Autoimmune Diseases: A Leading Cause of Death Among Young and Middle-Aged Women in the United States

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A B S T R A C T

Objectives. This study assessed the effect of autoimmune diseases on mortality among women.

Methods. Counts of autoimmune disease deaths were compared with frequencies of the 10 "official" leading causes of death among women in the United States in 1995.

Results. Autoimmune disease deaths exceeded the frequency of the 10th leading cause in every age category of women younger than 65 years and exceeded that for the eighth leading cause in the 15 to 24, 25 to 44, and 45 to 64 years age groups.

Conclusions. Autoimmune diseases constitute a leading cause of death among young and middle-aged women. This fact is obscured by current methods used to identify leading causes. (*Am J Public Health.* 2000;90:1463–1466)

The National Center for Health Statistics annually identifies the 10 leading causes of death in the United States.[1] Leading causes are diseases or health events cited most frequently as underlying causes on death certificates. Candidates for leading causes are drawn from a subset of 37 "rankable" categories within the List of 72 Selected Causes of Death.[1] This list is based on the structure of the *International Classification of Diseases, Ninth Revision (ICD-9)*.[2]

Autoimmune diseases are caused by an immune response against constituents of the body's own tissues. They occur predominantly in women.[3] There is disagreement concerning which diseases satisfy the definition of autoimmunity. However, Jacobsen et al.[3] recently characterized 24 diseases as having direct, indirect, or strong circumstantial evidence of autoimmune pathogenesis. Although these diseases are generally rare, several of them have high case-fatality rates. Despite this, within the List of 72 Selected Causes of Death, 16 of the 24 autoimmune diseases are included in "nonrankable" categories. The 8 remaining autoimmune diseases are absorbed into broader categories for the organ systems in which they occur.

In this report, we compare the frequency of deaths from autoimmune diseases with counts for the "official" 10 leading causes of death to address the question "Do autoimmune diseases cause sufficient mortality among women to constitute a leading cause of death?"

Methods

The 24 autoimmune diseases identified by Jacobsen et al.[3] were divided into 2 groups to determine "lower bound" and "midrange" estimates of mortality. Group 1 included diseases with *ICD-9* categories and codes that refer specifically to the disease of interest: autoimmune hemolytic anemia (283.0), glomerulonephritis (580.0–583.9), Graves disease (242.0), multiple sclerosis (340), myasthenia gravis (358.0), myocarditis (130.3, 422.0, 422.9, 429.0), polymyositis/dermatomyositis (710.3, 710.4), rheumatic fever and heart disease (390–398.9), rheumatoid arthritis (714.0–714.2), scleroderma (710.1), and systemic lupus erythematosus (710.0). Group 2 consisted of those with *ICD-9* categories that include the disease of interest and other nonautoimmune diseases: Addison disease (255.4), chronic active hepatitis (571.4), Goodpasture syndrome (446.2), idiopathic thrombocytopenia purpura (287.3), type 1 diabetes mellitus (250.0–250.9), myocarditis (36.4, 74.2, 93.8), pemphigus vulgaris (694.4), pernicious anemia (281.0), primary biliary cirrhosis (571.6), relapsing polychondritis (733.9), Sjögren syndrome (710.2), thyroiditis (245.2), uveitis (364.0–364.3), and vitiligo (709.0). Categories for myocarditis were included in both groups because some *ICD-9* codes are specific for myocarditis and others are not.

Female deaths in 1995 that cited as an underlying cause one of the *ICD-9* codes for the 24 autoimmune diseases were identified with the Wonder Internet site of the Centers for Disease Control and Prevention.[4,5] Summary counts were stratified into age categories used by National Center for Health Statistics in tabulating leading causes.[1] Tallies of autoimmune disease deaths in each age category were compared with the number of deaths for the official 10th leading cause in that category for 1995.[6]

It was impossible to obtain accurate counts of deaths from type 1 diabetes, because the *ICD-9* categories for diabetes mellitus do not distinguish between type 1 (insulin dependent with an autoimmune pathogenesis) and type 2 (non–insulin dependent and, presumably, without an autoimmune pathogenesis). In an effort to isolate deaths from type 1, only diabetes deaths in persons younger than 35 were counted, and all were treated as deaths from type 1 disease.[7–10]

Results

In 1995, the total number of deaths attributable to the autoimmune diseases in

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This brief was accepted February 24, 2000.

TABLE 1—Counts of Deaths of Women With an Autoimmune Disease as the Underlying Cause, Compared With Official Counts for the 10th Leading Cause of Death, by Disease Category and Age: United States 1995

Autoimmune diseases	Age, y						All ages[a]
	1–4	5–14	15–24	25–44	45–64	>65	
Group 1 (diseases with specific *ICD* categories)							
Autoimmune hemolytic anemia	0	2	1	2	11	77	93
Glomerulonephritis	3	6	5	44	88	745	893
Graves disease	0	0	2	4	3	15	24
Multiple sclerosis	0	0	3	254	620	514	1391
Myasthenia gravis	0	0	1	9	14	150	174
Myocarditis (I)	24	20	26	97	78	126	401
Polymyositis and dermatomyositis	0	0	1	13	46	112	172
Rheumatic fever and heart disease	1	1	17	177	582	2832	3613
Rheumatoid arthritis	0	0	1	14	183	1244	1442
Scleroderma	0	5	4	85	318	490	902
Systemic lupus erythematosus	0	9	62	338	353	356	1118
Subtotals for group 1	28[b]	43	123[b]	1037[b]	2296[b]	6661	10223
Group 2 (diseases without specific *ICD* categories)							
Addison disease	0	0	2	11	15	61	89
Chronic active hepatitis	1	1	1	12	51	135	201
Goodpasture syndrome	0	0	1	8	15	34	58
Idiopathic thrombocytopenia purpura	1	0	3	21	29	134	188
Type 1 diabetes mellitus	1	8	52	269[c]	0[c]	0[c]	330[c]
Myocarditis (II)	0	0	0	0	0	4	7
Pemphigus vulgaris	0	0	0	0	2	28	30
Pernicious anemia	0	0	0	0	2	68	70
Primary biliary cirrhosis	0	0	1	10	78	308	398
Relapsing polychondritis	0	0	0	0	3	24	27
Sjögren syndrome	0	0	0	1	16	43	60
Thyroiditis	0	0	2	2	2	0	6
Uveitis	0	0	0	0	0	0	0
Vitiligo	0	0	0	0	0	0	0
Subtotals for group 2	3	9	62	334	213	839	1464
Totals	31[b]	52[b]	185[b]	1371[b]	2509[b]	7500	11687
10th leading cause of death counts	23	45	75	800	1380	10135	11974

Note. ICD = International Classification of Diseases.
[a]All ages includes persons younger than 1 year and of unknown age.
[b]Subtotal or total count for autoimmune disease deaths exceeds the count for the 10th leading cause of death.
[c]Diabetes mellitus deaths were included only for persons younger than 35 years.

groups 1 and 2 exceeded the count for the 10th leading cause in all age groups of women younger than 65 years (Table 1). With the exception of the 5 to 14 years age group, these results persisted when the counts were restricted to include only the *ICD-9* categories in group 1.

The relative position of autoimmune diseases among the 10 leading causes of death in each age group of women younger than 65 years is shown in Table 2. Counts for other disease categories in the table were not adjusted to exclude autoimmune diseases, but the table does indicate which categories include autoimmune diseases and the number of autoimmune disease deaths in those categories. Subtraction of autoimmune diseases from other disease categories sometimes altered ranks within the leading causes but, except for diabetes mellitus, did not alter the categories included among the leading causes. Table 2 establishes that in 1995, autoimmune diseases were at least the eighth leading cause of death for women between 15 and 64 years of age.

Discussion

Our investigation found that autoimmune diseases constitute 1 of the 10 leading causes of death among US women younger than 65 years. The significant contribution of autoimmune diseases to mortality has gone unrecognized, because the process used to establish leading causes of death systematically excludes them from consideration or obscures their presence by aggregation with nonautoimmune diseases.

Many autoimmune diseases do not have specific *ICD-9* categories or codes. Therefore, we cannot claim to have counted autoimmune disease deaths with high accuracy. Instead, we calculated both more and less conservative tallies of mortality. The counts that were restricted to autoimmune diseases with unique *ICD-9* categories provided lower bounds for mortality. Counts that referred to all 24 autoimmune diseases provided midrange estimates. In both cases, autoimmune disease mortality was sufficiently high to constitute a leading cause of death.

Estimation of an upper bound for autoimmune disease mortality was precluded by several factors. One factor is the difficulty of identifying diseases with an autoimmune pathogenesis. More than 60 diseases may have such an etiology.[11] Another factor relates to the process of death certificate completion. Deaths from chronic diseases other than cancer and heart disease are often unreported and undercounted.[12] Studies specifically document this phenomenon for rheumatoid arthritis and scleroderma.[13–15] Two studies showed that when rheumatoid arthritis and scleroderma are reported on death certificates, they are frequently listed among "contributing" causes (i.e., as significant comorbid conditions) rather than as the underlying cause of death.[14,15]

TABLE 2—Position of Autoimmune Diseases Among the Official 10 Leading Causes of Death in Women Younger Than 65 Years: United States 1995

Age, y	Official Rank	Disease Category	Death Count
1–4	1	Accidents and adverse effects	926
	2	Congenital anomalies	321
	3	Homicide and legal intervention	199
	4	Malignant neoplasms	198
	5	Diseases of heart (25)[a]	115
	6	HIV infection	114
	7	Pneumonia and influenza	87
	8	Certain conditions originating in the perinatal period	42
	8	Septicemia	42
	—	Autoimmune diseases[b]	31
	10	Anemias (0)	23
5–14	1	Accidents and adverse effects	1256
	2	Malignant neoplasms	439
	3	Congenital anomalies	219
	4	Homicide and legal intervention	188
	5	Diseases of heart (21)	131
	6	HIV infection	86
	7	Suicide	77
	8	Pneumonia and influenza	70
	9	Benign neoplasms; neoplasms of uncertain behavior	53
	—	Autoimmune diseases	52
	10	Chronic obstructive pulmonary diseases	45
15–24	1	Accidents and adverse effects	3529
	2	Homicide and legal intervention	1060
	3	Suicide	652
	4	Malignant neoplasms	633
	5	Diseases of heart (43)	380
	6	HIV infection	252
	7	Congenital anomalies	194
	—	Autoimmune diseases	185
	8	Chronic obstructive pulmonary diseases	113
	9	Pneumonia and influenza	88
	10	Cerebrovascular diseases	75
25–44	1	Malignant neoplasms	11916
	2	Accidents and adverse effects	6564
	3	HIV infection	5139
	4	Diseases of heart (274)	4796
	5	Suicide	2445
	6	Homicide and legal intervention	2370
	7	Cerebrovascular diseases	1629
	—	Autoimmune diseases	1371
	8	Chronic liver disease and cirrhosis (12)	1190
	9	Diabetes mellitus (269)[c]	1037
	10	Pneumonia and influenza	800
45–64	1	Malignant neoplasms	62007
	2	Diseases of heart (660)	30401
	3	Cerebrovascular diseases	6843
	4	Chronic obstructive pulmonary diseases	6071
	5	Diabetes mellitus (0)[c]	5722
	6	Accidents and adverse effects	4575
	7	Chronic liver disease and cirrhosis (53)	3046
	—	Autoimmune diseases	2509
	8	Pneumonia and influenza	2137
	9	Suicide	1657
	10	HIV infection	1380

[a]The presence of a number in parentheses following an official leading cause indicates that the cause-of-death category includes deaths from 1 or more of the 24 autoimmune diseases considered in this study. The number represents the count of such deaths.
[b]Death counts for the autoimmune diseases category include both group 1 and group 2 diseases.
[c]Only diabetes mellitus deaths in persons younger than 35 years were considered to result from an autoimmune disease.

Jacobsen et al.[3] estimated a 5% prevalence for autoimmune diseases among US women. Our study reflects the effect of that level of prevalence on mortality among young and middle-aged women. Together, the prevalence and mortality estimates support the contention that the etiology, diagnosis, and treatment of autoimmune diseases constitute important issues in women's health. □

Contributors

S. J. Walsh planned the study, supervised the data analysis, and wrote the paper. L. M. Rau obtained and analyzed the data and prepared the tables.

Acknowledgments

This study was supported by a Faculty Research Grant from the University of Connecticut Health Center Research Advisory Committee.

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