Original article

Running Title: Delay Causes in Referral and Diagnosis in Cancer

Delays in Initial Referral, Diagnosis and Treatment in Children with Cancer

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Abstract

Background: Cancer has been one of the most critical health problems during the past decades which require serious consideration, especially in developing countries.

Methods: 80 parents of the children with different types of cancers were studied via both questionnaire and person-to-person interview after announcing their informed consent.

Results: The highest delay in patients' initial referral was due to the following factors: lack of attention or ignoring the first symptoms, delay in referring to the physician, low economic status and even lack of family support for the patient. In addition, visiting several doctors after the initial diagnosis, uncertainty about the first proposed method, and high cost of treatment can be mentioned as the main causes of delays in the start of treatment.

Conclusion: Education plays an important role in identifying the signs of cancer. In addition, proper relationship and cooperation between the health system and physicians as well as provision of adequate information to patients could lead to the long-term cooperation of these patients in continuing their treatment.

Keywords: cancer, delay in referral, children, delay in diagnosis, delay in treatment.

Introduction

Since the diagnosis and treatment of this disease in its early stages can reduce the related mortality rates and complications and reduce the costs tangibly, it was attempted to investigate the factors affecting the patients' delay in referring to physicians in the beginning and subsequently propose some solutions to tackle this problem and reduce its resultant injuries.

Cancer has been defined as "uncontrollable growth of cells" and it has been recognized as a major problem in human societies. It has caused the highest mortality rate after heart disease[1]. It was Hippocrates (460-370 BC), the Greek physician who used the term "carsino" for the first time to refer to this disease. Later, Celsus (50-28 BC) changed it to "cancer", which means Scorpion in the Latin and since then the term cancer has been used to date [2].

Initially, cancer was determined as a problem for the health systems of developed countries; however, in the last decades; 1975 to 2012, its rate has been trending in developing countries.

Cancer prevalence rates increased   in all age ranges by 0.6% per year. In contrast, death rates have dropped constantly, from 6.5 in 1970 to 2.4 in 2012 ,per 100,000 population[1]. For example, the percentage of the patients with breast cancer has increased from 75% in 1977 to 90% in 2009 [3].

The high rates of mortality, economic and psychological consequences as well as the disabilities created by cancer impose a huge cost on the health system of the society. This has motivated the conducting of a plethora of studies for the rapid diagnosis of cancer in its early stages for effective treatment [4, 5]. With advances in screening, the diagnosis of cancers in their early stage has been made possible. Therefore, today many of patients can enjoy good quality of life because this disease is diagnosed and treated in early stages [6].

The delay in the diagnosis mainly hinges upon two different components:

1. Inattention to the illness symptoms and patient's delay in referring to physician (the factors related to the patient).

2. The physician's delay in the initial definitive diagnosis of the disease, which includes the inattention of some physicians to the initial and non-specific symptoms related to cancer and it is -sometimes due to the deceptive and inertial nature of some types of cancers in the early stages (the factors related to the health care system) [7, 8]. Delay in the diagnosis of cancer leads to indicating unreal incidence rate of cancer.

We know that the health strategic plans are based on this information and will be influenced by them. These causes lead to the delay in the initiation of early effective treatment, the increased relapse of the disease, no response to treatment and long-term increase of mortality. The present study tried to

distinguish the causes of delay in initial referral, diagnosis and onset of treatment.   In this way, we can identify the local factors and take a step forward regarding the achievement of the goals set by the World Health Organization in 2014, which emphasizes the early diagnosis with the start of education and training in schools and the implementation of an early perfect treatment plan [8]. Particularly, this issue bears high importance in Iran which is currently involved with cancer tsunami.

Methods

In the present study, the participants were selected within one year from 2015 to 2016 through person-to-person interviews with parents of the patients in the children age group. A total of 93 patients were examined consecutively. The children were divided into two groups, i.e. patients - above 7 years of age, 7 years old and below 7 of age. From all patients, 58 were male and 22 were female with mean age of 5.93 ±3.25 years old. Graphical abstract is shown in (Fig. 1).

The criterion for the inclusion of participants into the study was cancer development for the children who had referred to or had been asked to refer to Children's Hospital of Tabriz for the first time for the diagnosis of cancer or onset of treatment.

The patients who were not willing to be interviewed or the ones, who had gone through some part of the diagnosis and treatment process in another country, were eliminated from participation in this study. The data were collected through questionnaire, which was completed through interviews by the researchers. Those parents who did not provide the researchers with accurate information or opted out the interview during the interview were also excluded from the interview.

Figure 1: Graphical Abstract

In this study, each of the delayed referrals, delayed diagnoses, and delayed treatments were identified via the following definitions. The Delay in Referring: a delay of more than 30 days from the emergence of symptoms up to physician visit. The Delay in diagnosis: a delay of more than 30 days from the first physician visit to diagnosis. The Delay in treatment: a delay of more than 14 days from diagnosis to treatment.

Statistical analysis

Normality of data was calculated by Kolmogorov-Smirnov test and expressed by mean and standard deviation in tables. Non-normal variables were implied as median (max & min). The causes of delays difference between 2 groups; with delay and without delay were assessed by independent sample T-test. P-values less than 0.05 were considered statistically significant. All statistical analyses were done using the Statistical package for the Social Sciences (SPSS), version 16.0 (SPSS Inc, Chicago, IL, USA).

Ethical considerations

The theme of the study was described to all the patients' parents or patients in simple language and the questionnaires and written informed consent were completed with them. The participants were assured that their information would be treated as confidential, would be protected at all research stages, and dissemination of the results would be done in an anonymous manner.

Results

From among 93 patients under study, 13 patients were excluded from the study due to their non-compliance with the inclusion criteria and, thereby, a total of 80 patients were finally evaluated. In generally (Table 1) shows the information about number of patients' interns each delay groups.

Table 1: Number of patients in Each of Delay groups

Causes of delay in the initial referral

In total, the delay of more than one month from the first referral was observed in 5% of the patients. In this study, the relationship of this delay with age, gender, place of residence, occupation, and education of parents was assessed and the following results were obtained:

The relationship between patients' gender and delay in the initial referral

There was no significant correlation (p>0.05) in different groups. (Table 2) demonstrated correlation between genders by each delay.

Table 2: Correlation between Gender and Delay groups

The relationship between parents' occupation and delay in the initial referral

In this group, similarly, no significant relationship was found; thus, it can be concluded that there is no significant difference between different occupation groups (P> 0.05). (Table 3) represents relevance of Parent's occupation and each of delay.

Table 3: Relevance of parent's occupation and delay groups

The relationship between education level of parents and delay in the initial referral

Parents with elementary education referred to the physician with significantly further delays (P = 0.037) in comparison with other educational groups. On the contrary, those with secondary and higher education had the lowest delay. (Table 4) shows relation parent's education and kinds of delay groups.

Table 4: Relation parent's education and variety of delay groups.

The relationship between children's age and delay in the initial referral

The patients were divided into two age groups, i.e. patients' above7 years of age, and patients - below 7 years of age (based on school age of onset), however there was no significant difference in any of the groups. (Table 5) demonstrated relationship age range of children and each delay.

Table 5: Children age range and variety of delays

The relationship between residence location and delay in the initial referral

Regarding residence location of patients, there was no significant difference between urban and rural residents in referring to the physician, diagnosis, and treatment of cancer. (Table 6) displays relation between distance of residence and variety of delays.

Table 6: Relation between distance of residence and variety of delays.

Effective factors in delay in the first visit to the physician

About 5% of the patients had a delay of more than one month in physician visit.

Causes of delayed diagnosis

A large number of factors are at play in this regard. Here, the patients' demographic characteristics were evaluated where delayed diagnosis was not significantly correlated with patients' age and gender as well as parents' occupation.

Causes of delayed onset of treatment

Generally, 3.7% of the children had a delay more than a month regarding the onset of treatment.

In this study, the reasons that led to delay in the onset of treatment include:

Visiting several physicians after the final diagnosis

From among 18 patients who had a delay more than 16 days in the onset of treatment, 77.7% of them have referred to two or more physicians after the final diagnosis; therefore, these patients had significant delays in the onset of treatment.

Use of witchcraft, bet and making spell as a method of treatment

The parents of 88.8% of the children had also used this method for recovery, but only 7.8% of the parents mentioned the use of witchcraft as the reason for delay in the onset of treatment. Most of them did not refer to witchcraft as a method for the treatment of cancer; in fact, they mentioned   witchcraft as a complementary way for treatment of cancer. They acknowledged that cancer should be treated with medical and surgical procedures and this referral continued after the start of treatment, but it has not had any preventive power in the continuation of the treatment.

Denial of the reality

It was revealed that there is no significant relationship between the normal process of psychological reactions to the acceptance of the disease and delay in the onset of treatment.

Mistrust in the treatment

From among the patients who had a delay in the onset of the treatment, 33.3% of them referred to this factor as the reason for their delay; thus, a long time has been spent on searching for other methods to treat the disease.

It should be mentioned that the parents were asked about the distance of the route, their psychological problems after being informed of the cancer diagnosis, high cost of treatment and the reaction of relatives as the possible reasons for delayed treatment. However, they did not mention any of these factors as the ones that might have led to the delay in their referral or in the onset of treatment, but they found these factors a major cause of continued treatment.

Decision to discontinue treatment

In response to the question whether or not the parents have decided to discontinue treatment, 25% of children, they stated that they had made such a decision at least once, 68% of them referred to despair of recovery and treatment-related side effects as the reasons, 23% of them have referred to economic factors, and 9% of them have referred to other factors, such as family problems and lack of family support as the causes of delay.

In comparison with kinds of all delays and factors influencing on delays illustrates in (Table 7).

Table 7: In comparison with kinds of all delays and factors influencing on delays

Discussion

With the increase of human longevity and the change of environmental conditions, the improvement of cancer diagnostic methods has witnessed an increasing trend, especially in developing countries where there is a lower quality of environmental factors, food safety, health, and life. However, advances in diagnostic methods have contributed to the identification of cancer patients and this along with the betterment of treatment methods has brought a higher degree of hope for the treatment and increased quality of life in these patients. Since the quick and timely diagnosis has a very important role in the treatment process of cancer, this study sought to evaluate the amounts of the aforementioned delays from the incidence of the first symptoms and to determine the causes of these three types of delays so that basic strategies would be presented aimed at the reduction of patients' delay in referral, diagnosis, and treatment.

In the present study, no relationship was found between children's age and delay in referring to the physician; however, a similar study was carried out in Nigeria in 2015 where the results represented the existence of a negative significant correlation between children's age and the delay in diagnosis. In another study which was conducted in South Africa in 2010 by Dr. Stefan's team, delay in initial referral was found to hold no significant association with age, gender, and ethnicity [9, 10] . Similar results with the current finding were also obtained in terms of gender that may lead to the conclusion that most parents did not discriminate between their children in this regard despite the culture of gender discrimination in most societies.

Few studies have been done on the role of parents' education and knowledge, especially on children; however, Dr. Stephen also reported similar results [9]. In contrast, various studies have been conducted on the overall role of education in diagnosis and treatment at various age groups and the majority of these studies have lent support to the positive effect of education, training, and knowledge in this area [8, 11] .

In relation to the difference between urban and rural areas in terms of the initial referral and onset of treatment, Bain and Campbell conducted a study in 2000 at Oxford University and reported that rural patients are less hopeful about treatment and start their treatment later under the belief that they are faced with more obstacles in receiving intensive care [12]. In the same way, a study was undertaken on 200 women with breast cancer at Tehran University in 2005 and residence in rural areas was referred to as the cause of delay in initial referral [13].

In comparison with the result of the present study which is carried out a decade later and due to the non-significance of distance from treatment centers as one of the causes of delay in referral, it can be argued that the expansion of health centers, establishment of family doctor even in the most remote rural areas, and a referral system have played an effectively positive role in this domain. In fact, these patients have mentioned other factors, such as referral to multiple physicians after the final diagnosis, denial of the reality, lack of confidence in the treatment method, and high costs of treatment as the reasons for their delays. According to the research findings and considering the culture of our country, spell and making spell are not regarded as an acceptable treatment method for cancer. In fact, patients have stated other applications for making spell and have acknowledged that cancer should be treated with medical and surgical methods. However, they have emphasized the positive impact of making spell on their spirit and psyche [14, 15].

In a systematic study which was conducted in 2015, the following four factors were identified as the most important causes of delays in referral and seeking treatment: caregiving barriers, coordination of

the health system with patients, the type of communication, the interactions of the caregiving system with patients, and patients' personal values and relationships [16].

Conclusion

In the population of the present study, such characteristics as age, gender, occupation, and rural residence did not cause any delay in referring to the physician, but other factors, including the assignment of no importance to the primary symptoms and/or the serious consideration of these symptoms, habitual delay in referring to the physician, low level of economic status, lack of   —family support for the patient, and family problems have been found as the main reasons for such delays.

Suggestion

According to the research results, the following suggestions are recommended:

1) Necessary training and education should be taken more seriously to familiarize the public, especially school students and university students with warning signs of cancer.

2) Patients and their family who have undergone mental problems after the diagnosis and try to deny the reality should be helped immediately to improve this trend through psychoanalysis and social work services.

3) If the physician and the treatment system provide the patients and their relatives with necessary information and assurance regarding diagnostic methods and treatment procedures, patients can spend time on the treatment rather than on visiting several doctors.

4) The poor and low-income strata should be financially supported and their insurance situation should be improved.

5) Convincing the patients about the side effects of treatment will cause them not to think of stopping the continuity of treatment or not to think of treatment discontinuation immediately after the relative recovery.

6) The early diagnosis of cancer is important for preventing the rising death rate from cancer. In order to avoid this rate, it requires timely visit to the physician, timely diagnosis of the disease, and the improvement of treatment methods.

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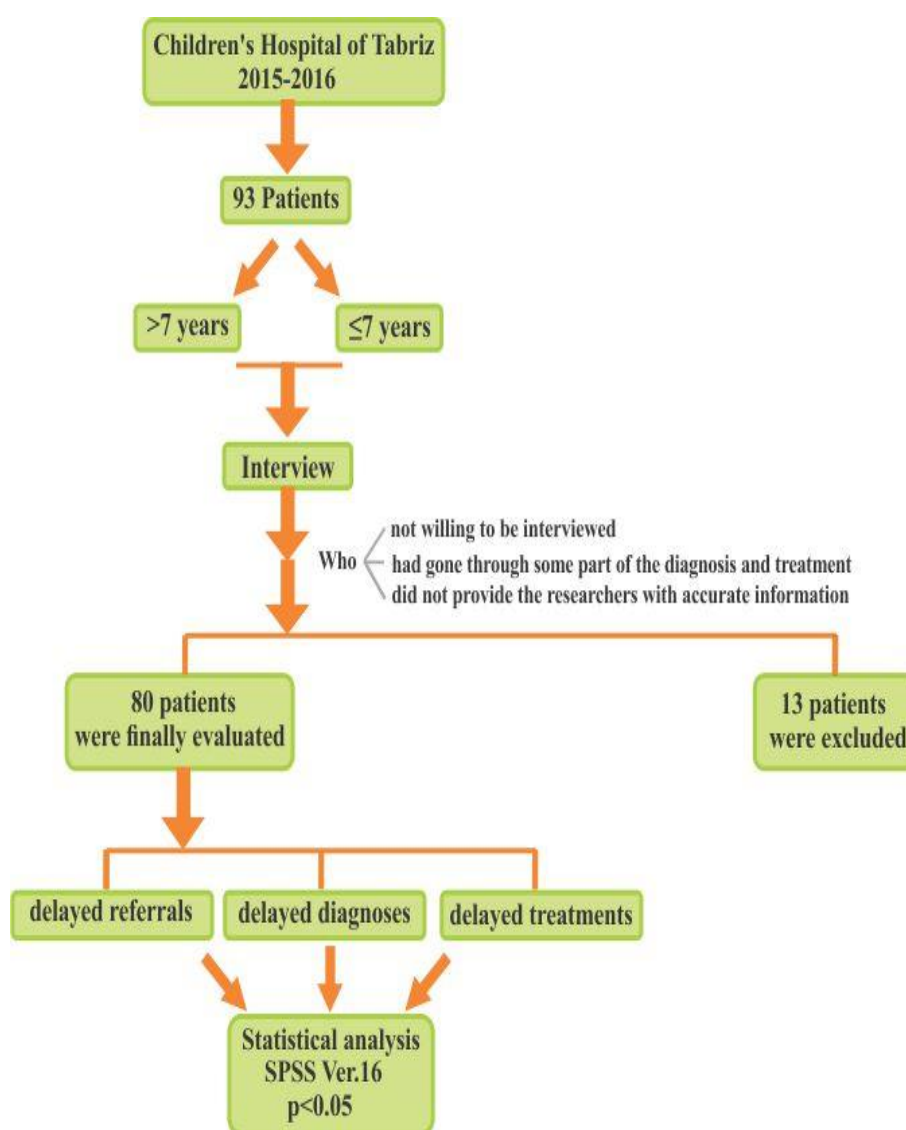
Figure 1. Graphical Abstract

Table 1. Number of patients in Each of Delay groups

Type of delay	Number of patients	≤ 30 days	> 30 days
Delayed referral	80	71	9
Delayed diagnosis	80	60	20
		≤ 14 days	**> 14 days**
Delayed treatment	80	71	9

Table 2. Correlation between Gender and Delay groups

Type of delay	Gender	≤ 30 days	> 30 days
Delayed referral	Male	51	**7**
	Female	20	2
Delayed diagnosis	Male	42	16
	Female	18	4
		≤ 14 days	**> 14 days**
Delayed treatment	Male	53	5
	Female	18	4

Table 3. Relevance of Parent's occupation and Length of Delay

Type of delay	Parent's work	≤ 30 days	> 30 days
Delayed referral	Mother:		
	Employee	5	-
	Farmer	13	-
	House wife	60	2
	Father:		
	Employee	14	-
	Farmer	42	5
	Businessman	16	1
	Unemployed	1	1
Delayed diagnosis	Mother:		
	Employee	5	-
	Farmer	12	1
	House wife	59	3
	Father:		
	Employee	12	2
	Farmer	35	12
	Businessman	15	2
	Unemployed	2	-
		≤ 14 days	**> 14 days**
Delayed treatment	Mother:		
	Employee	5	-
	Farmer	12	1
	House wife	59	3
	Father:		
	Employee	14	-
	Farmer	42	5
	Businessman	17	-
	Unemployed	2	-

Table 4. Relation parent's education and kinds of delay groups

Type of delay	Parent's education	≤ 30 days	> 30 days
Delayed referral	Mother:		
	Illiterate	32	7
	Diploma	18	1
	Academic	21	1
	Father:		
	Illiterate	37	3
	Diploma	15	4
	Academic	19	2
Delayed diagnosis	Mother:		
	Illiterate	28	11
	Diploma	14	5
	Academic	18	4
	Father:		
	Illiterate	31	9
	Diploma	14	5
	Academic	15	6
		≤ 14 days	> 14 days
Delayed treatment	Mother:		
	Illiterate	37	2
	Diploma	13	6
	Academic	21	1
	Father:		
	Illiterate	37	3
	Diploma	14	5
	Academic	20	1

Table 5. children Age range and Length of Delay

Type of delay	Distance	≤ 30 days	> 30 days
Delayed referral	Urban	29	2
	Rural	42	7
Delayed diagnosis	Urban	27	4
	Rural	33	16
		≤ 14 days	> 14 days
Delayed treatment	Urban	30	1
	Rural	41	8

Table 6. Relation between distance of residence and variety of delays

Type of delay	Age	≤ 30 days	> 30 days
Delayed referral	< 7 years ≥ 7 years	41 30	5 4
Delayed diagnosis	< 7 years ≥ 7 years	32 28	14 6
		≤ 14 days	**> 14 days**
Delayed treatment	< 7 years ≥ 7 years	40 31	6 3

Table 7. In comparison with kinds of all delays and factors influencing on delays

	Age	Gender	Mother work	Father work	distance	Mother education	Father education
Delay refer	.917	1.000	1.000	.410	.470	R=-.191 .090	R=+.054 .637
Delay diagnosis	.650	.389	.311	.450	**.048**	R=-.094 .408	R=+.060 .596
Delay treatment	.337	.250	1.000	.097	.143	R=+.043 .707	R=+.006 .955

P<0.05 is significant

R= *Pearson's correlation that can range from -1 to 1*