Prevalence of thyroid dysfunction and autoimmunity in adults with Down syndrome

V. P. Prasher

Lecturer in Psychiatry
University of Birmingham
U.K.

This study investigated thyroid dysfunction in 160 adults with Down syndrome; mean age 43.4 years, 57.5% over the age of 40 years. Thirty-five percent had evidence of thyroid dysfunction with subclinical hypothyroidism (11.9%) and definite hypothyroidism (8.1%) being the commonest abnormalities. An association between thyroid dysfunction and thyroid autoimmunity was found (P= 0.01). Monitoring of thyroid status in subjects on thyroxine replacement was found to be poor. Recommendations are discussed.

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Introduction

A pathological association between Down syndrome and thyroid disorders was first described by Bourneville in 1903, with subsequent confirmation by others (Hill, 1908; Gordon, 1930). During the last 30 years a clinical association between Down syndrome and thyroid disorders has been established with many reports demonstrating abnormalities of thyroxine (T4), triiodothyronine (T3) and thyroid stimulating hormone (TSH) (Table 1). Case reports of hypothyroidism (Maranon et al, 1951; Aarskog, 1969; Schindler, 1989) and hyperthyroidism (Gilchrist, 1946; Hayles et al, 1965; Blumberg and Ruskin, 1987) in subjects with Down syndrome have been published. The prevalence of hypothyroidism has been found to be greater than that of hyperthyroidism; a ratio of 9% to 1.8% was proposed by Kinnell et al (1987).

An association between Down syndrome and immunological disorders, including thyroid autoimmunity, has been reported (Gershwin et al, 1977; Kennedy et al, 1992). The relationship between Down syndrome and autoimmune thyroid disease was first described by Mellon et al (1963) and has been confirmed by subsequent reports (Burgio, 1965; Hollingsworth et al, 1974; Dinani and Carpenter, 1990).

This study reports the findings of thyroid screening in adults with Down syndrome, especially in elderly subjects and patients on thyroxine replacement for whom information of thyroid status is lacking. A possible association between thyroid autoimmunity and thyroid status was investigated.

Methodology

Adults with Down syndrome, aged 16 years and over, resident in hospital and the community (family or small group homes) were assessed. Subjects were involved in a longitudinal study investigating healthcare in adults with Down syndrome in the West Midlands. This cohort was a large (>200 subjects) sample, with a wide age distribution, investigating both hospital and community residents, from a wide geographical region and who had been clinically and cytogenetically screened for Down syndrome.

Thyroxine (T4) and thyroid stimulating hormone (TSH), along with thyroid antibodies (anti-thyroglobulin [ATA] and anti-microsomal [AMA] antibodies) were measured. Reference values for T4 were 12-26 pmol/l, for TSH 0.3-4.0 microIU/ml and thyroid antibodies were positive at 1:1600 to 1:400. Whether subjects were prescribed thyroxine replacement was recorded. Frequency of the differing results for thyroid status was calculated and comparative analysis using Chi-square was undertaken to investigate any association between thyroid status and thyroid autoimmunity. Thyroid status of subjects on thyroxine replacement was assessed.

Results

Two-hundred and one subjects were enrolled into the study but thyroid status was only available for 160 subjects; 89 (55.6%) male and 71 (44.4%) female. Forty-one subjects were either uncooperative with venesection or venesection failed on two attempts. The mean age of the 160 subjects was 43.4 years (standard deviation [SD] 12.58; standard error [SE] 9.88; age range 17-76 years). Ninety-two individuals (57.5%) were aged 40 years and over and 34 (21.3%) were over 50 years of age.

Author (Ref)	(Year)	Number of subjects in study	Age range in years	Male/Female	Number of patients with thyroid dysfunction (abnormalities in one or more value of T4/T3/TSH*)	
					No.	%
Pearse et al	(1963)	151	6-21	-	25	17
Hillman	(1969)	35	12-39	24/11	0	0
Hollingsworth et al	(1974)	60	9-65	39/21	17	28
Piffanelli et al	(1974)	73	6-24	-	15	21
Baxter et al	(1975)	11	44-65	6/5	7	66
Murdoch et al	(1977)	82	19-65	44/38	34	41
Sare	(1978)	121	13-48	81/40	23	20
Korsager et al	(1978)	24	41-60	8/16	10	42
Quinn	(1980)	49	8-59	-	3	6
Lobo et al	(1980)	101	5-47	-	7	7
Samuel et al	(1981)	54	9-12 days	20/34	10	18
Hughes et al	(1982)	38	16-65	27/11	8	21
Vladutiu et al	(1984)	42	18-64	22/20	23	55
Fort et al	(1984)	1130	3-16 days	-	12	0.12
Ziai et al	(1984)	62	5-16	40/22	7	11
Coleman & Abbassi	(1984)	206	<18	-	16	8
Pueschel & Pezzullo	(1985)	151	3-21	92/59	41	27
Cutler et al	(1986)	49	4/12-3	24/25	18	37
Kinnell et al	(1987)	111	22-72	56/55	16	14
Mani	(1988)	55	24-67	32/23	12	22
Sharav et al	(1988)	147	4/12-27	-	88	60
Tirosh et al	(1989)	44	2-51	31/14	9	20
Dinani & Carpenter	(1990)	106	20-67	61/45	43	41
Zori et al	(1990)	61	5/12-48	34/27	40	66
Pozzan et al	(1990)	108	3/12-38	55/53	40	37

* (T4 = Thyroxine; T3 = Tri-iodothyronine; TSH = Thyroid Stimulating Hormone)

Table 1. Studies of prevalence of Down syndrome and thyroid disorder

The majority of the individuals were living in the community with 59 (36.9%) living in supervised community units and 64 (40.0%) living in their family homes. Thirty-seven (23.1%) were resident in the hospital setting. Thirty (18.8%) individuals had mild learning disabilities, 106 (66.3%) had moderate and 22 (13.8%) had severe impairment and two were unknown.

One hundred and four individuals (65%) had normal thyroid function tests (normal T4 and normal TSH) with 56 (35%) individuals having an abnormality of T4 and/or TSH. The commonest abnormality present was sub-clinical hypothyroidism (normal T4 and increased TSH) and this was present in 19 cases (11.9%). Definite biochemical hypothyroidism (low T4, increased TSH), requiring immediate management was seen in 13 (8.1%) cases. Definite hyperthyroidism (raised T4, decreased TSH) was found in five cases (3.1%). Overall results are given in Table 2 (on page 70).

Results for anti-microsomal antibodies (AMA) were available for 104 (65%) of individuals. Twelve individuals (11.5%) had positive antibodies and 92 (88.5%) were negative. For anti-thyroglobulin (ATA) antibodies there were similar findings with results available for the same individuals, with seven individuals (6.7%) positive and 97 (93.3%) negative. For all seven cases where AMA were positive, ATA were also positive. This suggests there is an association between positive ATA and positive AMA results and negative ATA and negative AMA results. However, the numbers are too small for further statistical analysis.

For the 12 individuals with positive thyroid antibodies, four (33.3%) had normal plasma levels of thyroid hormones (thyroxine and TSH) and eight (66.7%) had abnormal levels, either sub-clinical hypothyroidism (normal thyroxine, raised TSH) or definite hypothyroidism (low thyroxine and raised TSH). No case of positive thyroid autoimmunity and hyperthyroidism was found. Although the numbers are small, these findings suggest there is a clinical association between the finding of positive thyroid autoimmunity and subclinical or definite hypothyroidism (Chi-squared with Fishers Exact probability P= 0.01).

Thirty (14.9%) subjects were on thyroxine replacement, with thyroid status results available for 25 individuals. Eighteen (72%) of this group had plasma thyroxine levels within the normal range. Six (24%) had plasma levels above the upper limit of the therapeutic range and one person had levels below the lower limit of the therapeutic range (Table 3). Five (20%) fulfilled criteria for biochemical hyperthyroidism and oneperson for biochemical hypothyroidism.

Discussion

As previously reported, this study too found a high prevalence of thyroid dysfunction (35%) in people with Down syndrome. Previous studies have reported varying rates in adults (0-66%, Table 1). However, this is the largest study of adults with Down syndrome to be reported and the first to investigate a significantly older population with Down syndrome . Hypothyroidism was found to be the commonest abnormality (evidence in 20%). This was approximately six times more frequent than for hyperthyroidism; a similar finding to that by Kinnell et al (1987).

Approximately 11% had positive antibodies, which is much lower than reported in previous studies (4%-85%; Cutler et al, 1986; Hollinsworth et al, 1974). An association was found between the presence of thyroid antibodies and resulting hypothyroidism (sub-clinical or definite). This has been reported by some researchers (Baxter et al, 1975; Lobo et al, 1980; Dinani and Carpenter, 1990), but not by others (Cutler et al, 1976).

The findings for thyroid screening for subjects on thyroxine replacement highlights the need for professional carers to monitor people with Down syndrome closely. Twenty-four percent were under-medicated and one person over-medicated. In summary, the prevalence of thyroid dysfunction is high in adults with Down syndrome but subjects on thyroxine replacement are poorly monitored. These findings suggest the medical profession needs a “high index of suspicion” for thyroid dysfunction in people with Down syndrome.

Table 2. Thyroid function results for study sample

Thyroid function result	Frequency	Percentage
Normal T4 Normal TSH	104	65.0
Normal T4 Increased TSH	19	11.9
Normal T4 Decreased TSH	2	1.3
Increased T4 Normal TSH	2	1.3
Increased T4 Decreased TSH	5	3.0
Decreased T4 Normal TSH	13	8.1
Decreased T4 Increased TSH	13	8.1
Decreased T4 Decreased TSH	2	1.3
TOTAL	160	100

T4 = Thyroxine TSH = Thyroid Stimulating Hormone

Table 3. Thyroid function results for those on thyroxine replacement

Thyroid function result	Frequency	Percentage
Normal T4 Normal TSH	12	48.0
Normal T4 Increased TSH	4	16.0
Normal T4 Decreased TSH	2	8.0
Increased T4 Normal TSH	1	4.0
Increased T4 Decreased TSH	5	20.0
Decreased T4 Increased TSH	1	4.0
Total	25	100

T4 = Thyroxine TSH = Thyroid Stimulating Hormone

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Address for correspondence:

Dr V P Prasher, MB, ChB, MMEDSc., MRCPsych., MD,
Department of Psychiatry
The University of Birmingham
Queen Elizabeth Psychiatric Hospital
Mindelsohn Way
Birmingham, B15 2QZ
U.K.