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Thalassemic syndromes in Latium: epidemiological evaluation

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ABSTRACT

Background and Objective. **After the first National Census of transfusion-dependent thalassemics (1984), in 1992 the *Italian Association of Pediatric Hematology and Oncology and the National Health Institute* organized its 3rd edition. Here, results concerning Latium are presented and discussed.**

Design and Methods. **Data for Latium, as in the rest of Italy, were collected by a single reference center; among all eventual care centers for thalassemia initially contacted, only those with patients were sent data forms. For new cases, a questionnaire was submitted to parents to obtaining social data, and information on their knowledge of thalassemia.**

Results. **Collected data were divided into 2 groups: old cases, before June 30, 1988, and new cases, between July 1, 1988 and December 31, 1992. On the whole, 262 transfusion-dependent thalassemics (127 m., 135 f.) could be counted. Sixteen percent were affected with thalassemia intermedia, severe enough as to need regular transfusions. New patients (last 5 years): the birth of almost 80% of them was due to combined mistakes of parents and doctors. Disease evolution: 19/262 patients had been submitted to BMT (presently transfusion-free). Causes of death: 22 patients died in the considered period, mostly for cardiologic complications.**

Interpretation and Conclusions. **Data emerging from censuses on specific pathologies of high social impact (such as thalassemia) may help health plans to rationalize public expenditure, especially by improving working conditions of care centers.**

Key words: thalassemia, epidemiology, census, health policy

Thalassemia may be justifiably referred to as a *syndrome* in view of the fact that the severity of the clinical picture may vary considerably as the result of different genic disorders. The condition refers to a group of hereditary, recessive and autosomal anemias, characterized by deficient (+form) or total lack (°form) of synthesis of one of the peptide chains forming the globin component of hemoglobin synthesis.

From a genic point of view, a truly homozygous state is rare; a *double heterozygous* or *genic compound* state is much more commonplace. This explains why, considering that over 100 different forms of genic variants have been identified, an essentially clinical description appears to be the most useful (based on phenotypes) according to the severity of the condition: thus thalassemia is described as major, intermediate or minor.[1] The seriousness depends on various factors: the age at which the deficient Hb synthesis becomes clinically apparent, the extent of the α/non-α synthesis' ratio disorder that conditions the seriousness of the defective erythropoiesis, and the existence of other types of hemoglobin in red blood cells, which may compensate in part for the deficient synthesis.

In Italy, the most common form of the disease is β-thalassemia. Like sickle-cell anemia, the disease that occurs in the same areas as malaria, thus the areas most affected are the Po delta, Sicily, Sardinia, Calabria and Campania. The co-existence of the two illnesses is explained by partial protection against *Plasmodium* afforded by the heterozygous phenotype (sick gene/healthy gene). Moreover, on account of internal migration, thalassemia has reached new areas of Italy where no cases of malaria have been recorded.

The clinical manifestations of thalassemia syndromes are now well known,[1] as are main therapies.[2] As a result, over 95% of properly treated patients live to the age of 15, and over 80% live to over 20. Complete recovery, once possible only for the youngest patients, is now a feasible prospect for patients of all ages and is achievable by means of a bone marrow transplant.

In terms of prevention and its consequences on affected populations, researches conducted in Sicily, Sardinia, Latium and Ferrara have shown that there has been a fall in the number of young people affected and a rise in older sufferers.[3-5] As a result of correctly applied preventive screening programs in Sardinia over the past 15 years, the specific birth rate went from 1:250 to 1:1200 born alive,[6,7] to further fall to 1:4000 in 1996, when 94% of the cases were prevented.[8] In Sicily, the birth rate per 10,000 inhabitants fell from 9.7 to 1.7 between 1981 and 1988.[9] In Latium, in the same period, the birth rate decreased from 1.2 to 0.5, up to reach 0.3 in 1992 (ref. #5, see this reference also for a broader review of the results of prevention programs up until 1994 in all of Italy).

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An outline of the epidemiology of thalassemia major

Thalassemia syndromes, once considered to be an exclusively Mediterranean disease are, in reality, spread throughout the world. Consequently, numerous authors in many countries have conducted epidemiological studies on their distribution.[10] In 1984,[11] it was calculated that there were over 200 million carriers of a gene responsible for hemoglobinopathy, equivalent to 4% of the world's population. According to the same author, 240,000 babies born worldwide every year were affected by a major form of β-hemoglobinopathy, and of these 20% was affected by β-thalassemia.

In Asia,[12,13] there is a high frequency of both β and α thalassemia. In particular, it was calculated that in Thailand, out of a population of some 45 million inhabitants, over 28,000 affected babies are born in each generation, whilst in India, there are at least 25 million carriers of the gene (with an average prevalence of 3.3%) and a specific birth rate of 9,000/year. Of these affected children, no more than 10-15% will receive adequate treatment.

In Europe, thalassemia is not restricted to the Mediterranean, but has also reached the continent as a result of internal migration. In France, research conducted between 1989 and 1992 by Lena-Russo *et al.*[14] identified 241 cases of thalassemia out of a population of 56.6 million (prevalence = $1.544 \cdot 10^{-5}$), 29.8% of which were concentrated in the Paris area, whilst the remaining 70.2% of cases were distributed in 40 other metropolitan areas. The highest incidence was found in the capital of Belgium also;[15] the authors point out that the 2.9 new cases of the disease every year are almost entirely attributable to the lack of an effective campaign to prevent the disease amongst immigrants since 59.7% of foreigners living in Belgium come from endemic areas. To confirm the importance of migration and effective prevention, Modell *et al*.[11] demonstrated that the most affected ethnic groups in Great Britain are Cypriots and Asians, that Italian and Chinese are affected to a lesser extent and that native Britons very rarely suffer from the disease. The same study points out that 17% of Anglo-Cypriots are heterozygous for β-thalassemia, a figure which roughly corresponds with the figure for Cyprus from 1973-1980;[16] according to this study, 17.2% of the population suffers from microcythemia. In Portugal, Martins *et al*.[17] conducted a random study, analyzing 15,208 blood samples; they discovered that the average prevalence of β-thalassemia trait was 0.45% and that the incidence was higher in the South of the country where a greater number of African immigrants had settled, especially during the colonial period. This factor also played an important role in Spain,[18,19] where a total of 894 carriers of the disease were identified.

The first figures on the diffusion of microcythemia in Italy have revealed that insular areas of Southern Italy have the highest incidence of microcythemia.[20] Furthermore, within these areas, the incidence was highest in coastal areas. However, massive shifts of the population from the South to the industrial areas of the North in the fifties gave rise to new hotbeds of microcythemia in outlying areas of Genoa, Milan and Turin. Cao *et al*.[22] have also conducted detailed and more recent studies on the thalassemia trait: the highest concentrations were found to be in the Po Delta, Sardinia, Sicily, Calabria and Southern Apulia (7-13%) whilst the figure fell to 5-7% in Northern Apulia, Campania and Piedmont, to 2-5% in Latium and Northern industrial areas and less than 2% in the remaining Central/Northern areas.

Despite the vast diffusion of the thalassemia trait and consequently the existence of a large number of people affected by Cooley's disease, the *National Register of Thalassemics* was only set up in 1984. Sicily alone had set up its own regional observatory in order to carry out a census of the disease (*Sicilian Register of Thalassemia and Hemoglobinopathy* [also known as RESTE]).[23] In 1984, the AIEOP began gathering data for a national census of transfusion-dependent thalassemics (unpublished data). Fifteen Italian regions participated in the census by sending in data, even though incomplete at times. It was thus possible to identify 2,962 proven cases, a figure that corresponds to the number of carriers throughout Italy. If we add the estimated number of patients in the regions for which no figures or only incomplete figures are available, the overall (estimated) number of sufferers is between 5,000 and 5,500.

Specific epidemiological studies in the Latium region

A prevention and screening campaign, sponsored by the *Regional Health Council*, has been underway since 1975. The campaign is organized by the *Fondazione per la Lotta alla Microcitemia in Italia* (i.e. *Foundation for the Fight against Microcythemia in Italy*) and particularly by *Rome's Microcythemia Research Center*. The results of this screening program,[20] involving all pupils attending the second year of intermediate school, gave a very clear idea of the frequency of the thalassemia trait amongst the population of Latium. The prevalence was found to be 2.5% of all the forms of microcythemia, form β accounts for 90% of cases; interestingly, there is evidence for a quite high incidence of silent or sub-silent phenotypes of both α and β thalassemias, which in Latium reach the figure of 15.27% of all phenotypes.[21] The thalassemic trait is not evenly distributed throughout the various provinces, with the lowest incidence in Rieti (1.3%) and the highest in Latina (2.9%).

The above-mentioned *National Census of Transfusion-Dependent Thalassemics* had revealed that in the region, where the response rate was lower than 50%, there were 117 cases of the disease, with a specific birth rate of 0.02. As other surveys had already revealed,[14,15]

there appeared to be an uneven distribution of cases in the province, with the highest number of cases in the capital.

The census was repeated in 1987 (unpublished data). In the case of Latium, the census revealed only 3 new cases in Latina, Frosinone and Rome, although again, the centers that took part in the census showed a general lack of enthusiasm.

Materials and Methods

Ten years after the creation of the *National Register of Thalassemics*, the AIEOP backed by the *Istituto Superiore della Sanità* (*National Health Institute*), organized the third national census of transfusion-dependent thalassemics throughout the whole of Italy.

The data for the Latium region were organised, collected and processed by the *Special Service for the Diagnosis and Treatment of Thalassemias and Hemoglobinopathies during Growing Age*, which is part of "La Sapienza" University in Rome.

Initially, all hospitals in the Latium region were contacted, irrespective of whether they had a blood transfusion centre, as well as the *Microcythemia Center*, the *Italian Red Cross* in Latina and the *National Blood Transfusion Center* in Rome, in order to discover whether each individual hospital or center was treating transfusion-dependent thalassemia sufferers. With the sole exception of the *Microcythemia Center*, whose patients can be traced easily since they have to attend other centers for blood transfusions, all hospitals with thalassemics patients in their care declared to be interested in taking part in the census (see Table 1) and they were therefore sent data forms.

Once the forms were filled in and returned, an initial screening test was carried out in order to identify the cases that were being treated simultaneously by more than one center (a normal occurrence in such a chronic pathology); these patients were attributed to the center responsible for the majority of the treatment. The information was then subdivided into two groups:

- cases diagnosed before June 30, 1988, for which the causes of the disease were already known on account of earlier censuses;
- new cases diagnosed between July 1st, 1988 and December 31, 1992.

For both groups, the doctors in charge of the patients were re-contacted. Apart from personal details about the patients, doctors were also asked to provide general information on the patient's condition, state whether a bone marrow transplant had been carried out, advise if the patient had been transferred to or from other centers as well as give the reasons for the patient's death, if applicable.

In addition to a pure epidemiological survey, the parents of newly diagnosed patients were also asked to fill in a semi-anonymous questionnaire (patients were identified by their christian name + the first letter of their surname). The form included questions on the family's social/cultural/financial status (occupation, education, if any brother or sisters were also affected) as well as on information received on thalassemia, both before and during pregnancy. To complete the questionnaire, there was also a section on medical data which may have been underestimated during pregnancy (anemia, father's health, prenatal diagnosis and refusal of induced abortion).

Census results

The census established that there were 262 (127 male, 135 female) transfusion-dependent thalassemia sufferers in Latium at December 31, 1992. The prevalence rate for the period in question referred to the population residing in Latium at the time of the 1991 census, was found to be equivalent to $8.65 \cdot 10^{-5}$. The distribution of patients amongst the various treatment centers is given in Table 2. The distribution by diagnosis is given in Table 3.

Figure 1 shows the distribution of patients by five

Table 1. Treatment centers contacted during the 1992 census.

Rome	• Bambino Gesù Pediatric Hospital, I.R.C.C.S.
	• National Blood Transfusion Center
	• Pediatric Clinic, 'Umberto I' University Hospital
	• Sant'Eugenio Hospital
	• Traumatology and Orthopedic Center
	• San Camillo Hospital
	• Sandro Pertini Hospital
	• University Transfusion Center and Hematology Clinic, 'Umberto I' University Hospital
	• A. Gemelli Hospital, 'Sacro Cuore' Catholic University
Viterbo	• 'Bel Colle' Hospital
Velletri	• Hospital
Latina	• Hospital
	• Italian Red Cross

Table 2. Distribution of patients amongst the different treatment centers.

Treatment centers	No. of patients
Rome - Pediatric Clinic, Umberto I Hospital	55
Rome - Bambino Gesù Hospital	37
Rome - C.N.T.S.	16
Rome - C.T.O.	3
Rome - A. Gemelli Hospital	1
Rome - S. Camillo Hospital	1
Rome - Sandro Pertini Hospital	16
Rome - S. Eugenio Hospital	96
Rome - Hematology Clinic Umberto I Hospital	21
Viterbo - Hospital	4
Velletri - Hospital	3
Latina - Hospital	9
Total	262

Table 3. Distribution of patients by diagnosis.

Diagnosis	No. of patients
Major β°-homozygote	204
Major δ-homozygote	3
Major β+-homozygote	3
Major β/δβ	1
Major β/Lepore	2
Major β/βS	8
Major βS homozygote	1
Intermediate β-homozygote	23
Intermediate β/δβ	1
Intermediate β/βS	1
Intermediate (others)	15

Table 4. Normal demographical changes (births, deaths, moves in/out) of affected population during the five-year period 1988-1992.

Presents at Dec. 31, 1987	206	+
Newly diagnosed	18	+
Moved into Latium	43	+
Referred to Latium Hospital	32	=
Total 1	299	
Transplants	19	+
Deaths	10	+
Moved from Latium	8	=
Total 2	*37*	
Total 1	299	–
Total 2	37	=
Total to Dec. 31, 1992	*262*	

Table 5. Newly diagnosed patients in the period 1988-1992, subdivided according to the causes for their birth.

Causes of birth	*% patients*
Combined errors made by physicians and parents	76.3
Errors made by physicians	10.7
Risk taken by parents	8.6
Refusal of prenatal diagnosis	1.1
Refusal of induced abortion	0.0
Laboratory errors (microcythemia's diagnosis)	1.1
Laboratory errors (prenatal diagnosis)	2.2
Unknown father	0.0

year age groups (range: 1.41-75.08 years). The graph shows the pseudo-Gaussian distribution of the age of patients, where the left half of the curve reflects mortality and the right half of the curve reflects the fall in new pathologies as a result of preventive medicine. In view of the fact that during the five years in question,

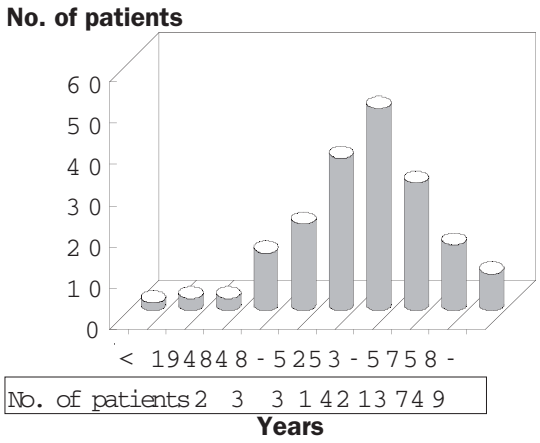

Figure 1. Distribution of patients by five year age groups.

the population was affected by normal demographical changes (births, deaths, moves in/out), Table 4 shows the extent of the phenomena with figures referring to the date of the census.

Table 5 shows newly diagnosed patients i.e. those diagnosed between 1988 and 1992, subdivided according to the causes of their birth. Of these, 76.3% were the result of combined errors made by doctors and parents. With regards to the remaining cases, it is worth pointing out that in 10.7% of cases, the error can be attributed exclusively to doctors who, despite knowing that one of the parents was a carrier, did not screen the other parent.

The specific birth rate from 1988 to 1992 is given in Table 6; it should be noted that the figures given for 1991 and 1992 are not final since the time-lag for diagnosing thalassemia can be as long as two years.

Specific population migration figures showing the provinces of birth and residence are summarized in tables 7 and 8 respectively. Four out of five patients born in Viterbo (=80.0%) choose their local hospital for treatment, with only one out of five preferring Rome for treatment. Of the 25 patients born in Latina, 47.8% are treated by the hospital in Latina and the remaining 62% of patients are treated by a hospital in Rome (most chosen for the Bambino Gesù hospital). Of the 11 patients born in the province of Frosinone, 18.2% (=2 cases) are treated by the hospital in Latina with the remaining 81.8% opting for Rome, the most popular again being the Bambino Gesù hospital (27.2%). The only patient born in Rieti attends the Umberto I hospital for treatment. Finally, the 130 patients born in the province of Rome are virtually all treated by hospitals in the capital (i.e. 33.8% go to the Sant'Eugenio for treatment, 21.5% to the Umberto I hospital, 7.7% to the National Blood Transfusion Center, 10.8% to the Bambino Gesù, 12.3% to the Chair of Hematology at the blood transfusion center, 7.6%

Table 6. Specific birth rate of thalassemic patients in Latium from 1988-1992 (source: ISTAT).

Year	Live birth (no.)	Total birth /1000	Thalass. Birth (no.)	Periodal prevalence Thal. birth /10^{-5} live birth	D%°
1978	61.432	12.2	19	30.9	.....
1979	59.148	11.7	2	3.4	-71.43
1980	56.622	11.1	3	5.3	-57.14
1981	53.586	10.7	6	11.2	-14.29
1982	54.462	10.8	6	11.0	-14.29
1983	53.265	10.5	6	11.3	-14.29
1984	55.173	10.2	2	3.6	-71.43
1985	50.175	9.8	1	2.0	-85.71
1986	48.424	9.5	3	6.2	-57.14
1987	48.687	9.5	4	8.2	-42.86
1988	50.957	9.9	2	3.9	-71.43
1989	49.850	9.6	6	12.0	-14.29
1990	50.897	9.8	1	1.9	-85.71
1991*	52.521	10.2	0	0	
1992*	51.421	10.0	0	0	

**The figures given for 1991 and 1992 are not final, considering that the maximum currently accepted delay for the diagnose of thalassemia is of two years.*
°Percentage change from the expected figure, based on mean number of births during the five-year period 1974-1978.

to the Sandro Pertini hospital and finally 2.3% go to the Center of Orthopedic Traumatology). The remaining 3.8% opts for Velletri (2.3%) and Latina (1.5%). With respect to the province of residence, the total number of transfusion-dependent thalassemics residing in Latium over the five year period is greater than the number of patients born there: the increase is distributed evenly throughout the provinces with the exception of Rieti where there are no resident thalassemics. Table 9 compares birth/residence figures. In Rome, the increase in the resident population compared to those born there is 43.6%; all these patients are treated by hospitals in the city.

Table 10 shows the municipalities in Latium with the greatest number of children born with thalassemia. If the figures for the municipalities are compared to those for the respective provinces, it emerges that approximately 1/10 of all patients born in the Roman province were born in Velletri, whilst over half of those born in the province of Latina were born in Fondi, Formia and Terracina, and over 1/4 of all those born in the province of Frosinone were born in Sora.

Regarding the evolution of the illness, 19/262 patients had been given a bone marrow transplant at December 31, 1992; 12/19 transplants were carried out by the Civil Hospital in Pesaro, 5/19 by the BMT Unit at the Civil Hospital in Pescara and 2/19 by the San Camillo Hospital in Rome. Twenty-two patients have died since the 1984 census (the causes of death are given in Table 11). The deaths are not evenly distributed over the years reaching a peak between 1985 and 1988.

Comments

Although the census figures require no special comments, it is worth mentioning a few aspects that do not emerge from a purely epidemiological assessment. First of all, a comment on the distribution of the diagnoses: a fairly substantial percentage of patients (16%) are affected by a form of intermediate thalassemia which is nonetheless serious enough to require regular blood transfusions. This fact demon-

Table 7. Distribution of thalassemic patients by treatment centers and province of birth.

	Viterbo		Rieti		Rome		Latina		Frosinone		
Treatment center	no	%	no	%	no	%	no	%	no	%	Totale
Bambino Gesù Hospital	0	0.00	0	0.00	14	10.77	5	21.74	3	27.27	22
Pediatrics Cl. Umberto I Hospital	0	0.00	1	100.00	28	21.54	4	17.39	2	18.18	35
C.N.T.S.	0	0.00	0	0.00	10	7.69	1	4.35	0	0.00	11
Hematology Cl. Umberto I Hospital	0	0.00	0	0.00	16	12.31	0	0.00	1	9.09	17
Velletri Hospital	0	0.00	0	0.00	3	2.31	0	0.00	0	0.00	3
"Bel Colle" - VT Hospital	4	80.00	0	0.00	0	0.00	0	0.00	0	0.00	4
Gemelli Hospital	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0
Latina Hospital	0	0.00	0	0.00	2	1.54	11	47.83	2	18.18	15
S. Camillo Hospital	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0
C.T.O. Rome	0	0.00	0	0.00	3	2.31	0	0.00	0	0.00	3
Sandro Pertini Hospital	1	20.00	0	0.00	10	7.69	1	4.35	0	0.00	12
S. Eugenio Hospital	0	0.00	0	0.00	44	33.85	1	4.35	3	27.27	48
Total	5	100.00	1	100.00	130	100.00	23	100.00	11	100.00	170

Table 8. Distribution of thalassemic patients by treatment centers and province of residence.

Treatment center	Viterbo		Rieti		Rome		Latina		Frosinone		Totale
	no	%	no	%	no	%	no	%	no	%	
Bambino Gesù Hospital	0	0.00	0	0.00	26	13.88	6	23.07	3	21.43	35
Pediatric Cl. Umberto I Hospital	1	16.67	0	0.00	38	20.33	4	15.38	4	28.58	47
C.N.T.S.	0	0.00	0	0.00	17	9.09	0	0.00	0	0.00	17
Haematology Cl. Umberto I Hospital	0	0.00	0	0.00	15	8.03	2	7.69	1	7.14	18
Velletri Hospital	0	0.00	0	0.00	2	1.07	1	3.85	0	0.00	3
"Bel Colle" Viterbo Hospital	4	66.66	0	0.00	0	0.00	0	0.00	0	0.00	4
Gemelli Hospital	0	0.00	0	0.00	1	0.53	0	0.00	0	0.00	1
Latina Hospital	0	0.00	0	0.00	1	0.53	12	46.15	2	14.28	15
S. Camillo Hospital	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0
C.T.O. Rome	0	0.00	0	0.00	4	2.15	0	0.00	0	0.00	4
Sandro Pertini Hospital	1	16.67	0	0.00	13	6.96	1	3.86	0	0.00	15
S. Eugenio Hospital	0	0.00	0	0.00	70	37.43	0	0.00	4	26.67	74
Total	6	100.00	0	0	187	100.00	26	100.00	14	100.00	233

Table 9. Comparison by place of birth and of residence, respectively.

Province	Born	Residents	Variation %
Viterbo	5	6	+20.0
Rieti	1	0	-100.0
Rome	130	187	+43.8
Latina	23	20	-13.0
Frosinone	11	14	+27.2

Table 10. Municipalities in Latium with the greatest number of children born with thalassemia.

Municipalities	No. of patients	Periodal prevalence rate ($x10^{-5}$)
Velletri	9	20.7
Fondi	5	16.0
Formia	4	11.4
Terracina	3	8.1
Sora	3	11.5
Rome	110	3.9
Viterbo	3	5.1
Latina	7	6.6

Table 11. Causes for twenty-two thalassemic patient deaths since 1984.

	No. of patients
Initial cause	
cardiopathy	10
infection	1
liver pathology	1
Final cause	
cardiopathy	12
unknown	10

strates the enormous variety of phenotypes for the pathology and the difficulty in establishing precise nosographical classifications.

A comment should also be made on the figure regarding the birth of certain thalassemics in the Latium region where a screening program has been underway since 1975. The distribution of the causes of new cases must also be underlined; despite the unacceptably high rate of laboratory errors (5%, though the figure probably cannot be furtherly reduced), it is much more serious that, at the moment the census was performed, 87% of new cases of thalassemia were attributable to the ignorance of medical staff (that of doctors alone or combined with the parents' ignorance). These statistics clearly demonstrate that widespread information was still not available on the disease.

As far as the migration of the population is concerned, it is easy to appreciate that Rome, the heart of Latium in terms of commerce and employment, absorbs the majority of patients who are non-residents in the region (or even coming from overseas) due also to a wider *choice* of facilities. It would be interesting to determine if the migration is fortuitous or determined by the illness. However, given its very nature, the census cannot provide information on this point. Non-conclusive evidence is provided by the experience of our own center: in the case of the Pediatric Clinic at the Umberto I hospital, all changes of residence were fortuitous, though this was not the

case for patients who did not live in the city or in the region: it is feasible that these patients move periodically to other parts of Italy, despite the fatigue and cost involved, in the hope of obtaining better treatment than in their cities of origin (mostly in Southern Italy).

With regards to the origins of patients born and/or treated in Latium, we have attempted to identify any clusters of new cases. This sort of assessment is outside the scope of the census since no information is given on the origins of the patients' parents, and the data on births does not take migration into consideration. Despite the limitations, it is interesting to see that in the province of Latina, there are clusters of new cases outside the provincial capital, in Fondi, Formia and Terracina, whilst in the case of Frosinone, new cases occurred in Sora and in the town of Frosinone itself. It would thus seem reasonable to assume that the formation of these clusters is due to the genic drift typical of geographical areas with a high level of endogamy.

Finally, here is an observation on the deaths. Although the survey goes back only 8 years, it confirms what empirical observations have taught health workers for a long time, i.e. that deaths tend to occur over a relatively brief period (3-4 years) followed by periods of relative *well-being*. A convincing explanation for the phenomenon is yet to be found. With regards to the age of the deceased, it should be noted that improved treatment over the past 8 years has made no change in the average age of death, nor has there been any change in the main cause of death, which is still cardiopathy.

Conclusions

Data emerging from censuses on specific pathologies, especially when they cover multiple and ultra-specialized areas such as thalassemia, arouse great interest not only in strictly scientific terms, but also in terms of health policy and thus financial terms.

Indeed, all chronic illnesses need to be monitored by doctors/specialists; in view of the need for frequent check-ups, the cost to the individual and society as a whole (as occurs in Italy) is never negligible. Considered from this angle, thalassemia is perhaps one of the best examples. For years, thalassemics have been considered to be completely *passive* in terms of economic productivity. Even if this is not entirely true, on the basis of the information available for Rome, it is reasonable to estimate that 70 to 90% of transfusion-dependent thalassemics are still classified as 100% disabled and entitled to social security benefits. Furthermore, even when the work force is potentially unaffected (e.g. individuals not classified as disabled or children have been recently diagnosed), the need for special treatment and care results on the one hand, in school days and/or working days being lost (both may be lost because children are usually accompanied by a working parent) and on the other hand, in an outlay for medical assistance. Given the complexity of the treatment offered for thalassemia, patients must almost invariably be admitted to hospital and treated either in wards or as outpatients. Whichever method is chosen, the treatment lasts one day for younger patients and 2-3 days for older patients at intervals of 20-25 days, but treatment may be required as often as every 7-15 days, i.e. for blood transfusions. In addition, patients may also be admitted for routine checks or following acute or chronic complications.

In view of the above, we believe that the data that has emerged from the census may influence health policy so helping to curb and rationalize public expenditure. This could be achieved by:

- improving working conditions in many centers, especially in the South of Italy. By offering better local treatment, the number of *commuter* patients could fall;
- classifying a select number of centers as level 2 centers capable of offering thalassemics full treatment; level 1 centres would be left to monitor and care for patients on a day-to-day basis. This could lead to a cut in the cost of clinical tests and a better management of existing resources;
- identifying the patients being treated by more than one center. This could be the first step in discouraging this phenomenon, undoubtedly extremely costly in terms of direct public expenditure (tests repeated by more than one centre where communications between centers are either poor or non-existent) and indirect expenditures (time spent by doctors and paramedics is doubled or tripled, expenses, reimbursement of transfer costs, etc.);
- acknowledging that serious deficiencies in prevention and information supplied to the general public can still be present, even if not to the same extent as it was in the past. This could be the best way to overcome these problems. In the long term, this approach could even result in gaining complete control over the disease.

A final comment, in order to explain the delay in presenting these data: transformed data and statistical analysis were first available only in the second half of 1995. Thereafter, according to a *gentlemen's agreement* with the census board, single regions were restrained from publishing their data until national figures could be formally presented. Only recently, this restraint was cast aside.

Contributions and Acknowledgments

AV was responsible for the conception and the design of the paper as well as the writing of the paper, and directing the recruitment of Latium's hospitals involved in the study. PC shared with the former one the responsibility of the recruitment and was directly responsible for day-to-day contacts with participants. FGS managed the collection of rough data and

their handling. RF and MP actively contributed to the execution of the study and to the writing of the paper. GB was mainly responsible for statistical analysis and results' interpretation, to which, however, all authors contributed too; moreover, he gave his final approval of the version to be published.

The order in which authors' names appear was chosen according to the importance attributed to their practical and intellectual contribution to the study, with the only exception of the last name, to which the same importance as the first name is to be attributed.

Disclosures

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