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BRIEF ARTICLE

Burden of celiac disease in the Mediterranean area

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Abstract

AIM: To estimate the burden of undiagnosed celiac disease (CD) in the Mediterranean area in terms of morbidity, mortality and health cost.

METHODS: For statistics regarding the population of each country in the Mediterranean area, we accessed authoritative international sources (World Bank, World Health Organization and United Nations). The prevalence of CD was obtained for most countries from published reports. An overall prevalence rate of 1% cases/total population was finally estimated to represent the frequency of the disease in the area, since none of the available confidence intervals of the reported rates significantly excluded this rate. The distribution of symptoms and complications was obtained from reliable reports in the same cohort. A standardized mortality rate of 1.8 was obtained from recent reports. Crude health cost was estimated for the years between symptoms and diagnosis for adults and children, and was standardized for purchasing power parity to account for the different economic profiles amongst Mediterranean countries.

RESULTS: In the next 10 years, the Mediterranean area will have about half a billion inhabitants, of which 120 million will be children. The projected number of CD diagnoses in 2020 is 5 million cases (1 million celiac children), with a relative increase of 11% compared to 2010. Based on the 2010 rate, there will be about 550 000 symptomatic adults and about 240 000 sick children: 85% of the symptomatic patients will suffer from gastrointestinal complaints, 40% are likely to have anemia, 30% will likely have osteopenia, 20% of children will have short stature, and 10% will have abnormal liver enzymes. The estimated standardized medical costs for symptomatic celiac patients during the delay between symptom onset and diagnosis (mean 6 years for adults, 2 years for children) will be about €4 billion (€387 million for children) over the next 10 years. A delay in diagnosis is expected to increase mortal-

ity: about 600 000 celiac patients will die in the next 10 years, with an excess of 44.4% *vs* age- and sex-matched controls.

CONCLUSION: In the near future, the burden of CD will increase tremendously. Few Mediterranean countries are able to face this expanding epidemic alone.

Key words: Pediatric; Celiac disease; Short stature; Anemia; Osteopenia; Purchasing power parity; Standardized mortality rate; Mediterranean area

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INTRODUCTION

Recent epidemiological studies show that the prevalence of celiac disease (CD) is underestimated not only in Europe, but also among the populations of Mediterranean regions such as the Middle East and North Africa[1-3], where its prevalence is similar to that recently observed in Western countries[4]. Indeed, in these two regions, a very high prevalence of CD has recently been reported both in the general population and in at-risk groups[2]. These high frequencies are associated with the widespread consumption of wheat and barley[1,5] and the high frequency of the DR3-DQ2 CD-predisposing haplotypes in these populations[6,7]. But these factors alone do not satisfactorily account for the spread of the CD epidemic in recent years[8,9]. The prevalence of CD among the general population varies from 0.14% to 1.17%[10-20]: 1%-1.3% in Turkey[10-12], 0.6%-0.96% in Iran[13,14], 0.5% in Egypt[15], 0.6% in Tunisia and Israel[16-19], and < 0.5% in Jordan, Lebanon and Kuwait[5,20]. Among high-risk groups [including patients with a positive family history, insulin-dependent diabetes mellitus (IDDM), thyroiditis] the prevalence of CD ranges from 2.4% to 44%, assessed by serological markers and biopsy[21-24].

Egypt, and indeed all North African countries, were significant producers of wheat, and largely used barley for beer brewing; they were considered the "granary" of Romans for over 4 centuries. Bread, mostly made of wheat flour and called "the survival" in some local languages[1], has been a staple food for thousands of years. Similarly, the widespread use of couscous [from grossly milled durum wheat (*Triticum durum*)] dates back over 2000 years. But the use of wheat and other gluten-containing cereals is also increasing in the countries where it has been a staple for centuries[25,26].

The diffusion of pasta across all the Mediterranean countries is relatively recent and stems from the industrial development of grain processing. Unfortunately, a side effect of this positive dispersal may be the enormous increase in gluten intolerance, which is at a truly epidemic level. CD is now a widespread public health problem that also involves the populations of developing countries, as well as China and India[27,28]. However, this epidemic is not fully recognized since a sizeable number of cases are neither diagnosed nor cared for. In many Mediterranean countries, few cases are diagnosed because of the low level of awareness, knowledge and skill to deal with the problem, the lack of diagnostic resources and the attribution of CD symptoms to other, similar, illnesses[5,20]. The low awareness of CD often leads to a delay in diagnosis, which contributes to an excess of medical costs (CD includes growth failure, infant malnutrition, gastrointestinal diseases, anemia and more than 20 associated symptoms and conditions) and mortality.

All partners taking part in this study agreed that, to date, the best available estimation of CD-associated medical cost was that reported by Long *et al*[29], and supported by Hershcovici *et al*[31]. The annual medical cost in the year preceding the diagnosis of CD, excluding diagnostic costs, was estimated to be $5023/patient, $1764 more than the cost of the same patients in the year after diagnosis[29]. In the four years preceding the diagnosis of symptomatic CD, the direct medical cost was estimated to be $11 037/patient. For a symptom- and age-matched control individual, not affected by CD, the cost after 4 years was estimated at $7073, with a difference of $3964 (about $1000/patient per year). This difference is due to increased in-patients admissions, out-patient cost, laboratory tests, radiology, and office visits[29]. The diagnosis of CD resulted in a 30% reduction in direct medical expenditure. A similar 30% reduction in direct medical costs after diagnosis of CD was reported by Green *et al*[30]; the mean medical expenditure decreased from $8502 per capita to $7133 for the 2 years after diagnosis of CD.

The CD epidemic is the largest epidemic of food-induced permanent disease in the Euro-Mediterranean region. Very few countries of this region are able to face this expanding problem. The aim of this study was to estimate what the burden of CD will be in the near future, and how the CD epidemic will affect morbidity, mortality and health costs. We aim to provide stakeholders with a reliable prediction of the incoming picture of CD in the Mediterranean area, and so enable them to take action to face this epidemic.

MATERIALS AND METHODS

Population statistics

For statistics regarding each country in the Mediterra-

nean area, we accessed authoritative international sources (World Bank, World Health Organization and United Nations). Population size, median age, number of children (0-14 years), population growth rate, birth rate, death rate, infant mortality rate and literacy were retrieved and validated across multiple sources. The projected population from 2010 to 2020 was computed by adopting the 2008 growth rate as a constant over the following decade because the predicted rate of change of the growth rate would have not significantly affected our estimate. The number of children was incremented yearly by the birth rate and corrected for the infant mortality rate although mortality from 1 to 14 years is minimal in all the countries included in this evaluation.

Celiac disease

The prevalence of CD among the populations of Mediterranean countries, such as the Middle East and North Africa[1-3], is similar to that recently observed in Western countries[4]. The prevalence of CD among the general population varies from 0.14% to 1.17%[10-20]: 1%-1.3% in Turkey[10-12], 0.6%-0.96% in Iran[13,14], 0.5% in Egypt[15], 0.6% in Tunisia and Israel[16-19], and < 0.5% in Jordan, Lebanon and Kuwait[5,20]. An overall prevalence rate of 1% cases/total population was finally estimated to better represent the frequency of the disease in the area, since none of the available confidence intervals of the reported rates significantly excluded this 1% rate. The rate of symptomatic *vs* asymptomatic patients was obtained from several reliable reports from the area[3,9,10,17]. In summary, 85% of symptomatic patients are likely to suffer from gastrointestinal symptoms, which include diarrhea, abdominal pain, vomiting, irritable bowel, and gastritis[5,13,20,32-37]. Among the non-gastrointestinal complaints, the available estimates suggest 20% of children are affected by short stature[5,20,33-35,37], 40% of all cases are affected by anemia[5,20,32,36,37], 30% are afflicted by osteopenia[32,33,35,37], and 10% by abnormal liver enzymes[37,38].

Mortality has been reported in excess of 1.8 compared to age- and sex-matched controls[31,39,40]. The risk of cancer in undiagnosed adults is significantly increased and the mortality is almost doubled in the total cohort of affected persons compared with the general population[41,44].

Crude medical costs

Crude health costs were estimated for the years between symptoms and diagnosis only for symptomatic adults and children, and were standardized for purchasing power parity (PPP) to account for the different economic profile among Mediterranean countries. Since gross national product is different across countries, the PPP is based on the law of one price; in the absence of transaction costs, identical goods will have the same price in different markets. The PPP equalizes the purchasing power of different currencies for a given basket of goods, thereby providing a standardized estimate of cost across countries.

We assume that the cohort of CD without symptoms does not increase the average medical cost compared to non CD individuals (but this should also be revised, since a significant number of patients identified by screening had a posteriori clinical symptoms). Therefore, medical costs are estimated only for 1:7 adults and 1:5 children with CD symptoms.

Table 1 Excess need of health resources before the diagnosis of celiac disease

	n	Adult cost (€)	*n*	Child cost (€)
In-patient admission	2	9818	1	2254
Out-patient admission	1	879	1	586
Medical consultations	3	100	3	150
Specialist consultations	2	150	1	50
Lab test	4	446	2	297
Total per patient		11 393		3337

For each individual adult we assigned (on the basis of the reports cited and the clinical experience of the study partners), a minimal period of 6 years of delay between symptom onset and diagnosis of the disease[45,46], while this delay was two years for each assigned child with CD[9,20]. During that period an adult with CD required, in excess of age- and sex-matched controls, at least: 2 in-patient admissions, 1 out-patient admission, 3 primary medical consultations, 2 specialized consultations, and 4 laboratory tests. Similarly, children needed at least: 1 in-patient admission and 1 out-patient admission, 3 medical consultations, 1 specialized consultation and 2 laboratory tests (Table 1).

Estimated medical costs

The costs of health services were estimated based on the 2007 costs of the Italian National Health Service (NHS) which is similar to that of several European countries. We summed the total costs of the medical services required for each child or adult patient to obtain a standardized cost/per patient before the diagnosis of CD was made (Table 1). In this way, we obtained an estimation of the financial load (only for medical expenses) of symptomatic patients. The estimated cost according to the Italian NHS was then standardized for each country according to its PPP index. The total load of medical expenses for each country was calculated by multiplying the individual cost by the number of symptomatic patients estimated (adults and children).

Summary of reference data

(1) CD prevalence = 1%; incidence: new cases/year estimated at 1% of the live births, corrected for infant mortality rate; (2) symptomatic adults: 1 of every 7 cases, children 1:5 cases; (3) mortality of the total CD cohort: standardized mortality rate 1.8 compared to age- and sex-matched population; (4) delay between symptoms and diagnosis: adults 6 years, children 2 years; (5) associated conditions: 10%-15% of the total cohort - autoimmune disorders 30% (Turkey 1.9%, Iran 33%) and IDDM 10% (6.7%-18.5%); (6) complications: 16% of symptomatic CD patients; and (7) non gastrointestinal

Table 2 Populations now and after 10 years

	Population	Children 0-14	Median age (yr)	Population growth rate (%)	Children 0-14 in 10 yr	Total population in 10 yr
Albania	3 619 778	853 883	29.9	0.5	901 667	3 822 345
Algeria	33 769 669	8 878 665	26.6	1.2	9 999 566	38 032 972
Bosnia	4 590 310	673 770	39.8	0.3	696 962	4 748 317
Cyprus	792 604	154 445	35.5	1.7	182 623	937 214
Croatia	4 491 543	708 683	41	-0.1	705 006	4 468 242
Egypt	81 713 517	25 983 672	24.8	2	31 776 575	99 931 053
France	64 057 790	11 894 698	39.4	0.5	12 564 088	67 662 729
Greece	10 722 816	1 531 606	41.8	0.1	1 551 169	10 859 777
Israel	7 112 359	1 989 312	29.1	1.7	2 347 869	8 394 303
Italy	58 126 212	7 870 226	43.3	0	7 833 314	57 853 596
Lebanon	3 971 941	1 032 888	29.3	1.1	1 153 096	4 434 197
Libya	6 173 579	2 048 548	23.9	2.2	2 539 599	7 653 427
Malta	403 532	66 112	39.5	0.4	68 805	419 967
Morocco	34 343 219	10 473 478	25	1.1	11 683 138	8 309 775
Syria	19 747 586	7 146 569	21.7	2	8 716 754	24 086 361
Slovenia	2 007 711	273 464	41.5	0	273 655	2 009 117
Spain	40 525 002	5 864 419	41.1	0.1	5 906 780	40 817 729
Tunisia	10 383 577	2 413 484	29.2	1	2 660 713	11 447 236
Turkey	71 892 807	17 545 890	27.7	1.3	19 965 025	81 805 009
Mediter	458 445 552	107 403 812	33.2	0.9	121 526 405	507 693 365

Table 3 Prevalence of celiac disease in the next 10 years[1]

	Estimated celiacs today	Estimated celiac children today at 1%	Projected prevalence of CD in next 10 yr	Projected celiac children in next 10 yr
Albania	36 198	8539	38 223	9017
Algeria	337 697	88 787	380 330	99 996
Bosnia	45 903	6738	47 483	6970
Cyprus	7926	1544	9372	1826
Croatia	44 915	7087	44 682	7050
Egypt	817 135	259 837	999 311	317 766
France	640 578	118 947	676 627	125 641
Greece	107 228	15 316	108 598	15 512
Israel	71 124	19 893	83 943	23 479
Italy	581 262	78 702	578 536	78 333
Lebanon	39 719	10 329	44 342	11 531
Libya	61 736	20 485	76 534	25 396
Malta	4035	661	4200	688
Morocco	343 432	104 735	383 098	116 831
Syria	197 476	71 466	240 864	87 168
Slovenia	20 077	2735	20 091	2737
Spain	405 250	58 644	408 177	59 068
Tunisia	103 836	24 135	114 472	26 607
Turkey	718 928	175 459	818 050	199 650
Mediter	4 584 456	1 074 038	5 076 934	1 215 264

[1]Population prevalence estimated at minimum rate of 1%. CD: Celiac disease.

symptoms: short stature 20% (only children), anemia 40% (20%-80%), osteopenia 30% (30%-50%), abnormal liver function 10% (Turkey 38%, Iran 25%)

RESULTS

Table 2 shows the population growth, number of children aged 0-14 years and the predicted figures for the year 2020, calculated based on a constant growth rate. The Mediterranean area will have about half a billion individuals by the year 2020, more than 100 million of which will be children aged 0-14 years. This estimate is likely to be in the low range, since some countries with a large population are likely to grow at a higher rate than this estimate before the year 2010.

Table 3 shows the prevalence of CD in each country in 2010 and the predicted prevalence in 2020. Within 10 years, the Mediterranean area will have to face more than 5 million cases of CD, one million of which will be in children. The large majority will not have clear symptoms and their diagnosis and care will be significantly delayed. Among the adult CD population, about 550 000 will present symptoms, while only 240 000 out of the 1 million estimated celiac children will be symptomatic. Table 4 shows the estimated number of clinical complaints associated with the CD epidemic. It is likely that more than 48 000 children will be affected by growth failure, there will be 317 000 cases of anemia and 238 000 individuals will be afflicted with osteopenia. Table 5 shows the estimated financial burden of the CD epidemic. There is no scope for a detailed calculation of costs, which will be related more to the availability of and access to medical services than to the actual cost of the service, but these figures help to understand the financial burden of the undiagnosed disease. European countries may not be impressed by these estimates but, for several other Mediterranean countries, these predicted costs might be a consistent load to the gross national product. More than €4 billion is a prudent estimate; only crude medical costs are included, not individual or social cost.

Table 6 shows the estimated number of deaths in the celiac disease cohort and the excess of deaths compared to age- and sex-matched controls. At the present rate, there will be more than 250 000 CD-related deaths in the Mediterranean area in 2020.

DISCUSSION

Celiac disease is a very common chronic disease that

Table 4 Symptoms and diseases associated with symptomatic cases

	Symptomatic adults next 10 yr 1:7	Symptomatic children next 10 yr 1:5	Gastrointestinal symptoms	Anaemia	Osteopenia	Abnormal liver	Children with short stature
Albania	4172	1803	5079	2390	1793	598	361
Algeria	40 048	19 999	51 040	24 019	18 014	6005	4000
Bosnia	5788	1394	6104	2873	2154	718	279
Cyprus	1078	365	1227	577	433	144	73
Croatia	5376	1410	5768	2714	2036	679	282
Egypt	97 364	63 553	136 779	64 367	48 275	16 092	12 711
France	78 712	25 128	88 264	41 536	31 152	10 384	5026
Greece	13 298	3102	13 940	6560	4920	1640	620
Israel	8638	4696	11 333	5333	4000	1333	939
Italy	71 458	15 667	74 056	34 850	26 137	8712	3133
Lebanon	4687	2306	5944	2797	2098	699	461
Libya	7305	5079	10 527	4954	3715	1238	1016
Malta	502	138	543	256	192	64	28
Morocco	38 038	23 366	52 194	24 562	18 421	6140	4673
Syria	21 957	17 434	33 482	15 756	11 817	3939	3487
Slovenia	2479	547	2573	1211	908	303	109
Spain	49 873	11 814	52 433	24 675	18 506	6169	2363
Tunisia	12 552	5321	15 193	7149	5362	1787	1064
Turkey	88 343	39 930	109 032	51 309	38 482	12 827	7986
Mediter	551 667	243 053	675 512	317 888	238 416	79 472	48 611

Table 5 Excess cost of undiagnosed symptomatic celiac patients

	Purchasing power parity	Standardized cost for an adult in 6 yr of delay, €	Standardized cost for a child in 2 yr of delay, €	Total cost for adults in the next 10 yr, €	Total cost for children in the next 10 yr, €	Total cost of symptomatic in the next 10 yr, €
Albania	7.164	2804	821	11 698 575	1 481 020	13 179 595
Algeria	6.869	2688	787	107 662 164	15 748 296	123 410 460
Bosnia	7.361	2881	844	16 673 654	1 176 265	17 849 919
Cyprus	17.7	6928	2029	7 468 819	741 246	8 210 065
Croatia	28.54	11 171	3272	60 057 866	4 613 886	64 671 751
Egypt	6.123	2396	702	233 320 214	44 609 799	277 930 013
France	33.68	13 181	3861	1 037 513 563	97 017 277	1 134 530 840
Greece	29.88	11 695	3426	155 520 664	10 627 416	166 148 080
Israel	28.39	11 112	3255	95 985 202	15 284 247	111 269 450
Italy	29.11	11 393	3337	814 080 086	52 279 538	866 359 625
Lebanon	14.23	5568	1631	26 097 336	3 761 033	29 858 369
Libya	14.33	5608	1643	40 966 178	8 342 757	49 308 935
Malta	23.58	9230	2704	4 630 407	372 044	5 002 450
Morocco	4.604	1802	528	68 540 194	12 332 575	80 872 769
Syria	4.7	1839	539	40 388 186	9 393 156	49 781 342
Slovenia	29.69	11 619	3403	28 807 411	1 862 767	30 670 178
Spain	33.7	13 189	3863	657 786 976	45 639 366	703 426 342
Tunisia	8.254	3230	946	40 548 541	5 035 255	45 583 796
Turkey	12.48	4883	1430	431 358 582	57 108 945	488 467 527
Mediter	17.92	7012	2054	3 879 104 619	387 426 887	4 266 531 506

affects adults and children in all wheat-consuming countries. It has also recently been reported in countries where its prevalence was previously unknown, such as China[27]. For more than two decades, we have been discussing the difference in the prevalence of CD among countries in Europe, North America and South America, and the conclusion is that there is no country where CD prevalence is significantly different from the overall prevalence of about 1%. Interestingly, the prevalence, at a global level, is not related either to the amount of wheat consumed by each country or to the prevalence of the human leukocyte antigen (HLA) DR3-DQ2 and DR4-DQ8 haplotype worldwide[47].

An excess prevalence of CD has been reported in an isolated population in North Africa and in a large population in Sweden, but again it is plausible that this excess prevalence reflects a bias related to the cohort rather than a true excess. The prevalence of CD is increasing worldwide, including in Europe[4], China[27] and India[28]. The only region where it has not yet been described is Central Africa, and this may be explained by the absence in this region of HLA predisposing haplotypes, and of polymorphisms of the major non-HLA genes, namely *SH2B3, IL12A, SCHIP, IL18RAP,* and *IL1RL1*, among others[47,48]. Recently, Barada *et al*[2] from Lebanon produced a comprehensive report of the situation in the

Table 6 Excess mortality in undiagnosed cases[2]

	Projected prevalence of CD in the next 10 yr	Death rate, deaths/1000 individuals	Population expected deaths (next 10 yr)	Celiac deaths in next 10 yr	Excess celiac deaths in next 10 yr
Albania	38 223	5.1	193 793	3488	1550
Algeria	380 330	4.6	1 764 730	31 765	14 118
Bosnia	47 483	8.6	409 780	7376	3278
Cyprus	9372	6.4	59 982	1080	480
Croatia	44 682	11.8	525 018	9450	4200
Egypt	999 311	4.9	4 876 635	87 779	39 013
France	676 627	8.6	5 791 930	104 255	46 335
Greece	108 598	10.5	1 141 363	20 545	9131
Israel	83 943	5.4	455 811	8205	3646
Italy	578 536	10.7	6 201 905	111 634	49 615
Lebanon	44 342	6	267 382	4813	2139
Libya	76 534	3.4	260 982	4698	2088
Malta	4200	8.4	35 193	633	282
Morocco	383 098	4.7	1 815 883	32 686	14 527
Syria	240 864	3.7	896 013	16 128	7168
Slovenia	20 091	9.2	184 839	3327	1479
Spain	408 177	10	4 077 691	73 398	32 622
Tunisia	114 472	5.2	595 256	10 715	4762
Turkey	818 050	6	4 908 301	88 349	39 266
Mediter	5 076 934	7	34 462 486	620 325	275 700

[2]Undiagnosed celiac patients have 1.8 standard mortality rate[39]. CD: Celiac disease.

countries that face the Mediterranean Sea, thereby increasing the awareness of CD in the area.

The EUROMED program supports several health-promoting activities across the Mediterranean, such as the surveillance of infectious diseases program and the Program for Transplants and Oncology EuroMed (Cancer Registries Network, Cancer screening and early diagnosis program, Mediterranean Transplant Network). Italy has requested that the CD epidemic be included in these programs (www.eeas.europa.eu/euromed/index_en.htm). The first step in facing this epidemic is to estimate the burden of CD in the area. Here we provide a reliable and simple picture of the present situation and a prediction of the development of the CD epidemic in the next 10 years, up to 2021.

The prediction obtained by simple straightforward calculations is impressive. Mediterranean countries will have to be prepared to deal with a considerable number of CD patients in the near future. There will be more than 5 million cases, one million of which will be children. But, more than the overall figures, each country will be especially concerned about the national figures. Our estimates are conservative figures, since we estimated a constant population growth over the next ten years, whereas the faster growing countries may have a more rapid growth rate than slower growing countries. Data on symptoms and common clinical problems are available only for symptomatic individuals, while a considerable percentage of so-called "asymptomatic" subjects notoriously report significant complaints a posteriori[49]. A limitation of this study is related to the uncertainties inherent in any prediction given the wide confidence intervals of rates. However, the starting 1% prevalence rate is not only very robust, because of innumerable replications, but it also probably underestimates rather than overestimates the problem[4,28,50]. The rate of symptomatic versus asymptomatic individuals is also fairly conservative.

The financial burden estimate is not aimed to acquire more precision; we provide a gross figure for the spectrum of resources needed in each country for the services required by symptomatic patients. The priority issue is the availability of services; in many African countries, services are mostly only available in large cities and specialized health institutions. In the rural areas, the availability of services can be far less than that required. Hence, the cost of these services should, sadly, be subtracted from the total financial burden. This impending cohort of CD patients does require, and moreover will require, access to health services as inpatients or outpatients, for medical consultations, laboratory tests and, after diagnosis, financial support for a lifelong gluten-free diet. There is universal concern and many countries demand the expertise and support for dissemination of know how and capacity building for the management of CD.

The EuroMed - MEDICEL project (www.medicel.unina.it) offers a platform to analyze the problem and develop strategies, but active national plans are required to face the burgeoning epidemic, and the heavy burden that it will place on the health and the finances of the population.

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COMMENTS

Background

The incidence of celiac disease (CD) (i.e., permanent gluten intolerance), is

increasing in all countries in which there is awareness of this intolerance. In all Western countries, including the United States and South America, the observed prevalence of the disease went from 1:1000 individuals to more than 1:100 individuals in two decades. However, large series of cases have recently been reported from "new" countries like India, China, North Africa and the Middle East. Celiac disease is expanding over and above any predicted trend, and has taken on the semblance of a real epidemic.

Research frontiers

This expanding "epidemic" raises a series of unanswered research questions related to the following hot topics: **(1) the weight of environmental factors in the** increase of CD; **(2) the genetic profile associated with predisposition to CD; (3)** population differences in terms of genetic and environmental factors; **and (4)** the development of "sensitivity" to gluten.

Innovations and breakthroughs

In next 10 years, the Mediterranean area will have about half a billion inhabitants, 120 million of whom will be children. The projected number of CD cases in 2020 will be 5 million cases (1 million celiac children), with a relative increase of 11% compared to 2010. At a 2010 constant rate, there will be about 550 000 symptomatic adults and 240 000 sick children: 85% of patients will suffer from gastrointestinal complaints, 40% are likely to have anemia, 30% will be afflicted with osteopenia, 20% of children will have short stature and 10% will have abnormal liver enzymes. The estimated standardized medical costs for symptomatic celiac disease during the years of delay between onset of symptoms and diagnosis (mean: 6 years for adults, 2 years for children) will be about €4 billion (€387 million for the children) over the next 10 years. A delay in diagnosis is expected to increase mortality; about 600 000 deaths will occur among individuals affected by CD in the next 10 years, with an excess of 44.4% compared to age- and sex-matched controls.

Applications

The data produced in this study provide a picture of the cohort of patients affected by CD that will develop over the next 10 years in each country of the Mediterranean Basin. Stakeholders and health professionals in each country now have the figures with which it is possible to base adequate plans to face this epidemic. The diagnostic protocol must be simplified and made available not only in specialized centers, usually in large cities, but it should be especially important in rural districts.

Terminology

CD: Celiac disease is a permanent intolerance to gluten based on a genetic predisposition; **Projected prevalence: The number of celiac cases that are** expected to be present over the next 10 years; **Excess mortality: Undiagnosed** celiac cases have twice the risk of death compared to age- and sex-matched controls. If the expected cases are not diagnosed, there will be more than 200 000 excess deaths in the Mediterranean area; **Growth failure: 20% of children** (about 50 000) with undiagnosed CD are affected by weight loss and short stature, due to a growth failure.

Peer review

The paper is well written and deals with an important problem people are continuously facing.

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