's possible that cancer and/or therapy led to these problems. Children with cancer who have received neurotoxic therapies such neurosurgery, cranial radiation therapy (CRT), high dosage methotrexate, intrathecal chemotherapy, and corticosteroids have been shown to have significant declines in their cognitive abilities [(2)].

Childhood cancer survivors' brain development may be influenced by a variety of sociodemographic, environmental, and biological factors. They can have a major impact on survivors' eventual functional outcomes, such as schooling, work, income, and marital status because of these neurocognitive difficulties [(3)].

We aimed at this study to evaluate the association between childhood cancer, antineoplastic treatment and neurocognitive dysfunction.

PATIENTS AND METHODS

In the Pediatrics Department of the Faculty of Medicine at Zagazig University, a case control study was undertaken on 25 cancer patients who had completed their treatment and on 25 healthy children between August 2020 and July 2021. Children of both sexes, aged 5-15, were enrolled in the study. The research examined individuals with all types of cancer, including children cancers, who had gone into remission after treatment.

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Patients were divided randomly into two groups:
Group A: 25 diagnosed with cancer who completed their treatment.
Group B: 25 normal healthy children.

Ethical considerations:
All participants' parents or relatives signed informed permission forms, and the study was given the green light by the Zagazig University Faculty of Medicine's Research Ethical Committee. The study was conducted in conformity with the World Medical Association's Code of Ethics for Human Research (Declaration of Helsinki).

Inclusion criteria:
All types of pediatric cancer are included in this study, as childhood cancer patients who had complete remissions following therapy and regularly attended outpatient clinics. Age: between (5-15) years old, both genders (male and female).

Exclusion criteria:
Prior neurodevelopmental or genetic disorders associated with cognitive impairment (e.g. Down syndrome) were present in patients, as were pediatric cancer patients who had relapsed, as well as those who later suffered a non-cancer related brain damage.
All patients underwent a thorough medical history examination (stressed on protocols of the chemotherapy, history of radiotherapy or surgery and the duration of the treatment), clinical and neurological examination, with qualified examiners and under the supervision of a board-certified clinical neuropsychologist, all participants performed neurocognitive testing. In order to minimize interference and tiredness, testing procedures adhered to ED's standard clinical guidelines, which include a predetermined test order and timelines that are tightly managed. The following was used to gauge the study's main outcome: a professional neuropsychologist oversees all neurocognitive testing conducted by certified examiners. Standard clinical guidelines were followed for the testing procedures, with a set test order and regulated timetables to reduce interference and tiredness effects on the subjects. Wechsler Intelligence Scale was used to measure the primary outcome of interest in the study, Tests of intelligence (IQ) [(4)], processing speed [(4, 5)], attention[(6)], memory[(5)] and fine motor dexterity[(7)] have also been completed.

Statistical analysis
We used Statistical Package for the Social Sciences version 24 to analyse the data (SPSS). Tables and graphs were used to display the data. We used mean, standard deviation (SD), range and median to convey continuous quantitative variables, as well as absolute frequencies (number) and relative frequencies (percentage) to express categorical qualitative variables. P value < 0.05 was considered significant.

RESULTS
Table 1 shows that there was statistically significant difference between the studied groups regarding age (higher in case group). There was statistically non-significant difference between the studied groups regarding gender, residence or number of sibling.

Table (1): Comparison of demographic data between the two groups

Parameter	**Case group** N=25 (%)	**Control group** N=25 (%)	**p**
Age (year):			
Mean ± SD	11.6 ± 2.5	9.68 ± 3.11	0.02*
Min – max	6 – 15	6 – 15	
Gender:			
Male	14 (56)	13 (52)	0.777
Female	11 (44)	12 (48)	
Residence:			
Rural	14 (56)	9 (36)	0.156
Urban	11 (44)	16 (64)	
Number of sibling:			
Median	2	2	0.084
Absent	2 (8)	6 (24)	0.247
Present	23 (92)	19 (76)	

*: Statistically significant

Table 2 shows that there was statistically significant difference between the studied groups regarding full, and performance IQ scale (significantly higher in control group).

Table (2): Comparison of full-scale, verbal, and performance IQ between the groups

IQ	Case group (N=25)	Control group (N=25)	p
	Mean ± SD	Mean ± SD	
Full scale	90.36 ± 7.89	98.4 ± 2.55	<0.001**
Verbal	100.24 ± 5.29	102.52 ± 4.74	0.115
Performance	89.32 ± 5.14	95.2 ± 5.45	<0.001**

**: Statistically highly significant

Table 3 shows that in terms of similarities and geometric design, there was a statistically significant difference between groups (significantly higher in the control group). However, in terms of information, vocabulary, arithmetic, comprehension, object assembly, picture completion and mazes or block design, there was a statistically non-significant difference between groups.

Table (3): Comparison of the groups under investigation with respect to the IQ subtest

Parameter	Case group (N=25)	Control group (N=25)	p
	Mean ± SD	Mean ± SD	
Information	11.76 ± 2.47	12.2 ± 2.33	0.544
Vocabulary	11.96 ± 2.99	11.8 ± 2.2	0.83
Arithmetic	8.44 ± 1.89	9.12 ± 2.28	0.257
Similarities	8.0 ± 1.76	9.52 ± 1.58	0.002*
Comprehension	10.28 ± 1.37	10.32 ± 1.65	0.926
Object assembly	10.68 ± 1.95	10.16 ± 1.75	0.326
Picture completion	9.76 ± 2.49	10.2 ± 2.1	0.503
Mazes	9.32 ± 2.94	10.24 ± 2.35	0.228
Geometric design	9.56 ± 1.98	11.28 ± 1.67	0.002*
Block design	7.92 ± 2.63	9.16 ± 1.65	0.053

*: Statistically significant

Table 4 and figure 1 show that treatment duration has no statistically significant relationship to verbal or performance IQ, there is a statistically significant link between the duration of treatment and full-scale intelligence.

Table (4): Correlation between treatment duration and the IQ scores of the patients

IQ	Duration of treatment (Months)	
	r	p
Full scale	-0.72	<0.001**
Verbal	-0.32	0.118
Performance	-0.268	0.195

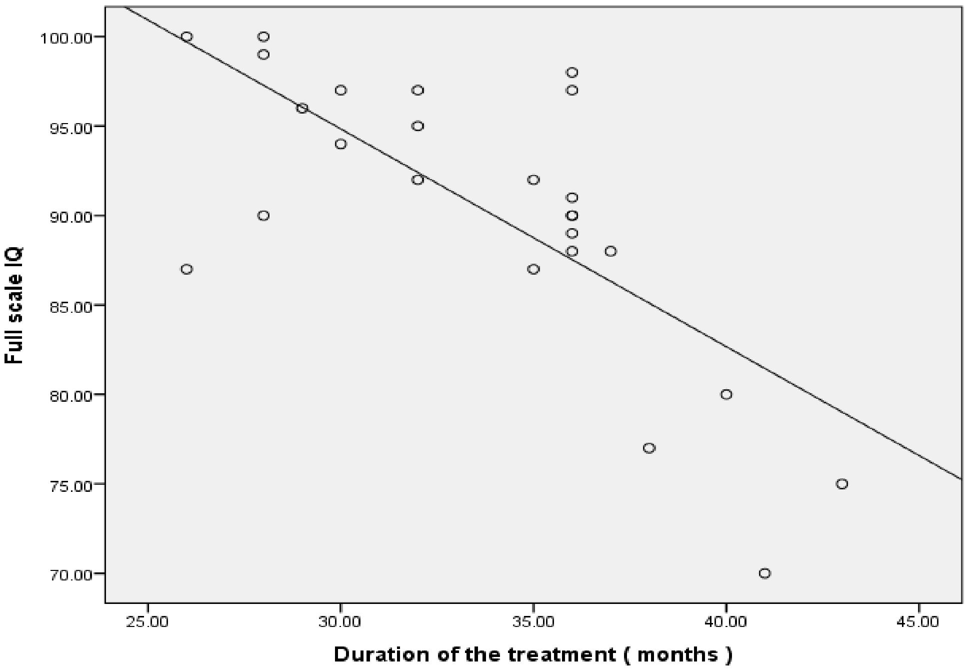

Figure (1): Scatter dot showing significant negative correlation between duration of treatment and full scale IQ

Table 5 and figure 2 show that both information, vocabulary, and geometric or block design were statistically significantly correlated to the duration of treatment, and the duration of treatment was not statistically significantly correlated with arithmetic, similarity, comprehension, object assembly, picture completion, mazes, block design or geometric or block design.

Table (5): Correlation between duration of the treatment and IQ subtest of the studied case group

	Duration of treatment (Months)	
	r	P
Information	-0.442	0.027*
Vocabulary	-0.43	0.032*
Arithmetic	0.177	0.389
Similarities	-0.371	0.068
Comprehension	-0.07	0.739
Object assembly	-0.377	0.063
Picture completion	-0.036	0.866
Mazes	-0.12	0.569
Geometric design	-0.66	<0.001**
Block design	0.358	0.079

*: Statistically significant, **: Statistically highly significant

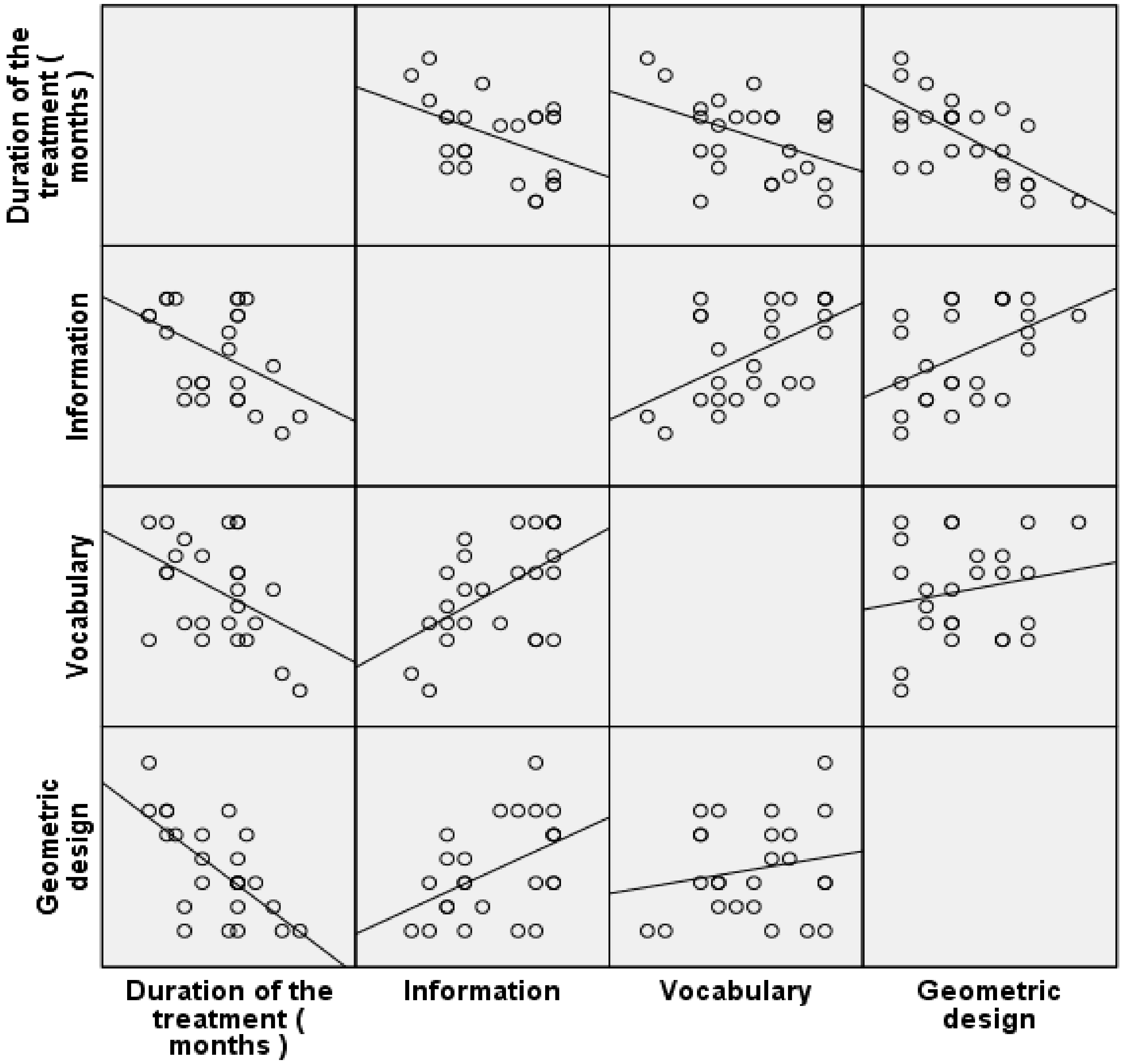

Figure (2): Scatter dot matrix showing correlation between duration of treatment, information, vocabularies and geometric design.

DISCUSSION

Recent advances in pediatric cancer therapy have been linked to extraordinary increases in 5-year survival rates, with over 80% of children and adolescents who receive a diagnosis today likely to live at least 5 years. More than 500,000 people will have survived pediatric cancer by 2020, according to current estimates [8]. Maintaining a good follow-up to examine various health-related problems after curative therapy for children cancer is one of the key concerns. Cancer and its therapeutic exposure have a wide spectrum of long-term impacts [9].

In this study, specifically, neurocognitive function was poorer in the case group compared to a healthy control group on a full and verbal IQ scale, although there was no statistical difference between groups in terms of full and performance. Analyses of the differences between the groups found a statistically significant difference between the groups in terms of similarity and geometric design in the IQ subtest (significantly lower in case group).

According to these findings, the prevalence of neurocognitive symptoms in acute lymphocytic leukemia (ALL) survivors was higher than previously thought, and this was in line with previous research conducted by **Vishwa *et al.*** [9]. 50% of children with cancer had a major neurocognitive deficit in full scale intelligence quotient (FSIQ 90), with the mean FSIQ used to assess the neurocognitive function being 86.1± 20.5. One-half of the survivors had deficiencies in verbal understanding, perceptual reasoning, working memory, and processing speed, while the other half had none of these problems.

Neurocognitive impairment occurred in 10–42.8% of survivors, mostly in the intellectual domain, according to a systematic study conducted by **Peng *et al.*** [3]. Compared to healthy controls, childhood cancer survivors had lower IQs on average, according to one study. In two investigations, attention, focus, executive skills, memory, and IQ were all found to be mildly to moderately impaired in children who had cancer in their childhood.

Our study showed statistically significant negative correlation between treatment duration and full scale IQ, and also with duration of treatment and information, vocabulary, and geometric design while there was statistically nonsignificant correlation between the duration of treatment and any of the following: arithmetic, similarities, comprehensions, object assembly and picture completion.

These results agreed with the study of **Sherief *et al.*** [11] where impaired neurocognitive functioning was observed as a significant long-term consequence of ALL treatment. Also, **Krull *et al.*** [12] in their large study on adult survivors of childhood cancer found worsening in executive function skills to be increased with time since diagnosis.

CONCLUSION

Neurocognitive function is affected in cancer survivors of children as there is statistically significant difference between the studied groups regarding full, and performance IQ scale (significantly higher in control group) but verbal scale was not statistically different between the groups. Regarding IQ subtests, there is statistically significant difference between the studied groups regarding similarities and geometric design (significantly higher in control group) but information, vocabulary, arithmetic, comprehension, object assembly, picture completion, mazes or block design were not different between the groups.

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