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The Financial and Social Impact of Thalassemia and Its Treatment in Iran

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ABSTRACT

Background: Health care funders are struggling to meet the rising costs of medical treatments. Thalassemia is a costly disease. We aimed to examine the economic burden of thalassemia treatment in Iran. ***Methods:*** All thalassemic patients, registered at two hematology clinics of Tabriz in 2009 were invited to the study. Those who consented (100 patients) completed a simple questionnaire. ***Results:*** The total cost of treating thalassemia was €1,730.52 per patient/year. Total annual direct cost was €146,621.49 and indirect cost was €26430.22 for 100 patients. Blood transfusion and nursing charges were the most costly expenditures. It is estimated that up to €26 million/year is spent for treatment of all registered thalassemic patients in Iran. ***Conclusion:*** This study showed that a large amount of money is paid for thalassemia treatment by the government and patients. When the income of an average Iranian is considered, the magnitude of problem emerges.

Introduction

Health care funders including governments, social security funds, and insurance companies are struggling to meet the rising costs of medical treatments. Expenditure on drug therapy is a particular target for their attention for several reasons such as the size of the drug bill; the ease of measurement of pharmaceutical costs and evidence of wasteful prescribing.[1]

Thalassemia is a disease which needs lifelong therapy. Thalassemia therapy includes regular blood transfusion, administration of several medications such as iron chelating agents and other concomitant medications.[2] The cost of therapy in these patients as well as any other disease does not only cover medication cost. These extra costs include the cost of medical consultation, laboratory tests, diagnostic tests, cost of preventative or treatments of side effects of therapies and many other indirect costs. Indirect costs include travel expenses, the cost attributable to the loss of productivity by the patients or their caregivers, the impairment of well-being and all other related aspects.

There are 25,000 registered thalassemic patients in Iran,[3] and it is considered in category of special diseases by Ministry of health. These diseases are in need of special attention regarding their treatments, preventions or prevalence. Some examples of this type of disease are multiple sclerosis and cancers. Patients are financially supported by government. Almost all medications in Iran are subsidized by the government and a small fraction of the total cost of treatment/care is paid by the patients such as iron chelating therapies (ICTs) in thalassemia treatment. There is also insurance coverage for these patients. Despite coverage of many of the costs of therapy, parts of the cost are not paid by the government or the insurance companies and are paid by the patients themselves.

In the present study we tried to examine the economic burden of thalassemia treatment on the government, insurance companies and the patients.

Materials and Methods

All beta-thalassemic patients attending two hematology clinics, were invited to the study. These two thalassemia centers cover patients from East Azerbaijan province and the neighborhood provinces. Patients were provided with information and those who consented, were included in the study. Because the study was not interventional, according to Iranian Ethics codes and rules, it did not need ethical approval, but every effort to protect the patients' rights, confidentiality and wellbeing was taken. The

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questionnaire was consisted of 3 sections; demographic information, treatments and cost of treatment. Patients' record provided information on number of physician visits and medication used. The cost of the medications, laboratory tests, and physician visits and blood preparations was obtained from pharmacies, laboratories, physicians, and blood banks, respectively. The history of the illness and the side effects was collected by the questionnaire completed by the patients. This information was used to estimate the direct and indirect cost of thalassemia therapy.

Direct Costs

Direct costs included costs of transfusion, iron chelating therapy (ICT), concomitant medications, hospitalizations, physician visits, nursing cost, laboratory tests, and instrumental tests using the previously mentioned sources.

The direct costs were analyzed and reported in two major subtypes; shared and individual costs. The costs were estimated for one year of therapy using the amount of the resource consumed during the observational period. The costs were reported as Euro, which equaled to 13,733 Rials (Iranian currency; date 10/06/2009).[4]

Indirect Costs

Indirect costs included transportation costs and costs of productivity losses. The travel cost was reported as mean cost paid by patients for a year for treatment related travels. The productivity losses was reported in two age groups; one for 6-18 years old as loss of education and another for over 18 as loss of income. Converting educational losses into monetary is impossible so we reported number of patients with educational retardation.

Productivity loss for over 18 years old patients was measured by the number of days patients and/or the parents missed working activities in the past 12 months because of the treatment. Iranian GNI (gross national income) per capita in 2008 was retrieved from World Bank website. The average daily income of each Iranian was assumed to be 1/365 of GNI per capita.[5] Figure 1 shows method of cost analysis in the present article. SPSS software, version 14 was used for analyzing the data.

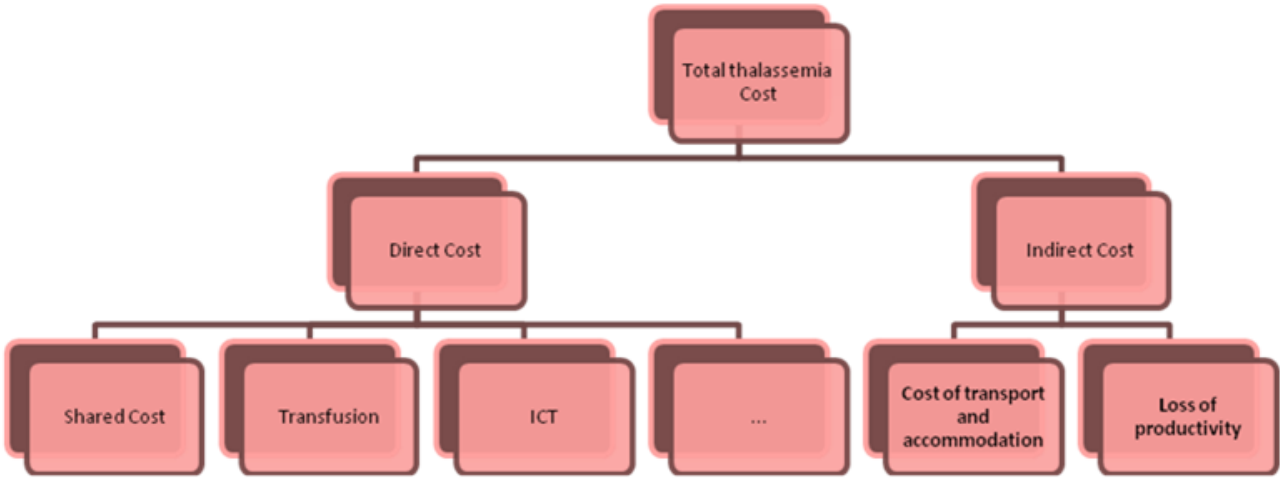

Figure 1. The costs of thalassemia treatment.

Results

Data was obtained between August 2008 and July 2009. Out of 148 registered subjects, 100 (67.56 %) patients participated in the study and 48 were excluded from the analysis because of irregular visits to the centers (44 patients) or refusing to take part in the study.[4] Eighty seven questionnaires were distributed among patients in pediatric center and thirteen in the adult center. The samples had a normal distribution of age; ranging from 4 months to 65 years old and with median age of 14.25±11.06 years. Forty three were female and 57 were male. Median ages of female and male subjects were 18.5±14.9 and 13.3±6.9 years, respectively. Out of 26 patients over 18 year-old patients, 38.5% were married but only 34.6% reported living with their spouse. 44 patients had familial history of the disease.

Mean age of diagnosis and age of beginning of treatment were 4.0±8.6 and 4.1±8.9 years, respectively. The mean duration of diagnosed disease and its treatment were 11.50±0.76 and 11.34±0.75 years, both ranging from 4 months to 32 years. Total duration of diagnosed disease and its treatment in 100 subjects were 1149.74 and 1133.74 years, respectively.

Number of visits to the hospitals was once a month for 81 patients and twice a month for the rest. 78% of the subjects filled their prescription from the hospitals' pharmacies and the rest from city pharmacies or the Red Crescent pharmacy. Number of medications received by the patients was 3.9±1.9 (0–9 medications).

Direct cost

Shared Costs

Some types of costs such as nurses and nurse assistants' salary, center physician were shared among patients. These included physician (general and specialist), nurses and assistant nurses' salary. Three part time nurses and three part time assistant nurses worked for each hospital for net annual salaries of €3652.96 and €1909.5, respectively. The total annual salaries of six nurses and 6 assistant nurses added up to €33374.76. Based on each patient's number of physicians' visits, the mean cost of the in-center physician visit in a year was €74.20 (±4.89), which added up to €7419.64 for all 100 patients/year. The total cost of physician visits for the duration of treatment for all patients estimated to be €8,530,656.89. Medical staff salaries were covered completely by the ministry of health and medical education.

Transfusion

The cost of preparing a blood bag is about €55.348 and the extra cost of preparing packed cells needed for thalassemic patients was estimated as €24.21 (Personal conversation with the head of laboratory of Tabriz Blood Bank). The annual cost of the necessary blood supply for all 100 patients was €58,104.0.

ICTs

Deferoxamine mesylate (DFO) was the only ICT used by these patients. Estimation of annual cost of DFO used by the thalassemic patients was a complicated issue. The treatment protocol, states a dose of 30-50 mg/kg (mean of 40 mg/kg) injected five times/week. But for patients younger than 18, protocol was changed slightly due to serum ferritin level and a dose of 20-40 mg/kg (mean of 30 mg/kg) injected five times/week was recommended.

For 2-10 years old patients, with median weight of 19.5 kg, on average 585 mg DFO was needed for each injection (30 mg/kg). This was equal to 1.17 vials (DFO vial is 500 mg), but in the current settings, this amount was rounded upward and each patient received 2 vials. This was performed routinely in these clinics to reduce the anticipated occurrence of hemosiderosis when treating for thalassemia. The excess DFO (about 0.83 vials) was the extra injection. It is expected that the extra DFO cause a reduction in prevalence of hemosiderosis in these patients but according to the centers physicians, still high number of hemosiderosis induced mortality is seen. Each year, about 520 vials were used by 31 patients aged 2-10 years old, of which 215.8 vials were extra. The median cost of DFO for each patient in this age group was €62.4 annually and €1,934.4/year for all 31 patients in this age group. According to our estimation €802.9 was just for the extra DFO in this group. Similar extra dose was seen in other age groups. Table 1 shows detail of cost of DFO used and extra dose in each age group and in all patients.

Table 1. Number of annual prescribed DFO vials and their cost

Age range group (years)	2-10	11-18	Over 19	Total
Number	31	43	26	100
Median weight (Kg)	19.5	36	55	-
Needed vials for each injection[1]	1.17	2.16	4.4	-
Number of prescribed vials for each injection	2	3	5	-
Number of annual prescribed vials per patient[2]	520	780	1300	2600
Number of annual prescribed vials for patients in age group[3]	16,120	33,540	33,800	83,460.00
The annual cost of prescribed vials per patient (Euro)	62.4	93.6	156	-
The annual cost of prescribed vials for patients in age group (Euro)	1,934.4	4,024.8	4,056	10,015.20
The annual extra vials number prescribed per patient[4]	215.8	218.4	156	-
The annual extra vials number prescribed for patients in age group	6689.8	9391.2	4,056	20137
The annual cost of extra vials prescribed per patient (Euro)	25.90	26.21	18.72	-
The annual cost of extra vials prescribed for the age group (Euro)	802.9	1127.03	486.72	2,416.65

[1] 30 mg/Kg of DFO vial for each injection was accounted in above table. For example the number of annual prescribed DFO vials and their cost for one patient in age range group of 2-10 years was accounted as below:

40 mg/Kg DFO * 19.5 Kg = 585 mg DFO (1.17 DFO vial) for each injection

[2] Number of prescribed vials for each injection * 5 injection each week * 52 weeks in a year

[3] Number of annual prescribed vials per patient * Number of age group

[4] Number of prescribed vials for each injection-Needed vial for each injection

* The extra vials number for patients in age group * 5 injection each week * 52 weeks in a year.

In summary, for the 100 subjects, 83,460 vials equal to €10,015.20 was used for iron chelating and equal to the content of 20,137 vials, which worth €2,416.65 was extra injected each year. The cost of infusion solution

used for diluting iron chelating agent was €9.19 per patient per year and total of €919.0 for all patients.

Co Committed Medications

Based on number of patients who received extra medication and dosage, monthly and annual cost estimated (Table 2).

Hospitalizations

Those who had been hospitalized in the past year (68 patients), reported that they had spent a mean of €54.60±12.70 (SE) on each time but many reported being hospitalized for free because of the circumstance of their illness. No highly cost surgery or hospitalization was reported for these patients in the past year. Total amount spent for hospitalization was €5405.00.

Table 2. Extra medications had taken by the patients and their annual and total cost.

Medication	Number of patients taking this medication	Annual cost (Euro)	Cost for the patients (Euro)
Folic acid	86	15.1	1298.60
Vitamin C	56	27.77	1555.12
Vitamin D	8	3.25	26.00
Vitamin K	35	156.1	5463.50
Calcium	66	7.57	499.62
Propranolol	6	2.52	15.12
Antibiotics	8	20.20	161.60
Insulin	4	378.78	1515.12
Furosemide	3	2.52	7.56
Hormonal Therapy	9	27.77	249.93
Levothyroxin	3	2.52	7.56
Calcitriol	1	580.81	580.81
Zinc Sulfate	3	0.09	0.27
Captopril	6	15.15	90.90
Digoxin	1	66.42	66.42
Ribavirin	1	18.68	18.68
Total cost per year: € 11,556.81			

Laboratory and Para-Clinic Tests

The annual cost for Para-clinical costs of each patients estimated as follow; routine laboratory tests (€16.36 ± 29.27), radiography (€13.83 ± 0.0), sonography and echocardiography (each €6.91±0.0). If these tests were performed at the laboratories of hematology centers, they would have been free of charge for the patients and would have been paid by the insurance company and the government (75:25) but if they were performed in private sectors, the cost would have been shared among the insurance company and the patients (50:50). The median cost of primary test for Bone Marrow Transplantation (BMT) was €133.35 and 12 patients had them done.

Instrumental Tests

Patients had some extra expenditure for used equipment with annual median costs of Syringe €33.20, injection set €6.91 and infusion pump €24.21 which was provided by the centers free of charge. Others included blood glucose test strips (€44.97), hearing aid (€41.51) and other equipments (€10.37) which were paid by the patients themselves. Any other equipment used by patients outside the centers was provided by the patients. We could not comment on these expenditures.

Medical Procedures

Despite that 12 patients reported having preliminary BMT; no one had tried BMT procedure itself. The 15 patients with splenectomy included 8 under 20 year-old male patients and 7 over 20 year-old female patients. Splenectomy was performed on these subjects at different times and it cost varied greatly over the years so we could not estimate this procedure cost.

Indirect Costs

Cost of Transport and Accommodation

The travel charge to and from the hospitals and pharmacy varied from case to case and it depended on the patients' condition and place of living. The travel costs of visit to and from the clinics each year ranged from €4.37 to €1048.57 with mean of €132.77±16.50. The total cost of travel for all patients was €13011.87/year. For the duration of their treatment up to the date of the study, it is estimated that €139,206.29 was spent for treatment related travels.

For those who had to pay for hotel during their treatment (2 patients), the annual cost was €348.69 which added up to €697.38/year.

Mean cost of travel to the pharmacy for those who lived in Tabriz was €120.06 while it was €348.69 for those who lived elsewhere. The total annual charge of travel to and from pharmacy for all patients was €1,680.85. The travel costs were paid by patients.

Loss of Productivity

Main income provider for patients and their families was the parent(s) (78%), husbands/wives (8%), patients (7%) and Imam Khomeini's Relief Foundation (3%). Patients reported that thalassemia caused financial problems (86%), social problems (66%), psychological problems (44%), while 5% reported having no problem. When all subjects were taken into account the earning reduction was observed in 8% of the patients and 63% of patients' parent(s). Imam Khomeini's Relief Foundation partly supported 5% of cases.

Out of 57 subjects aged 6-18 years old, 3.5% was illiterate, 78.9% and 17.5% had middle school and high school education. Most patients had fallen behind the level of the education they were supposed to be. Eighteen years old and older subjects (27 subjects) had greater and more obvious problems with their education. Out of these, 84.6% had less than 8 years of

education (primary or middle school), 42.3% had high school education and only 15.4% had university degrees. In total, the disease and its treatments had caused educational fallback for 60% of all subjects.

Out of 26 patients who were over 18 year-old, 26.9% reported being employed, 11.5% were students and 57.7% reported having no job. 45.5% reported having problems in performing/finding a job because of their disease. Conversion of setbacks in education or performing or finding a job into monetary unit is almost impossible so we only estimated the cost of missed days of work because of the treatment procedures. Number of days in which 100 patients or their parents missed work because of their treatment procedures especially blood transfusion were 130 days each month, which equaled to €11,040.12/year based on GNI per capita.[5]

Total cost

The total annual direct cost of therapy added up to €146,621.49 and the indirect cost was €26,430.22. The total annual cost of thalassemia treatment was €173,051.71 (Table 3). The cost of procedures done once or in a very limited times such as splenectomy or pre-BMT tests were not added to this amount.

Table 3. The costs of thalassemia treatment.

Cost		Number	Amount for all patients per year (Euro)	% of total annual cost
Direct costs: 146,621.49 Euro/Year	Transfusion	100	58,104.0	33.58
	ICT + diluting fluid	100	10,934.20	6.32
	Concommitted medications	100	11,556.81	6.68
	Hospitalizations	68	5405.00	3.12
	Physician visits	100	7419.64	4.29
	Nursing cost	100	33374.84	19.29
	Laboratory and Para-clinical tests	100	3710.00	2.14
	Instrumental tests	100	16,117.00	9.31
Indirect costs: 26430.22 Euro/Year	Transportation to/from hospital	100	13011.87	7.52
	Transportation to/from pharmacy	100	1,680.85	0.97
	Hotel	2	697.38	0.40
	Productivity losses	100	11,040.12	6.38
Total cost per year		-	173,051.71	100

Discussion

Although a considerable number of studies have estimated the cost of thalassemia prevention or ICTs costs, according to our knowledge; this was one of the few studies which tried to estimate overall impact of thalassemia management in Iran. The technique adopted for this study was not for making comparisons between alternative options such as cost-minimization or cost-effective analyses, but a survey of the impact of disease and current clinical practice.

The total cost of treating thalassemia was as far as we were able to gather €1,730.52 per patient/year. This means that up to €26 million for each year of thalassemia treatment of all 15,000 registered thalassemic patients in the country or in other terms almost €0.40 per Iranian/year is spent. In Abolghasemi and colleagues study, cost of prevention of birth of one child in two Iranian provinces was estimated to be 36,470 and 1568.25 $ for Sistan-Balouchestan and Fars Provinces, respectively.[6] As seen here, in a province with effective consultation (Fars), cost of prevention is less than cost of one year of thalassemia treatment of one patient. On the other hand in Sistan-Balouchestan province, because of ineffective consultation and religious marriages prior to official registration, prevention cost was 23 times more than Fars and almost equal to 21 years of treatment of a patient. Despite the latter estimated cost, prevention is far more economical than treatment especially if we consider life expectancy in these patients which is similar to non thalassemic patients and the duration of needed therapy.[7] Beside the financial effects of treatment, emotional effects of having a sick child or being sick for life could be a greater effect, which cannot put a price on.

Major part of thalassemia treatment was for blood transfusion and nursing charges, which was paid by government. It is customary practice to administrate thalassemic patients 2 bags of blood each month, so 2400 blood bags; equal to 480 liter of blood were needed for these patients each year. But these patients did not receive this amount of blood, mainly because of their number of visits to the clinics. We estimated the cost of blood transfusion based on the actual number of blood bags these patients received. In Iran blood is given free of charge by volunteer donors but costs of preparation of blood products are considerable.

For estimation of personnel costs, there are two important issues. First we did not add the bonuses that each staff might receive. Secondly, the nurses and assistant nurses did not work just for thalassemic patients and as any other hematology clinics, and these

costs were shared among all of those patients. But since presence of these staffs are necessary during the treatment of thalassemia patients, we decided to estimate the cost of nursing as if these patients were the only patients under care of the nursing staff. Similar issue was seen for physicians who visit several patients with different disease while receiving certain payment. Furthermore the physicians in the hematology clinics had different duration of work experiences and therefore received different salaries. We estimated physician visit cost based on the number of physician visits each patient received not based on each physician monthly salary to prevent the over estimation of the cost. Because the number of physician visit outside the centers was not available through patients records, we could only estimate this cost. Any undetected physician visit could be an element for under-estimation of the cost.

If a patient received his/her medicines from hospitals' pharmacy departments, they would be free of charge and the insurance companies paid 90% of its cost and the rest was paid by ministry of health and medical education but if they were bought from community pharmacies, the cost was covered by the insurance companies and the patients. Another important point is that the cost of ICT is much higher than its price tag in pharmacies and the government subsidizes its price to a great extent. If the subsidization did not exist, the cost of ICT would be about 5 times higher.

In a recent study among U.S. patients mean total medication costs were €59,233/year including €10,899 for DFO and €8,722 for administration of ICTs.[8] A previous study in Italy showed that the cost of items similar to the ones we studied was €4,911.92 patient/year and main payer in Italy was also the government.[9] The cost of thalassemia treatment in Iran was considerably lower than USA but this was close to what Italians spend on their patients.[9] Because of annual inflation and also changes in medical policies, cost has changed in the past and could change greatly in future. If we do not take annual inflation into account, overall cost of treatment for all 100 patients for years of treatment until the date of the study is estimated to be €2 million. This is without estimation of producibility or reproductively losses experienced by patients or their families. Preventative methods such as prenatal diagnosis can reduce number of these patients and as reported by WHO, the treatment/prevention cost ratio is 1.6.[10] Iran started its primary care thalassemia prevention program in 1996.[11] In Iran screening and offering selective abortion of pregnancy provides a practical option for reducing birth of new patients. Although the challenge of organizing such a program is difficult, especially because of the religious boundaries which are against abortion, the Iranian experience provides a good model to learn to many countries and even the developed ones.

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