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Original articles

The prevalence of Addison's disease in Coventry, UK

Andrew C Willis, Frank P Vince

Summary

The prevalence of Addison's disease (chronic adrenal failure) has not been widely investigated and is usually given as 39 in a million. We conducted a prevalence study using a postal survey of general practitioners in Coventry. Three quarters (139/188) replied, representing 79/85 (93%) of the practices. Thirty cases of Addision's disease were found from a total patient list of 323 852, of which a third were tuberculous in origin and two-thirds non-tuberculous (12/30 autoimmune, 8/30 unclassified). We conclude that Addison's disease is 2.4 times more common than previously reported. The tuberculous group was older, 65 *vs* 52 years ($p<0.05$), and had had the disease for longer than the non-tuberculous group, 20 *vs* 12 years ($p<0.05$). There was no significant difference in the age at diagnosis.

Keywords: Addison's disease, adrenal hypofunction, epidemiology, tuberculosis

Since Thomas Addison first described the condition of chronic adrenal failure, its prevalence has rarely been defined. In 1968, a hospital-based survey found a prevalence of 39 in a million.[1] This seemed likely to be an underestimate and we performed a prevalence study in a West Midlands industrial city in the UK.

Methods

In 1992 general practitioners (GPs) on the Coventry Family Health Services Authority (FHSA) list were asked by post if they had any patients with Addison's disease (chronic adrenal failure) on their practice lists. Non-responders were telephoned. We sought at least one reply per practice. Cases were also sought in a hospital endocrine clinic. The population size was taken from the FHSA patient list for July 1992. Medical records were examined for evidence of primary adrenal failure. These patients were divided into a tuberculous and an autoimmune group. Those cases that could not be placed in either group were added to the autoimmune group to form a non-tuberculous group. The statistics were performed using a Student's *t*-test.

Results

The survey was sent to 188 GPs in 85 practices, looking after 323 852 patients. Replies were received from 139 (74%) of the GPs in 79 (93%) of the practices. Of the six practices that did not reply, four were single-handed and two double-handed. A total of 30 patients with Addison's disease were identified, of whom 26 were found in general practice, two in the hospital endocrine clinic and two from other sources. All patients were registered with Coventry GPs. Ten patients were not being followed up in a hospital clinic. In 25 patients there was a description of their clinical state at presentation and 24 had recorded biochemical evidence of hypocortisolaemia. Of the six that did not have a record of their cortisol state at presentation, all were being treated for Addison's disease. One had bilateral adrenal calcification on X-ray, one had had a tuberculous kidney removed, one presented in an Addisonian crisis and with pulmonary tuberculosis, two were diagnosed elsewhere and for one no other information was available.

Of the 30 patients, 10 (five men, five women) were classified as tuberculous (table 1), 12 (two men, 10 women) were classified as autoimmune (table 2) and eight (five men, three women) had no evidence of tuberculous, autoimmune or other infiltrative disease, making 20 (seven men, 13 women) non-tuberculous cases. The prevalence was calculated as 93 in a million, 33% of whom were tuberculous. The majority (26/30) had one or more of the following features of primary adrenal failure: increased pigmentation at presentation, adrenal calcification on X-ray, no response to a

Table 1 Patients classified as tuberculous Addison's disease

Patient	*Sex*	*Treated tuberculosis*	*CXR*	*AXR*	*Mantoux*
1	F	peritoneal	neg	neg	N/A
2	F	cervical	neg	neg	N/A
3	F	renal	pos	neg	N/A
4	M	pulmonary	pos	N/A	N/A
5	M	cervical	neg	pos	N/A
6	M	pulmonary	pos	pos	pos
7	F	none	neg	neg	pos
8	F	none	pos	neg	N/A
9	M	none	pos	N/A	N/A
10	M	none	N/A	pos	N/A

Abbreviatons: CXR=chest X-ray, AXR=abdominal X-ray, F=female, M=male, pos=test positive, neg=test negative, N/A=test not recorded

Coventry and Warwickshire Hospital, Stoney Stanton Road, Coventry, West Midlands CV1 4FH, UK
AC Willis
FP Vince

Correspondence to Dr AC Willis, Research Registrar, The Diabetes Resource Centre, Selly Oak Hospital, Raddlebarn Road, Birmingham B29 6JD,UK

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Table 2 Patients classified as having autoimmune Addison's disease

Patient	Sex	Autoantibodies: Adrenal	Autoantibodies: Thyroid	Autoantibodies: Gastric	Thyroid disease	Diabetes mellitus	Other
1	F	pos	pos	N/A	pos	N/A	
2	F	pos	pos	neg	neg	neg	vitiligo
3	F	pos	neg	neg	N/A	neg	
4	F	pos	neg	pos	neg	neg	menopause at 30
5	F	pos	pos	neg	pos	neg	
6	F	pos	pos	neg	pos	neg	
7	F	N/A	pos	pos	pos	pos	
8	F	N/A	neg	neg	pos	pos	vitiligo
9	F	N/A	N/A	neg	pos	N/A	
10	F	neg	neg	N/A	pos	neg	PA
11	M	pos	N/A	N/A	N/A	pos	TB
12	M	pos	neg	neg	neg	neg	

Abbreviations: F=female; M=male; pos=test positive; neg=test negative; N/A=test not recorded; PA=pernicious anaemia; TB=tuberculosis; thyroid autoantibodies=thyroid microsomal ± thyroglobulin autoantibodies

Table 3 The mean ages of tuberculous and idiopathic Addisonian patients (ranges in parentheses)

	Tuberculous cases	Idiopathic cases	p
Age (years)	65 (43–80)	52 (39–62)	<0.05
Age at diagnosis (years)	43 (16–56)	34 (10–47)	NS
Length of disease (years)	20 (8–37)	12 (1–24)	<0.05

NS: not significant

prolonged adrenocorticotropin stimulation test, adrenal autoantibodies, a normal response to pituitary stimulation tests or raised levels of adrenocorticotropin at diagnosis or whilst on treatment. No patients have developed evidence of a pituitary tumour since diagnosis.

The tuberculous group was older than the non-tuberculous group and had had Addison's disease for longer, but there was no significant difference in the age at diagnosis (table 3).

Discussion

The causes and clinical features of Addison's disease are given in boxes 1 and 2. In the current study, we found Addison's disease to be 2.4 times more common than previously reported. This study had a high response rate (74% of GPs, 93% of practices) and a high detection rate by GPs (26/30, 89% of cases), who reported 10 cases not attending a hospital clinic. We cannot say if the prevalence of Addison's disease has changed but believe that the previous figure of 39 in a million was an underestimate because cases were not sought outside hospitals.[1]

This was a retrospective study and full details of the diagnosis were not always available. Of the 30 cases, 27 were diagnosed locally but in three cases the diagnosis was made elsewhere and has been taken on trust. These are limitations of the data.

Our evidence for classifying patients as tuberculous or autoimmune is summarised in tables 1 and 2. One-third of our cases were tuberculous, consistent with other series.[2,3] Of these, six had been treated for tuberculosis, three others had radiological evidence of old tuberculosis and one had had a strongly positive Mantoux test but had not been treated for tuberculosis. There was virtually no evidence of autoantibodies or associated autoimmune disease in these patients, which is consistent with findings of Kasperlik-Zaluska *et al.*[2] Patient 2 (table 1) became hypothyroid seven years after diagnosis and patient 8 had

Addison's disease: causes

Common
- autoimmune
- tuberculosis

Uncommon
- bilateral adrenalectomy
- infiltration: metastatic carcinoma, amyloidosis, fungal infection (eg, histoplasmosis), haemochromatosis
- meningococcal septicaemia
- haemorrhage/infarction
- adrenal vein thrombosis
- congenital: adrenoleucodystrophy (Schilder's disease), congenital adrenal hyperplasia, X-linked congenital adrenal hypoplasia
- drugs: rifampicin, ketoconazole
- AIDS

Box 1

Clinical features

Symptoms
- common: lethargy, dizziness, weight loss, nausea and vomiting
- less common: loss of appetite, abdominal pain, cramps, salt craving

Signs
- increased pigmentation
- postural hypotension

Associated conditions
- vitiligo
- hypothyroidism
- diabetes mellitus
- premature ovarian failure
- hypoparathyroidism

Box 2

Summary/learning points

- the prevalence of Addison's disease is 9.3/100 000
- the common causes are autoimmune and tuberculosis
- autoimmune Addison's disease is more common in women than men and it is associated with other autoimmune disease
- tuberculous Addison's disease affects men and women equally
- tuberculosis may be active and must be excluded at the time of diagnosis

Box 3

inconsistently positive antithyroglobulin autoantibodies (negative at the time of diagnosis). Only 30% of tuberculous cases had radiological adrenal calcification, similar to the 26% of Kasperlik-Zaluska *et al.*[2] Tuberculosis was previously a common disease and evidence of old tuberculosis does not exclude the possibility of autoimmune Addison's disease, as adrenal antibodies are only found within the first eight years of the disease.[2] In a series involving computed tomography and autopsy,[4] adrenal calcification was seen in 55% of tuberculous cases and 76% had evidence of extra-adrenal tuberculosis, but pulmonary tuberculosis was seen in 46% of cases considered to have idiopathic disease. Six of our tuberculous cases had evidence of extra-adrenal tuberculosis, in three there was only evidence of pulmonary tuberculosis and in one the site of the infection was not known. Of the 12 patients with autoimmune disease, eight had adrenal autoantibodies and the remaining four had evidence of other autoantibodies or autoimmune disease (table 2). In the non-tuberculous group the sex ratio (M/F) was 1.9/1 and 7/20 (35%) had clinical or subclinical thyroid disease. These figures compare with a sex ratio of 1.7/1 and 31% with thyroid disease in Kasperlik-Zaluska *et al*[2] and it is likely that our cases have been correctly classified.

The finding that two quite different disease processes produce adrenal failure at a similar age and that the tuberculous patients are older and have had Addison's disease for longer is interesting. We cannot tell from this work whether this is due to a change in the relative incidence of tuberculous and autoimmune adrenal disease or whether the latter has a higher mortality risk, perhaps due to an associated disease such as diabetes mellitus.

We would like to thank all the general practitioners in Coventry who helped us with this study.

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