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Adolescents with Cancer in Italy: Improving Access to National Cooperative

Pediatric Oncology Group (AIEOP) Centers

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Abstract

This analysis compared the numbers of patients treated at Italian pediatric oncology group (Associazione Italiana Ematologia Oncologia Pediatrica [AIEOP]) centers with the numbers of cases predicted according to the population- based registry. It considered 32,431 patients registered in the AIEOP database (1989–2012). The ratio of observed (O) to expected (E) cases was 0.79 for children (0–14 years old) and 0.15 for adolescents (15–19 years old). The proportion of adolescents increased significantly over the years, however, from 0.05 in the earliest period to 0.10, 0.18, and then 0.28 in the latest period of observation, suggesting a greater efficacy of local/national programs dedicated to adolescents.

Abbreviations

AIEOP Associazione Italiana Ematologia Oncologia Pediatrica

AIRTUM Associazione Italiana Registri Tumori

CNS central nervous system

SIAMO Società Italiana Adolescenti Malati Onco- ematologici

INTRODUCTION

The optimal management of adolescents with cancer remains a challenge. Various authors report little improvement in adolescents' survival rates compared with other age groups, and a worse survival for adolescents than for children with the same types of tumor.^{1, 2} This may stem from several factors, but differences in access to optimal cancer services and treatments delivered are believed to play a part.²⁻⁴ The Italian pediatric oncology community's awareness of this issue has been growing in recent years. In 2008, a Committee on Adolescents was established by the Italian Pediatric Oncology Association (*Associazione Italiana Ematologia Oncologia Pediatrica* [AIEOP]). A study published in 2009 of more than 22,000 cases treated from 1989 to 2006 revealed that

adolescent cancer patients' access to AIEOP centers had been distinctly limited: only 10% compared to 77% of children.⁵ Further research suggested that excessively strict upper age limits were preventing teenagers from being admitted to AIEOP centers.⁶ Various initiatives were consequently devised to improve awareness on adolescent cancer.⁷ This study compares the number of cases treated at AIEOP centers with the number of cases expected, to see whether these interventions have increased the proportion of adolescents treated at pediatric oncology centers over time.

RESULTS

We compared the numbers of adolescents (15–19 years old) and children (0–14 years old) with cancer treated at AIEOP centers with the numbers of cases expected to occur in Italy based on the incidence rates derived from the population- based Italian Network of Cancer Registries (*Associazione Italiana Registri Tumori* [AIRTUM]).

All malignant tumors were considered eligible. Astrocytomas of the central nervous system (CNS) were also included because differentiation between malignant and benign cases is not easy, and benign astrocytomas are often locally aggressive and therefore potentially just as invasive and lethal as malignant ones.

The observed cases were patients under 20 years old at diagnosis registered in the AIEOP Mod.1.01 database by 55 centers during the years 1989–2012. The study period was split into four diagnostic periods: 1989–1994, 1995–2000, 2001–2006, and 2007–2012. All pediatric oncology units in Italy are affiliated with AIEOP.

The cases of cancer expected in 1989–2012 was calculated using AIRTUM's site- specific incidence rates for 1989–2008 for the Italian population by age group (0, 1–4, 5–9, 10–14, and 15–19 years old) and diagnostic period (the rates for 2001–2006 were also adopted for 2009–2012).⁸ The AIRTUM includes 32 general and five specialized cancer registries (only two specializing in childhood and adolescent cancer). It monitors over 5.5 million children and adolescents (approximately 4 million children and 1.5 million adolescents),

corresponding to 47% of Italy's population in this age group. Our analyses were based on the International Childhood Cancer Classification ICCC- 3.9

The statistical significance of differences between observed (O) and expected (E) numbers of cases was tested by calculating confidence interval around the O/E ratio using the Sahai and Khurshid method. Statistical significance was set at 0.05. All statistical tests were two- tailed. The Breslow–Day test was used to assess O/E trends by diagnostic period. All analyses were conducted using the SAS 8.2 and Stata/SE 11.0 software.

During the study period, 32,431 cancer patients were registered in the AIEOP database, 29,337 children and 3,094 (9.5%) adolescents. Epidemiological data suggested that 57,672 cases could be expected in Italy during the same period. Table I shows the cases registered and expected by diagnosis and patient age. The O/E ratio for the entire time period was 0.79 for children (over 0.90 for many tumor types) and 0.15 for adolescents. Table II shows adolescent cases and the O/E ratios in the four diagnostic periods considered. The overall O/E ratio rose gradually from 0.05 in the first period to 0.10, then 0.18, and 0.28; with few exceptions, this improvement was statistically significant for all tumor types. In 2007–2012, the O/E ratio for adolescents was particularly high (≥ 1) for CNS primitive neuroectodermal tumors, neuroblastoma, hepatic tumors, osteosarcoma, and Ewing sarcoma. It was 0.82 for acute lymphocytic leukemia. The lowest O/E ratios were seen for carcinomas (0.04), lymphomas (0.24), and germ cell tumors (0.21).

DISCUSSION

Although adolescents are still less well represented than children at Italian pediatric oncology referral centers, the present study shows that the proportion of 15- to 19- year- olds treated at pediatric oncology facilities has improved significantly in recent years, and for almost all tumor types. Better O/E ratios demonstrate that, for some pediatric type tumors, most adolescent cases have recently been treated at centers affiliated to the AIEOP. The O/E ratios have remained low for malignancies more typical of

adult age, such as carcinomas. As a limitation of the study, no data are available on where and how patients not seen at AIEOP centers may have been treated.

Adolescents have often been described as a medically underserved population, in that they may be less likely to access the best possible treatment facilities compared to younger children.²⁻⁴ Many potential reasons for this state of affairs have been suggested. Some are patient related (e.g., a limited awareness of adolescents' healthcare options), but many are factors relating to the healthcare system, including primary care providers' limited awareness that cancer can occur in adolescents, arbitrary patterns of referral to pediatric or adult medical oncologists based on age alone, strict upper age limits set by pediatric hospitals, inadequate collaboration between pediatric and adult medical oncologists, and a shortage of organized healthcare networks focusing on adolescents.¹⁰⁻¹⁴

In Italy, alongside two local projects developed in Aviano ¹⁵ and Milan,¹⁶ an ad hoc AIEOP committee established in 2008 led to a nationwide program.⁷ Since previous Italian studies had found the AIEOP network far less effective in serving adolescents than children, and assuming that pediatric oncologists are in a better position to care for adolescent cancer patients (especially those with pediatric- type tumors),^{17, 18} the AIEOP committee aimed primarily to increase the proportion of adolescents accessing AIEOP centers. Action was taken to raise the upper age limit for admission to pediatric oncology centers and a broad- based communication strategy was implemented at various levels (community, media, family physicians, oncologists, and institutions).⁷ The rising O/E ratios of adolescent cancer cases treated at AIEOP centers in recent years demonstrate the efficacy of these actions.

The Italian oncology community nonetheless recognized a further crucial need to establish strong cooperation between pediatric oncologists and adult medical oncologists. In 2013, the AIEOP committee changed into a broad- based national task force focusing on adolescents and young adults, in close cooperation with adult oncology societies. Its new

project, called SIAMO (Società Italiana Adolescenti Malati Onco-ematologici, the Italian Society for Adolescents with Oncohematological Diseases),¹⁹ was formally established by the country's pediatric and adult hematological and oncological scientific societies, and also involves other stakeholders (nurses, psychologists, advocacy organizations, and parents associations). With the support of the Italian National Health Service, SIAMO aims to include the particular needs of adolescents in Italy's next National Oncology Plan, identifying the special criteria and facilities that centers (be they pediatric or adult units) need to treat adolescents with cancer (no restrictive age cut-offs, availability of clinical trials on the different types of tumor, training multidisciplinary staff, age-appropriate psychosocial support teams, dedicated spaces, fertility preservation, and transition in care programs).¹⁹

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