



Research Protocol: Cross-sectional Study (Survey)—The Fate of Moroccan Childhood Cancer Survivors

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Abstract: Background: Malignant tumors of the child represent one of the major causes of mortality in children between 1 and 14 years in the West. Young people recovering from childhood cancer may have complications related to the disease itself or treatment. Complications can be somatic, psychic or socio-occupational and familial. The current study aims to know the current status of young children treated in the oncology unit of PHOU (Pediatric Hemato-Oncology Unit), Rabat Children Hospital is exclusively or jointly between 1978 and 2004. Material and methods: It will be a cross-sectional study conducted among childhood cancer survivors treated between 1978 and 2004 at the Pediatric Oncology Unit of Children's Hospital of Rabat. Medical and demographic data will be collected through questionnaires completed by phone or internet, by the survivor, his parent or his physician. Discussion: To our knowledge, there is no previous study about the fate of Moroccan childhood cancer survivors before our study. Hence, it will be a cross-sectional study to have a quick picture on the situation in Morocco. It would be necessary to establish a follow-up strategy in Morocco.

Key words: Childhood, cancer, survivors, Morocco.

1. Background

Malignant tumors of the child represent one of the major causes of mortality in children between 1 and 14 years in the West [1]. Considerable progress has been made over the last few decades, which makes it possible today to cure four of five children on average, this number can vary according to the type and extent of cancer at the time of diagnosis [1, 2].

According to data from the literature, childhood cancers are dominated by leukemia, CNS (central nervous system) tumors, bone and soft tissue tumors [2]. Young people recovering from childhood cancer may have late effects complications related to the disease itself or treatment. The complications can be somatic, psychic or socio-occupational and familial.

On the somatic level, cardiovascular disease is the leading non-cancerous cause of death among survivors of childhood cancer [3]. Childhood survivors and young adult cancer remain at an increased risk of cardiovascular disease compared to the general population [4]. Thus, in post-chemotherapy, children have abnormal myocardial characteristics despite normal overall cardiac function by standard transthoracic echocardiography [5].

The presence of hormonal disorders is common especially after radiation therapy of the head and neck: growth retardation; delayed or advanced puberty, thyroid disorders [8].

Infertility in women has been strongly associated with radiation treatment of the genital sphere and especially with alkylating chemotherapy [9]. In men, many childhood cancer survivors, especially Hodgkin Disease survivors, are at risk of azoospermia [10]. A

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better understanding of infertility after cancer is crucial for counseling and decision-making on future attempts to design and preserve fertility [11].

On the neurocognitive level, clinically significant and potentially treatable apathy occurs relatively frequently in adult survivors of a posterior fossa childhood tumor, especially women [12]. Survivors of malignant neoplasms of the CNS were found to be at high risk for neurocognitive impairment which continues into adulthood and is correlated with lower socio-economic success [13].

Other somatic disorders such as osteopenia have been observed in young adults who have been the victims of childhood cancer. Many studies showed that antineoplastic treatments in childhood and adolescence hinder the acquisition of bone mass [14].

Survivors of childhood cancers may also suffer from neuropsychological complications, so survivors of childhood medulloblastoma often suffer from severe persistent deficits in a wide range of neuropsychological functional areas. These serious neuropsychological and psychological impairments justify efforts to reduce or delay the use of cranio radiotherapy for childhood medulloblastoma [15].

In Morocco, according to the Cancer Registry of Casablanca, childhood cancer accounted for 3% of all cancers. By gender, the boy was hit in 56.2%. The incidence was 12.7/100,000 children/year [16, 17]. Leukemia, lymphoma, nephroblastoma were the most frequent childhood cancers in the pediatric oncology units before 2005. Brain tumors, which were treated only in neurosurgical departments, are becoming the second cancer after leukemia. Presently, childhood cancer patients are treated in 5 PHOU (pediatric hemato-oncology units) and their disease free survival is about 60%. Survivors are seen in PO clinics at the same time with the undergoing treatment patients, about 5 years after stopping treatment. Then survivors do not have long term Follow Up and their late effects are diagnosed late.

2. Objectives of the Study

2.1 Primary Objective

To know the current status of young children's cancer treatments in PHOU, Rabat Children Hospital is exclusively or jointly between 1978 and 2004.

2.2 Secondary Objectives

Establish a database of Moroccan childhood cancer survivors.

Gather information about their current status.

Respond to their treatment or prevention needs.

Implement a long-term monitoring strategy for survivors in terms of information, prevention, early detection, medical treatment and socio-emotional support.

3. Material and Methods

3.1 Type of Study

It will be an exhaustive, cross-sectional study designed to assess the physical, psychological and social outcomes of young people treated and cured of childhood cancer between 1978 and 2004 at the PHOU, Rabat Children Hospital.

3.2 Study Population

The study population consists of young people recovered from childhood cancer (between 0 and 15 years old) treated in the unit of onco-pediatrics at the CHU in Rabat either exclusively or jointly between 1978 and 2004. These young people are in CCR (Continuous Complete Remission without relapse), Complete Remission 2 or CR2 (remission after 1 relapse) Complete Remission 3 or CR3 (remission after 2 relapses).

It is an exhaustive study where all the subjects, all the young people treated and cured of childhood cancer at the onc-pediatric unit of the CHU Avicenne in Rabat between 1978 and 2004 will be included.

4. Data Collection

4.1 Collection Tools

- Source: Questionnaires
- Data management: Data will be anonymous and transcribed from the questionnaires into excel sheets by two grabbers' data. The data will be validated by a data manager.
- Each subject included in the study will be contacted by phone, email, postal mail, Face Book or by home visit. In this sense a newsletter was made explaining the purpose of the survey.
- After obtaining their agreement, we will send the questionnaires that had to be completed by the patient himself, the parents or the attending physician. For some patients, the questionnaire will be completed over the telephone by the project directors or a trained volunteer.
- The revival will be made for subjects that have not responded by phone, email, social networks and mail.

4.2 Collected Variables

(1) Sociodemographic characteristics of the child in the treatment of cancer, as well as in adult age: age, sex, parents' occupation, urban or rural housing, educational attainment, occupation, marital status, and number of children...

It is through the questions discussed in this section that we can establish the causal link that may exist between childhood cancer and socio-familial and professional reintegration.

(2) The major somatic and psychological complications associated with childhood cancer or treatment: This section will provide an overview of

the major somatic complications occurring in adults with childhood cancer. These complications may be related to the disease itself or treatment.

It will also enable us to judge the effectiveness of psychological support and thus be able to offer more relevant assistance.

4.3 Statistical Analysis

All variables will be summarized by using descriptive statistics. Categorical variables will be described in terms of proportions and quantitative variables will be described in terms of average, extreme values and standard deviation.

The association between certain dependent variables and several potential explanatory variables will be investigated. Bi-variate analysis will be used and the association between two categorical variables will be searched by chi-square test, the association between a categorical and quantitative variable will be searched by T-test and we will select as the significant level with p -value of 0.05.

A binary logistic regression will be made by including in the model all variables found significant at the bivariate analysis with $p < 0.05$ and all variables found at the bivariate analysis with $p < 0.20$. The multivariate analysis will be used (logistic regression).

Statistical analysis will be done on SPSS Version 17.

5. Timeline (2015)

++++	January	February-March	April	May-September	October	November-December
Writting the protocol						
Validate the protocole/obtaining IRB approval						
Pilote survey						
Survey						
Seizure and analysis of the questionnaire						
Publication of the results						

6. Safety Monitoring Plan

Data will be saved in hard disc, paper form and external drive in three separate locals.

7. Ethics Guidelines

7.1 Risks

- Physical: None;
- Psychological: Minimal;
- Social: Minimal;
- Legal: Minimal;
- Economic: Minimal.

7.2 Confidentiality and Data Protection

- Questionnaires will be anonymous;
- Data will be protected in 3 closed rooms;
- Access to data will be possible only for the researcher's team.

7.3 Consent Process

- Informed consent will be made in Moroccan Arabic;
- Informed consent will be distributed to all participants who will agree to join voluntarily the survey;
- An oral informed consent will be taken from each participant after full explanations of the objective of the study and their right as participant (withdraw, confidentiality, privacy...);
- A written informed consent would not be necessary as it's hard to collect it from each participant (many participants will be contacted only by phone or social media) and it's a minimal risk research;
- Approval will be taken from the local IRB of the University Hospital of Fès.

8. Budget

	Cost dh	Cost \$
Print questionnaires	4.5×1,000 = 4,500 dh	500\$
Data collection	2,500 dh	300\$
Data entry (*2)	(100 dh/day × 25) × 2 = 5,000 dh	550\$
Nadia (coordinator) payment	48,000 dh	5,000\$
Publication fees	10,000 dh	1,000\$
Total	65,000 dh	7,350\$

9. Declarations

9.1 Ethical Approval

- This study will be presented to the local ethics committee of University Hospital Hassan II of Fez who agreed it. Approval will be taken from the local IRB of the University Hospital of Fès;
- An oral informed consent will be taken from each participant after full explanations of the objective of the study and their right as participant (withdraw, confidentiality, privacy...);
- A written informed consent would not be necessary as it's hard to collect it from each participant (many participants will be contacted only by phone or social media) and it's a minimal risk research;
- These points will be clearly stated in the informed consent so that the survivor of childhood cancer was not reluctant to give confidential information.

9.2 Consent for Publication

Not applicable.

9.3 Availability of Data and Materials

Not applicable.

9.4 Competing Interests

The authors declare that they have no competing interests.

9.5 Funding

This survey was funded by the Avenir Association. Terry Fox Foundation through a Terry Fox runs in Rabat.

9.6 Author Contribution Nadia BENAICHA: Writing the Protocol, Drafting the Questionnaire, Writing the Consent Form, Conducting the Survey, Statistical Analysis

Fouzia MSEFER ALAOU: Conception and writing the survey project, drafting and reviewing the questionnaires, reviewing the protocol, conducting

and supervising the survey, reviewing the article; Karima ELRHAZI: Reviewing the protocol; Abdessalam DIARRA: Statistical sampling Chakib; NEJJARI: Reviewing the protocol, reviewing the questionnaire, reviewing the Consent Form.

9.7 Acknowledgement

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10. Endnotes

10.1 What Is Already Known on This Topic

- Children's malignant tumors are major causes of death in children under 15 years old.
- Young people cured of childhood cancer may develop late complications related to the disease itself or the treatment.
- Many survivors report many physical, psychological and social difficulties in comparison with siblings' populations.

10.2 What This Study Will Add

- To our knowledge, there is no previous study about the fate of Moroccan childhood cancer survivors before our study.
- This study will help us to know the current status of young children's cancer treated in the oncology unit of the Rabat Children Hospital exclusively or jointly between 1975 and 2005.

References

- [1] <http://www.e-cancer.fr/cancerinfo/les-cancers/le-cancer-chez-l-enfant/complications-tardives-et-sequelles-eventuelles>.
- [2] Msefer Alaoui, F., and Benaicha, N. Jeunes marocains guéris d'un cancer de l'enfance, Que Deviennent-ils? *Doctinews*: 32-6.
- [3] <http://www.e-cancer.fr/cancerinfo>.
- [4] Dietz, A. C., Sivanandam, S., Konety, S., Kaufman, C. L., Gage, R. M., Kelly, A. S., Neglia, J. P., and Mulrooney, D. A. "Evaluation of Traditional and Novel Measures of Cardiac Function to Detect Anthracycline-Induced Cardiotoxicity in Survivors of Childhood Cancer."
- [5] Van Laar, M., Feltbower, R. G., Gale, C. P., Bowen, D. T., Oliver, S. E., and Glaser, A. "Cardiovascular Sequelae in Long-term Survivors of Young Peoples' Cancer: A Linked Cohort Study."
- [6] Toro-Salazar, O. H., Gillan, E., O'Loughlin, M. T., Burke, G. S., Ferranti, J., Stainsby, J., Liang, B., Mazur, W., Raman, S. V., and Hor, K. N. 2013. "Occult Cardiotoxicity in Childhood Cancer Survivors Exposed to Anthracycline Therapy." *Circ Cardiovasc Imaging* 6 (6): 873-80.
- [7] Venkatramani, R., Kamath, S., Wong, K., Olch, A. J., Malvar, J., Sposto, R., Goodarzian, F., Freyer, D. R., Keens, T. G., and Mascarenhas, L. 2013. "Correlation of Clinical and Dosimetric Factors with Adverse Pulmonary Outcomes in Children after Lung Irradiation." *Int. J. Radiat Oncol. Biol. Phys.* 86 (5): 942-8.
- [8] Tantawy, A. A., Elbarbary, N., Ahmed, A., Mohamed, N. A., and Ezz-Elarab, S. 2011. "Pulmonary Complications in Survivors of Childhood Hematological Malignancies: Single-Center Experience." *Pediatr. Hematol. Oncol.* 28 (5): 403-17.
- [9] <http://www.cancer.org/treatment/childrenandcancer/when-your-child-has-cancer/children-diagnosed-with-cancer-late-effects-of-cancer-treatment>.
- [10] Barton, S. E., Najita, J. S., Ginsburg, E. S., Leisenring, W. M., Stovall, M., Weathers, R. E., Sklar, C. A., Robison, L. L., and Diller, L. 2013. "Infertility, Infertility Treatment, and Achievement of Pregnancy in Female Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study Cohort." *Lancet Oncol.* (9): 873-81.
- [11] Green, D. M., Zhu, L., Zhang, N., Sklar, C. A., Ke, R. W., Kutteh, W. H., Klosky, J. L., Spunt, S. L., Metzger, M. L., Navid, F., Srivastava, D., Robison, L. L., and Hudson, M. M. 2013. "Lack of Specificity of Plasma Concentrations of Inhibin B and Follicle-stimulating Hormone for Identification of Azoospermic Survivors of Childhood Cancer: A Report from the St Jude Lifetime Cohort Study." *J. Clin. Oncol.* 31 (10): 1324-8.
- [12] Barton, S. E., Najita, J. S., Ginsburg, E. S., Leisenring, W. M., Stovall, M., Weathers, R. E., Sklar, C. A., Robison, L. L., and Diller, L. 2002. "Achievement of Pregnancy in Female Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study Cohort." *Am. J. Obstet. Gynecol.* 187 (4): 1070-80.

- [13] Hopyan, T., Laughlin, S., and Dennis, M. Emotions and Their Cognitive Control in Children with Cerebellar Tumors.
- [14] Ellenberg, L., Liu, Q., Gioia, G., Yasui, Y., Packer, R. J., Mertens, A., Donaldson, S. S., Stovall, M., Kadan-Lottick, N., Armstrong, G., Robison, L. L., and Zeltzer, L. K. 2009. "Neurocognitive Status in Long-term Survivors of Childhood CNS Malignancies: A Report from the Childhood Cancer Survivor Study." *Neuropsychology* 23 (6): 705-17.
- [15] Vassilopoulou-Sellin, R., Brosnan, P., Delpassand, A., Zietz, H., Klein, M. J., and Jaffe, N. 1999. "Osteopenia in Young Adult Survivors of Childhood Cancer." *Med. Pediatr. Oncol.* 32 (4): 272-8.
- [16] Maddrey, A. M., Bergeron, J. A., Lombardo, E. R., McDonald, N. K., Mulne, A. F., Barenberg, P. D., and Bowers, D. C. 2005. "Neuropsychological Performance and Quality of Life of 10 Year Survivors of Childhood Medulloblastoma." *J. Neurooncol.* 72 (3): 245-53.
- [17] RCRC 2005-2008.
- [18] Msefer Alaoui, F. "Moroccan Childhood Cancer Survivors: A Medical and Demographic Survey." *Eposter SIOP* 2015.
- [19] Msefer Alaoui, F. "The Fate of Childhood Cancer Moroccan Survivors' Survey Project." *Eposter SIOP* 2014.