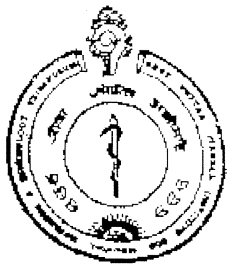

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES & TECHNOLOGY

THIRUVANANTHAPURAM - 695 011

PROJECT REPORT

NAME : **DR. JACOB GEORGE**

PROGRAMME : **D.M. NEUROLOGY**

MONTH & YEAR OF SUBMISSION : **NOVEMBER 1999**

CERTIFICATE

I, **DR.JACOB GEORGE** hereby declare that I have actually performed all the procedures listed / carried out the project under report.

Signature.....

Place : Trivandrum

Date : 08.11.1999

Name in capital letters

JACOB GEORGE

Forwarded. He has carried out minimum requirement of procedures/etc.

Signature Dr. C SARMA

Head of the Department 9.XI.99.

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCINES AND TECHNOLOGY TRIVANDRUM 695 011	Name	
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	Date	

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I sincerely acknowledge the help of Pixel Graphics for typing out the manuscript and giving this work its final form.

JACOB GEORGE

PROJECT REPORT DONE

TITLE

A RETROSPECTIVE STUDY OF THE AETIOLOGICAL PROFILE AND CLINICO ANATOMICAL CORRELATIONS OF DYSTONIC DISORDERS SEEN DURING 10 YEARS IN A TERTIARY REFERRAL CENTRE.

NAME : **Dr.Jacob George**

PROGRAMME : **D.M. NEUROLOGY**

MONTH & YEAR
OF SUBMISSION : **NOVEMBER 1999**

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY
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INTRODUCTION & REVIEW OF THE LITERATURE

One of the earliest description of dystonia was provided by Gowers (1888) who coined the term tetanoid chorea to describe the movement disorder in two siblings later found to have Wilson's disease[1]. In 1901, Destarac used the term "torticollis spasmodique" to describe the twisting neck and pelvic movements in a 17 year old girl [2]. In 1911 oppenheim introduced the term dystonia to indicate that muscle tone was hypotonic at one occasion and in tonic muscle spasm at another, usually elicited upon volitional movements[3]. in the same year as oppenheim's publication, Flatau and sterling described two boys with this disorder emphasizing that it is an organic disease and likely to be inherited. They objected to the term dystonia because they did not believe that varying muscle tone was the clinical hallmark of the condition[3]. However, oppenheim's term dystonia was adopted for this disorder. However since it is not a disease of muscles and since not all patients progress to have fixed postural deformities, objections have been raised over the use of the term dystonia musculorum deformans. The term dystonia is used to indicate both a disease as well as a symptom adding more confusion to the use of this term.

Definition

Dystonia as defined by the Ad Hoc committee of the Dystonia Medical Research Foundation, is a syndrome of sustained muscle contractions, frequently causing twisting and repetitive movements, or abnormal postures [4].

Pathophysiology of Dystonia

Clinical and electrophysiological observations have shown that dystonic movements and postures are due to prolonged abnormal cocontraction of agonist and antagonist muscles with abnormal recruitment ('overflow') of distal muscles during movement[5]. Normally, during contraction of a set of synergist muscles, the antagonist muscles do not behave passively but are actively inhibited by both central and peripheral mechanisms. This inhibition is mediated largely by the inhibitory interneurons of the intermediate laminae of the spinal gray matter. During voluntary contraction of an agonist muscle, the descending commands not only excite the agonist motor neurons, but also excite these inhibitory interneurons which project to the motor neurons of the antagonist muscles. In addition, contraction of the agonist is often associated with an increase in spindle discharge due to alpha-gamma coactivation. Ia afferents from the agonist project to the same group of inhibitory interneurons and constitute a second source of excitatory input to these interneurons. The result is that the antagonist motor neurons are actively inhibited through the inhibitory interneurons by input from both central and peripheral sources[6].

Torsion dystonia is generally considered to be a basal ganglia disorder. How dysfunction of the basal ganglia results in dystonia is unclear. In dystonia, basal ganglia dysfunction may result in an inability to target the inhibition to opposite set of neurons in the cortex, thus producing excessive motor output, particularly during movement[7]. Ridding et al have reported that ipsilateral cortico cortical inhibition is abnormal in patients with Writer's cramps, which could represent a disturbance in the excitability of local intracortical inhibitory interneurons[8]. In addition to these alterations in the cortex, many reflex abnormalities have been described in dystonic patients and these are greatest in muscles affected by dystonia. In cranial, laryngeal & cervical dystonia, blink reflex and masseter inhibitory reflex abnormalities have been documented, suggesting that both excitatory and inhibitory interneuronal pathways in the brainstem are perturbed. In limb dystonia, reciprocal inhibition studied in the flexor and extensor muscles of the forearm is reduced suggesting an abnormality at the spinal inhibitory interneuron circuitry[9].

The picture that emerges from physiological studies is that the brainstem and spinal interneuron circuitry are functioning abnormally in patients with focal dystonias, resulting a change in the tonic control of reflex excitability. An abnormal input from the basal ganglia via cortical or subcortical connections on the brainstem and spinal interneurons could result in these static abnormalities[9].

Anatomical basis of dystonia

There are no consistent morphological abnormalities in idiopathic torsion dystonia as seen on brain imaging or histological examination. A number of pathological studies have been carried out on patients who died with primary torsion dystonia. Even though a few histological abnormalities in the brain stem have been reported by zweig et al[10], the inconsistency of the histology in patients with primary dystonia makes it difficult to interpret the significance of these observations.

The identification of brain structures involved in symptomatic dystonias is based on neuroimaging and pathology. Magnetic resonance imaging (MRI) and positron emission tomography (PET) are more sensitive than computerised tomography. Three regions are most often involved: the basal ganglia, thalamus and brainstem[11]. Dystonia has also been reported with intramedullary spinal cord lesions[12].

Obeso and Gimenez Roldan[13] in a study of 71 patients (39 from their series and 32 from the literature) with symptomatic dystonia have made the following conclusions regarding the anatomic localisation of lesions in dystonia - i) Generalised symptomatic dystonia is usually associated with widespread pathological lesions in the brain. The lesion are bilateral and usually involve the putamen and globus pallidus. ii) Hemidystonia is more often associated with a large caudato capsulo lenticular lesion or hemiatrophy, but also may be secondary to a small putamenal lesion. ii) Hand dystonia is mainly related to a lesion in the posterolateral thalamic nuclei. Lesions of the caudate nucleus and

parietal cortex have also been rarely associated with dystonia of the hand or arm. iv) Torticollis is related to a lesion in the head of the caudate nucleus. v) Foot dystonia is due to large lenticular or caudo-capsulo-lenticular lesion. vi) Mesodiencephalic region is likely to be the main anatomical basis of symptomatic blepharospasm and perhaps cervical dystonia.

In summary, the appearance of symptomatic dystonia from focal brain lesions suggests that structural basis of dystonia lies in the basal ganglia - thalamocortical motor circuit and this has led to the current concept of dystonia as a dysfunction of this loop".

Classification of dystonia

Dystonia can be classified by the

a) Age of onset

b) Distribution.

c) Severity and

d) Aetiology

Classification by age of onset

Classification by age of onset is desirable because this is the most important single factor related to prognosis of idiopathic dystonia[3]. In general, the younger the age at onset the more likely that the dystonia will become severe and also spread to involve multiple parts of the body. The ad hoc committee set up the category by age at onset as

follows : childhood (0-12 years); adolescent (13-20 years) and adult (> 20 years). The relationship between age at onset and clinical progression is illustrated in a large series of 2431 patients with idiopathic torsion dystonia (ITD) seen at the Dystonia Clinical Research Centre; generalised dystonia occured in 47.5% of patients with childhood onset ITD, in 13.5% with adolescent onset and in only 1.9% with adult onset[14].

Classification by distribution[7, 14]

I. Focal dystonia : affects a single body part and is exemplified by blepharospasm, oromandibular dystonia, spasmodic torticollis, spasmodic dysphonia, writer's cramps etc.

II. Segmental dystonia: Two or more contiguous areas are affected. Common examples include cranial (face + Jaw + tongue + Vocal Cords), cranial + cervical, cervical + brachial, bibrachial and axial, neck + trunk etc.

III. Multifocal dystonia: Two or more noncontiguous body regions are involved. An example is a combination of torticollis and dystonia of a leg. Hemidystonia (unilateral dystonia) is a type of multifocal dystonia.

IV. Generalized : Both leg $\pm$ trunk are involved and at least one other region OR one leg + trunk and atleast one other region.

C. Classification by severity[7]

Idiopathic dystonia usually begins as a task specific focal dystonia. As the dystonia progresses, task specific dystonia evolves into action dystonia, then to an overflow dystonia, then to dystonic movements present at rest and finally to fixed postures.

For example, when idiopathic dystonia begins in a leg, it is seen only while walking. It is often absent with running or walking backwards (task specific dystonia). As the dystonic condition progresses less specific actions of the affected leg may activate the dystonia eg. tapping the floor (action dystonia). Later action in other parts of the body can induce dystonic movements of the involved leg (overflow dystonia). With still further worsening, the affected limb can develop dystonic movements while it is at rest (dystonia at rest). Eventually the leg can have sustained posturing.

d. Classification by aetiology

The aetiologic classification divides dystonia into two major divisions, idiopathic (or primary) and symptomatic (or secondary).

Primary dystonia : The primary dystonias are characterised by dystonic movements or postures without associated ataxia, parkinsonism, weakness, spasticity, reflex abnormalities or cognitive changes[7]. Primary dystonias are either sporadic or inherited. most patients with adult onset dystonia have primary sporadic dystonia. Most cases of childhood

onset dystonia are inherited as autosomal dominant disorders. Though Eldridge 15 had proposed an autosomal recessive form of inheritance occurring chiefly in the Ashkenazi Jewish population, this was later challenged by pauls and korczyn[16]. who reanalyzed Eldridge's data and showed that the Jewish form of dystonia was inherited in an autosomal dominant fashion. Bressman et al[17] also showed an autosomal dominant mode of transmission with a penetrance of 32.6% among Ashkenazi jews. X-linked recessive dystonia has been reported only in the natives of Panay island in the Philippines. The gene that causes this form of inherited dystonia has been mapped to the pericentromeric region of the x-chromosome[18].

Secondary dystonia : Wheras primary dystonias usually begin gradually as action dystonias, secondary dystonia often begin suddenly and occur at rest from the onset[7]. There are many clues that may help to make a diagnosis of symptomatic dystonia.

Table 1

Clues to symptomatic dystonia
1. Sudden onset & rapid progression
2. Onset in infancy
3. Cranial onset in childhood
4. Onset in legs in adulthood
5. Abnormal neurological findings : dementia, apraxia, seizures, ocular or visual disturbances, ataxia, weakness, amyotrophy, spasticity, areflexia, sensory deficits, parkinsonism, dysautonomia, skeletal anomalies etc.
6. Hemidystonia
7. Fixed Postures
8. Early speech involvement
9. Evidence for psychogenic actiology
10. Abnormal brain imaging
11. Abnormal laboratory studies
12. Etiologic histories (perinatal problems, encephalitis, head/neck trauma, peripheral injury, toxin/drug exposure etc.)
13. Onset as rest dystonia

AIMS OF THE STUDY

1. To study the aetiological profile of dystonic disorders seen in the department of Neurology, Sree Chitra Thirunal Institute of Medical Sciences and Technology, Trivandrum, over a period of 10 years from 1988 January to 1997 December.

2. To classify the dystonic disorders, based on the

   a. age of onset (childhood, adolescent and adult onset),

   b. distribution of dystonia (focal, segmental, multifocal, generalised or hemidystonia) and

   c. Severity (task specific, action induced, at rest, fixed postures etc)

3. To attempt a clinico anatomical correlation in secondary dystonias based on neuroimaging findings.

MATERIALS AND METHODS

Using a computerised retrieval system, all cases of primary and secondary dystonias seen in the department of Neurology from January 1988 to December 1997 were identified. The completeness of the retrieval was verified by checking the in-patient admission and discharge registers as well as the out patient register of the movement disorder clinic where all patients of dystonia are seen an follow-up. For identifying patients with dystonias, all the specific causes were separately searched (eg: Wilson's disease, Dopa responsive dystonia etc). Data were collected from inpatient or outpatient records and whenever possible also by personal interview of patients and their families, during follow up in the movement disorder clinic. CT scan & MRI scans were rated based on the reports of experienced Neuroradiologists.

Dystonia was diagnosed based on the clinical definition of the adhoc committee of the dystonia medical research foundation[4]. Dystonia was classified as primary when it occurred in the absence of other neurological signs, with the exception of tremor and investigations for secondary dystonia were negative. Secondary dystonia was diagnosed if dystonia was associated with other neurological signs, or if a specific aetiology was detected by laboratory tests or if neuroimaging was abnormal.

All the cases were entered into a proforma (see Appendix 1).

RESULTS

During the period 1988-1997, one hundred and eleven cases of dystonia were seen at SCTIMST.

Among the III patients studied, 77 (69.4%) were men and 34 (30.6%) were women with a male: female ratio of 2.26:1.

The mean age of patients was 34.9 years (range 1-70 years).

The age and sex distribution of the study group are depicted in table 1.

Maximum occurence of dystonia was seen in the age group of 41-50 years, which comprised 30% of all patients. Only 4% of patients were below 10 years of age.

Clinical Features

The age at onset of symptoms varied from 2 months to 66 years (mean = 31.04years). The condition was static in 27 patients (24.3%) and progressive in 84 patients (75.6%).

Site of onset

The most common site of onset was the upper limbs (47%), followed by neck in 28%, face in 10% and lower limb in 8%. No patient complained of an onset in the trunk. Four patients had a generalised onset of dystonia and another four patients had hemdystonia at the onset.

The commonest site of onset of symptoms was the upper limbs seen in 53 patients (47%). Out of these 53, 35 patients (66%) had dystonia confined to the upper limbs. 32 of them had task specific dystonia (writer's cramps), and other three had action induced or at rest dystonia. One of these three patients had dystonic tremor of the upper limb, and one had drug induced dystonia.

Only two patients out of 54, who had a symptom onset in the upper limbs progressed to have a primary generalised dystonia (3.7%) and another two patients had progressed to segmental dystonia (3.7%). Two patients who had an upper limb onset dystonia had features of secondary genralised dystonia.

The diagnosis of other patients who had an upper limb onset dystonia were Wilson's disease in three, drug induced in two, paroxysmal dystonia in two, drug induced in three, PSP in one, and contralateral basal ganglia infarct in one. One patient who had bilateral basal ganglia calcification on CT scan had presented only with writer's cramps.

The second commonest site of onset was in the neck seen in 32 patients (29%). Out of these 32 patients, in 23 patients it was primary (72%). Six of these patients had dystonic tremor, four had a segmental dystonia and one had generalised dystonia, and one had associated hemifacial spasm. The diagnosis of the other nine patients who had a cervical dystonia onset were progressive supranucler paldy in 3, drug induced dystonia in three, contralateral basal ganglia infarct, Wilson's disease and psychogenic dystonia in one each.

Eleven patients had onset of dystonia in the feet. Three of these patients had Meige's syndrome, one of whom also had essential tremor. Blepharospasm was seen in five patients, three of whom had PSP, one had primary blepharospasm and one had a psychogenic basis. One patient had tardive dystonia, one had a secondary generalised dystonia, and one had primary spasmodic dysphonia.

Seven patients had onset of dystonia in the lower limbs (6.3%). Two of these patients had primary generalised dystonia and one had dopa responsive dystonia. One patient subsequently evolved to have a secondary generalised dystonia with chorea and three had Hallwerworden spatz disease.

No patient had a dystonia onset in the trunk.

Four patients had a generalised onset of dystonia. Two of these patients had Wilson's disease, one was post encephalitic and in one it was of unknown cause.

Four patients had hemidystonia at the onset, three of which were secondary to infarct in the contralateral basal ganglia. One of these patients had polyarteritis nodosa. One patient had a paroxysmal nonkinesigenic hemidystonia.

Site of onset of dystonias in the 111 patients is depicted in table II.

Family History

A positive family history of dystonia or any other movement disorder was seen in only 10 of the 111 patients (9%). A family history of tremor was seen in 3 patients. A family history of dystonia was seen in 7patients. Two patients had a family history of writer's cramps. The inheritance in these patients could not be decided, since both these patients had only one another affected sib. These was no history of consanguinity in either of these two families. Two patients had a family history of Wilson's disease. One of them had features of autosomal recessive transmission and in the second patient, the pattern of inheritance could not be determined. Two brothers of probable Hallervorden spatz syndrome were also seen. They were issues of a nonconsanguinous parentage and again the exact pattern of inheritance could not be decided. one patient who had a syndrome of generalised dystonia with choreoathetosis of undetermined cause was product of a consanguinous union with three other sibs affected (autosomal recessive transmission).

Mode of onset

The mode of onset was acute in only ten patients, whereas it was insidious in 101 patients. in 4 out of these 10 patients dystonia was due to infarct. other patients who had complained of an acute onset of symptoms were one patient with Wilson's disease, one with Hallerworden spatz disease, one patient with post encephalitic dystonia, one with psychogenic dystonia and one each with Meige's syndrome and writer's cramps. But the majority of the patients (104) had a chronic onset.

Dystonia was the onset symptom in 87 patients (76%) whereas 24 patients (21%) had other neurological abnormalities before the onset of dystonia. A definite aetiological history was obtained in only 14 patients (12%). Three patients had a history of encephalitis, two had perinatal problems, two patients had a history of trauma and seven patients had a history of drug exposure.

Only seven out of 114 patients had given a history of fluctuations. In only one of them with dopa responsive dystonia was there a definite diurnal variation. Evidences for a psychogenic aetiology such as inconsistent neurological findings, history of psychiatric disturbances, response to placebo etc were found in three patients. The neurological examination was normal in 79 patients (71%) whereas it was abnormal in 33 patients (29%).

Muscles Involved : Commonest site of dystonia seen in this study was the upper limbs. Upper limbs were involved in 71 of the 111 cases studied (64%). Out of these 71 patients, 33 had writer's cramps. Rest of the patients with upper limbs dystonia had a variety of aetiologies.

The second commonest site of dystonia observed was in the neck. Cervical dystonia was seen in 43 patients (39%). Rotational torticollis was seen in 41 of these 43 patients. Nine patients had a combination of torticollis and retrocollis, whereas pure retrocollis was seen in one patients. Anterocollis alone was seen in one patient.

The third commonest site of dystonia was the lower limbs - seen in 24 patients (22%), followed by truncal dystonia in 20 patients (18%),

laryngeal dystonia in 12 patients (11%), blepharospasm in 11 patients (10%), jaw dystonia in 11 patients (10%), lingual dystonia in 10 patients (9%), and facial dystonia in 7 patients (6%) . Hemidystonia was seen in 4 patients (3.5%). The frequency of muscle involvement is show in table III.

Neuroimaging

Neuroimaging was done in 41 patients (37%). In 26 out of this 41 it was normal. Abnormal imaging findings were seen in 15 patients. The abnormalities seen in 3 patients of progressive supranuclear palsy, two with focal dystonia and one with segmental dystonia in another was nonspecific cerebral cortical atrophy. (A correlation between the distribution of dystonia in the other 12 cases and the neuroimaging abnormalities are given in table IV).

Abnormal Imaging

Abnormal neuroimaging findings were seen in three patients of focal dystonia, 2 patients of hemidystonia and seven patients with generalised dystonia.

Focal dystonias : One patient with writer's camps had bilateral basal ganglia calcification. One patient with left upper limb dystonia had an AVM in the region of the right basal ganglia. A third patient with torticollis had a left putamino capsular infarct detected on MRI.

Hemidystonias : There were two patients of hemidystonia who had abnormal neuroimaging findings. One patient had an infarct in the

contralateral thalamus seen on CT scan and the second patient had an infarct in the contralateral cerebral peduncle extending superiorly into the thalamus.

Generalised dystonias : There were seven patients with generalised dystonia who had abnormal imaging findings. All these seven patients had bilateral basal ganglia lesions. The diagnosis of these seven patients were Hallervorden Spatz disease in two, Wilson's disease in two, Leigh's syndrome in one, one patient with post encephalitic sequelae and one patient of polyarteritis nodosa with bilateral basal ganglia infarcts. Five of these patients had undergone MRI and two had undergone CT scans of brain.

Normal imaging

A normal neuroimaging or imaging with nonspecific findings were seen in 29 of the 42 patients who had undergone imaging (71%). These included 4 patients of PSP, 5 patients of torticollis, 4 patients of writer's cramps, 4 patients of secondary generalised dystonia, 3 patients of idiopathic generalised dystonia, 2 patients of Wilson's disease, 2 patients of blepharospasm, and one patient each of Dopa responsive dystonia, Hallervordem spatz disease, idiopathic segmental dystonia, drug induced dystonia and paroxysmal nonkinesigenic dystonia.

Classification of Dystonia

I. Classification by age

Seventy seven of the 111 cases were adult onset dystonias (69%). Twenty patients had an onset in childhood (18%) and 14 patients had an onset in adolescence (13%).

Out of the 77 patients who had an onset in adulthood, 59 had idiopathic dystonias (74%). Secondary dystonias which started in adulthood included 21 patients - 6 with progressive supranuclear palsy, 5 with drug induced dystonia, 2 patients of hemidystonia, 2 patients of Wilson's disease, 1 patient with torticollis following basal ganglia infarction, 1 patient of psychogenic dystonia and 1 patient of secondary generalised dystonia of unknown actiology.

Out of the 20 childhood onset cases, 6 had a secondary generalised dystonia of unknown aetiology, 4 had Hallervorden Spatz disease, 3 had Wilson's disease and one patient each had idiopathic torsion dystonia, dopa responsive dystonia, post encephalitic dystonia, bilateral basal ganglia infarcts secondary to vasculitis, Leigh's disease and a basal ganglia A.V. malformation. One child had dystonic torticollis at the age of 2 months of undetermined cause.

Out of the 14 patients with adolescent onset dystonia, 9 had idiopathic dystonia, two had paroxysmal nonkinesigenic dystonia, one had tardive segmental dystonia, one had Wilson's disease and one had writer's cramps with CT showing bilateral basal ganglia calcification.

The classification of dystonia by age is depicted in table V.

II. Classification by distribution : The commonest distribution of dystonia was focal, seen in 66 patients (59%), followed by generalised dystonia in 24 patients (22%), segmental dystonia in 14 patient (13%), multifocal in 3 patients and hemidystonia in 4 patients.

Out of the 67 patients with focal dystonias, 57 (85%) had idiopathic dystonia. Three patients with focal dystonia had drug induced dystonia, three had progressive supranuclear palsy, and one each had basal ganglia A.V. malformation, torticollis secondary to an infarct and writer's cramps due to bilateral basal ganglia calcification.

Out of the 25 patients with generalised dystonias only three had features of a primary generalised dystonia. Six patients had a secondary generalised dystonia of unknown actiology, 4 had Hallervorden spatz disease, 4 had Wilson's disease and one patient each had post encephalitic dystonia, vasculitis, dopa responsive dystonia, psychogenic dystonia, Leigh's syndrome, drug induced dystonia and progressive supranuclear palsy.

Fourteen patients had segmental dystonia. Out of these, 9 had idiopathic segmental dystonia, 2 were drug induced and 2 were seen in patients of progressive supranuclear palsy. One patient had a paroxysmal dystonia involving both the upper limbs.

Four patients had multifocal dystonia, two of which were due to Wilson's disease and one idiopathic.

Four patients had hemidystonia, 2 of which were due to contralateral infarcts and 2 of which were paroxysmal dystonias.

The classification of dystonias by distribution is shown in tableVI.

III. Classification by severity

The commonest severity grade of dystonia seen was at rest dystonia seen in 59 patients (53%), followed by task specific dystonia in 34 patients (31%), action dystonia in 13 patients (12%), fixed postures in 4 (4%) and overflow dystonia in one patient (1%).

Out of the 59 patients of, at rest dystonia, 26 had primary dystonias (44%) and the remainder (56%) had secondary dystonias of varying aetiologies.

All the 34 patients with task specific dystonia had writer's cramps. out of the 13 patients with actiondystonia, 7 had primary dystonia, 7 had primary dystonia, 2 had paroxysmal dystonia, 1 had action dystonia of right upper limb as a consequence of bil basal ganglia calcification and one each had Wilson's disease, and progressive supranuclear palsy respectively.

Overflow dystonia was recorded only in one patient of Young onset Parkinson's disease. Fixed postures were seen in 4 patients viz. one with post encephalitic dystonia, one with dopa responsive dystonia, one with Wilson's disease and one with Hallervorden spatz disease.

Classification of dystonias based on severity is given in table VII.

IV. Classification by aetiology

Out of the 111 patients, 71 were classified as primary dystonias (64%) and 40 as secondary dystonias (36%).

Out of the 71 patients with primary dystonia, 59 (83%) were classifiable as idiopathic adult onset focal dystonias - viz. writer's cramps in 34 patients, cervical dystonia in 17 patients, action/at rest upper limb dystonia in 2 patients, blepharospasm in 3 patients, spasmodic dysphonia in 1 patient, Meige's syndrome in 1 patient and oromandibular dystonia in one patient. Seven patients had primary segmental dystonia, three had generalised dystonia and are had primary multifocal dystonia. Only one patient had dopa responsive dystonia.

Forty patients had secondary dystonia. Six patients had secondary generalised dystonia of unknown actiology, six each had PSP, Wilson's disease and drug induced dystonia,four patients had Hallervorden spatz disease, two had hemidystonia secondary to infarct, and two had paroxysmal dystonia. One patient each had post encephalitic dystonia, vasculitic dystonia, Leigh's syndrome, basal ganglia A.V. malformation, bilateral basal ganglia calcification, and tortiocollis due to putamino capsular infarct.

The classification of dystonias by actiology is shown in table VIII, and the spectrum of aetiologies of secondary dystonias encountered in table IX.

Age of onset and distribution of dystonia in primary and secondary dystonias

The mean age of onset of primary dystonia was 35.22 compared to the mean age of onset in secondary dystonias viz 23.41.

In the group of secondary dystonias, 51% had generalised dystonia and 24% had focal dystonias. In contrast, in the group of primary dystonias, 80% had focal dystonias and only 4% had generalised dystonias. The distribution of dystonia in the groups of primary and secondary dystonias are given in table X.

Table I

Age and Sex distribution (n = 111)

Age	Males	Females	Total	Percent
1 - 10 years	4	1	5	4
11 - 20 years	14	10	24	21
21 - 30 years	12	3	16	14
31 - 40 years	12	3	24	30
41 - 50 years	24	10	34	30
51 - 60 years	5	5	11	10
61 - 70 years	6	2	8	7

Table II

Site of onset of symptoms (n = 111)

Site	Number	Percent(%)
1. Cervical	32	29
2. Upper limbs	53	48
3. Face	11	10
4. Lower limb	7	1
5. Trunk	0	0
6. Generalised	4	3.6
7. Hemidystonia	4	3.6

Table III

Frequency of muscles involved in dystonia in 114 patients

Site of involvement	Number of patients	Percentage %
1. upper limb dystonia	71	62%
2. Cervical dystonia	43	38%
3. lower limb dystonia	24	21%
4. truncal dystonia	20	18%
5. Laryngeal dystonia	12	11%
6. Blepharospasm	11	10%
7. Jaw dystonia	11	10%
8. Linguel dystonia	10	9%
9. Facial dystonia	7	6%
10. Hemidystonia	4	3.5%

Table IV

Correlation between distribution of dystonia and the neuroimaging abnormalities in 12 cases

No	Clinical feature	Imaging	Finding
	Focal dystonias		
1.	Right upper limb dystonia	CT	Bilateral basal ganglie calcification
2.	Left upper limb dystonia	CT	Right basal ganglie A.V. malformation
3.	Torticollis	MRI	Left putamino-capsular infarct
	Hemidystonias		
1.	Right hemidystonia	CT	Infarct left thalamus
2.	Right hemidystonia	MRI	Infarct left cerebral peduncle extending into left thalamus
	Generalised dystonia		
1.	Post encephalitic	MRI	Bilateral basal ganglia hypointensities
2.	Vascultitis	CT	Bilateral basal ganglia infarcts
3.	Hallervorden Spatz disease	MRI	Bilateral basal ganglia hypointensities
4.	Wilson's disease	MRI	-do-
5.	Wilson's disease	MRI	-do-
6.	Hallervorden Spatz disease	MRI	Bilateral basal ganglia hypointensities
7.	Leigh's disease	MRI	Bilateral basal ganglia and midbarain hypertensities

Table V

Classification of dystonia by age (n = 111)

Age category	Number of patients	Percentage
1. Childhood (0 - 12years)	20	18%
2. Adolescent (13 - 20 years)	14	13%)
3. Adult (>20 years)	77	69%)

Table VI

Classification of dystonias by distribution (n = 114)

No	Distribution	Number of Pateints	percentage
1.	Focal	66	59%
2.	Segmental	14	12%
3.	Multifocal	3	3%
4.	generalised	24	22%
5.	Hemidystonia	4	4%

Table VII

Classification of dystonias by severity (n = 111)

No	Severity	Number of patients	Percentage
1	Task specific	34	31%
2	Action induced	13	11%
3	Overflow	1	1%
4	At rest	59	53%
5	Fixed postures	4	4%

Table VIII

Classification of dystonias by aetiology (n = 111)

No	Aetiology	Number of patients	Percentage
1	Primary	71	64%
2	Seconday	40	36%

Table IX

Spectrum of secondary dystonias n = 40

No	Actiology	Number	Percentage
1	Wilson's Disease	6	15
2	Progressive supranuclear Palpy	6	15
3	Hallervorden Spatz disease	4	10
4	Drug induced	6	15
5	Infarct	3	8
6	Paroxysmal	2	5
7	Vasculitis	1	2.5
8	Leigh's syndrome	1	2.5
9	Encephalitis	1	2.5
10	Basal ganglia AVM	1	2.5
11	Basal ganglia calcification	1	2.5
12	Unknown cause	8	20%

Table X

No	Distribution	Primary diagnosis (n = 71)		Secondory diagnosis (n = 40)	
		Number	%	Number	%
1.	Focal	57	80%	8	20%
2	Segmental	10	14%	4	10%
3.	Multifocal	1	2%	3	7.5%
4.	generalised	3	4%	21	52.5%
5.	hemidystonia	0	0%	4	10%

This study was undertaken to see the pattern of dystonic disorders seen in a tertiary referral centre. The institute where the cases in this study were seen is situated in the southern most part of Kerala, a South Indian state. The institute forms a referral center for the whole of Kerala state as well as the Southern parts of the neighbouring state of Tamil Nadu. Each patient registered in this institute is given a diagnostic code which is entered into a computer. All cases with a diagnosis of primary dystonia and all secondary causes of dystonia could thus be easily retrieved.

One hundred and eleven cases of dystonia were seen in a ten year period from 1988-1997. The male: female ratio seen in this study was 2.3:1. This is unusual as the majority of dystonic disorders in which there is a gender difference, are more common in females. For example, idiopathic adult onset focal dystonias typically affect women more than men (3:1). Reported female to male ratios for idiopathic spasmodic torticollis is 2:1[19]. A survey of 250 blepharospasm patients found a 3:1 predominance for women 20. In 300 patients of cervical dystonia studied at Baylor college of Medicine, houstan 61% were women[21]. There is also a definite female predominance in dopa responsive dystonia of 2-3:1 due to a higher penetrance of the abnormal gene in women, compared to that in men[22]. Considering the fact, that a good majority of our patients had idiopathic adult onset focal dystonia, our finding of a male predominance is unusual. This is most probably related to the socio-cultural aspects of the population in this country, where the women are dependent on men and hence seek medical attention less often when compared to the male population.

DISCUSSION

Majority of the patients in our study had adult onset dystonia (69%). Seventy seven percent of patients with adult onset dystonia had primary dystonias, whereas only 23% had secondary dystonia (18 patients). Most of these patients had an acquired actiology. Only one patient in this group had an actiology of uncertain nature (1.5%). In contrast to this out of the 20 childhood onset dystonias, only one had a primary dystonia (5%). In six of the patients with secondary dystonias in this group, the actiology could not be identified (30%). Thus majority of the patients with adult onset dystonias have primary focal dystonias, and the aetiologies of secondary dystonias in this category can be easily identified, whereas majority of the childhood onset dystonias are secondary (symptomatic), and in a larger proportion of them the actiology cannot be identified. This is probably because of a lack of complete work up of the secondary dystonias. Facilities for genetic work up, lysosomal enzyme assays, electron microscopic examination of tissue biopsy etc were not available during the time period included in this study.

The commonest site of onset of dystonia seen in this study is in the upper limbs, seen in 54 patients (47%). In this group 65% had dystonic symptoms confined to the upper limbs and in 35% it had progressed to become segmental, multifocal or generalised. In contrast out of seven patients who had an onset of dystonia in the lower limbs, six had progressed to a generalised dystonia (85%). It seems that those patients with leg onset dystonia are more likely to evolve into

generalised dystonia compared to those patients with dystonia starting in the arm. This is similar to the observation in patients with idiopathic torsion dystonia where patient with leg onset are more likely to evolve into generalised dystonia[14].

A positive family history of any movement disorder was seen in only 9% of patients. Only 6% of patients had a family history of dystonia. In the group of primary dystonias, only two patients of writer's cramps had a similar illness in their brothers. This accounts for only 2.8% of the group of primary dystonias. The rates of dystonia, reported in the literature in patients with late onset primary dystonias vary from 5% to 9%[23]. Overall, the low occurrence a positive family history in our patients could be because that 62% of our patients had primary dystonias. Even in the group of secondary dystonias, a majority of patients (75%) had an acquired cause of dystonia.

The most common site of occurrence of dystonia seems to be in the upper limb, followed by the neck and lower limbs. Cranial dystonias were much less commonly seen in this study. This is in contrast to the observation of Jankovic according to whom cranial and cervical structures are most frequently affected by dystonia (78% of patients with dystonia)[24]. Even though upper limb dystonia was the commonest in this series, cervical or cranial dystonias occurred in 84% of our patients (see table III).

Neuroanatomical correlation

Neuroanatomical correlations of the dystonic disorders seen in this study could be made only based on structural imaging studies. Functional imaging or autopsy studies were not performed on any of the cases. Though imaging was done for 42 cases, positive findings which could correlate with dystonia were seen in only twelve patients.

In seven patients of generalised dystonia, bilateral basal ganglia lesions were seen. In one of these patients (Leigh's disease) there were additional lesions in the brainstem also. In two patients of hemidystonia, abnormalities were observed in the contralateral thalamus, one of them also had an additional lesion of the contralateral cerebral peduncle. One patients of upper limb dystonia had contralateral basal ganglia lesion, whereas another patient had bilateral basal ganglia calcification. One patient with torticollis had a contralateral putamino capsular infarct.

Three regions are most often involved in dystonia, viz-the basal ganglia especially the putamen, the thalamus and the brainstem[11]. Rarely dystonia may also occur with intramedullary spinal cord lesions[12]. Our finding of bilateral basal ganglia lesions in seven patients with generalised dystonia is consistent with the finding of obeso and gimenez Roldan[13]. In the study of obeso and Gimenez Roldan, hemidystonia is more often associated with a large caudato capsulo-lenticular lesion or hemiatrophy or a smell putaminal lesion. According to jankovic[24], about 75% of patients with hemedystonia have CT or MRI evidence of contralateral basal ganglionic lesion, a history or hemiparesis or both. Infarction or

hemorrhage involving the putamen precedes the onset of hemidystonia in a third of the patients. In our series there were only 4 patients of hemidystonia, 2 of whom had paroxysmal dystonia, in one of whom MRI was normal. In the other 3 patients imaging had shown infarction of the contrlateral thalamus. This is not difficult to explain as the structural basis of dystonia lies in the basal ganglia thalamocortical motor circuit. Interestingly one of our patients with torticollis had a putaminocapsular infarct whereas in the observations of obeso and Gimenez Roldan[13], torticolis is related to a lesion in the head of the candate nucleus.

Classification of dystonia

i) Classification by age : It is important to classify dystonia by the age of onset, since it is the single most important factor which can be used to prognosticate whether the dystonia will generalize or not[3]. This important fact is observed in this study also. In the 20 cases of childhood onset dystonia, in this study, excepting one patient who had a focal dystonia due to a contralateral basal ganglia AVM, all the other 19 patients had a multifocal or generalised dystonia. In the adult onset group, on the other hand the majority had idiopathic focal or segmental dystonias. Our study also shows that adult onset dystonia is much more common than childhood dystonia occuring in a ratio of 4:1.

ii. Classification by distribution : In our study focal dystonias are approximately three times more common than generalised dystonias. Segmental dystonia, focal dystonia and hemidystonia are much less

common. it is also observed that focal dystonias are much more common in adults whereas generalised dystonias are more common in childhood. Also, generalised dystonias are most often secondary (symptomatic), whereas focal dystonias are most often primary.

iii. Classification by severity : Dystonia occurring at rest is the most common form of dystonia based on severity seen in this study, followed by task specific and action dystonia. Fixed postures and overflow dystonia were only rarely seen. Dystonia occurring at rest is slightly more commonly seen with secondary dystonias rather than with primary dystonias. Task specific dystonias on the other hand, seen in this study mostly primary. Action dystonias also are more often primary rather than symptomatic.

iv. Classification by aetiology : In this study primary dystonias were more commonly seen than secondary dystonias in a ratio of 1.65:1. The spectrum of aetiologies for secondary dystonia is quite wide (see table IX). Secondary (symptomatic) dystonias have an younger age of onset when compared to primary dystonias. Also, symptomatic dystonias are more often generalised rather than focal, whereas primary dystonias are more often focal than generalised.

Limitations of this study

The major limitation of this study is the retrospective collection of data. Actiological histories, family history, history of fluctuations,

aggravating factors etc would have been given less stress by the physicians who attended to these patients is an outpatient setting. The exact recording of the muscles involved in the dystonia may also not be perfect in this situation.

The number of patients with dystonia seen in this study is likely to be much less than the actual number of cases seen. This is because dystonia as a minor symptom or sign may occur in a large variety of conditions. Even though we had gone through the case files of many patients with these conditions, dystonia would have been missed if the treating physician had not recorded the finding of dystonia in the presence of other major neurological findigs.

The spectrum of secondary dystonias seen in this study are likely to be far from complete due to lack of investigative facilities for these disorders

This retrospective study of dystonic disorders seen at SCTIMST in the time period 1988-1977 reveals the following

i Male patients with dystonia are more commonly seen than females (male: female ratio = 2.3:1)

ii. Adult onset dystonias are much more common than childhood and adolescent onset dystonias

iii Adult onset dystonias are more commonly primary, whereas childhood dystonias are more commonly secondary

iv Focal dystonias are the most common forms of dystonia, followed by generalised dystonia. Segmental, multifocal, and hemidystonias are much less commonly seen.

v Dystonias occurring at rest are the most common forms of dystonia classified by severity, followed by task specific and action induced dystonias. Overflow dystonias and fixed postures are only rarely seen

vi Primary dystonias are much more common than secondary dystonias. The age of onset of secondary dystonias is less than that of primary dystonias. Secondary dystonias are more often generalised, whereas primary dystonias are more often focal.

vii The proportion of patient of dystonia showing abnormalities on neuroimaging is few. Generlised dystonic disorders show bilateral basal ganglia lesions. Hemidystonias and focal dystonias may show lesions of the contraleral basal ganglia or thalamus.

CONCLUSIONS

1. Gowers W R. A manual of diseases of the nervous system. vol2. London: Churchile, P 656,1888.

2. Destarac. Torticolis spasmodique et spasmes functionelles Rev neurol 9: 591, 1901.

3. Fahn S. Concept and classification of dystonia Adv Neurol 50: 1-7; 1988.

4. A Barbeau, D.B.Calne, S. Fahn, C.D. Marsden, J Menkes, G.F.Worten. Ad Hoc Committee of the Dystonia Medical Research Foundation Feb 1984.

5. Rothwell JC, obeso JA, Day BL, Marsden CD. Pathophysiology of dystonia. Advances in neurology, 39, 851-863, 1983.

6. Rothwell JC, Day BL, Obeso JA, Berardelli A, Marsden CD. Reciprocal inhibition between muscles of the human forearm in normal subjects and in patients with idiopathic torsion dystonia. Adv. Nurol 50, 133-139. (1988)

7. Jankovic J, Fahn S: Dystonic disorders, in Jankovic J, Tolosa E eds: Parkisan's disease and movement disorders, 2nd ed. Baltimore: Williams & Wilkins, 1993, Chap 21, pp 337-374.

8. Ridding MC, Sheean G, Rothwell IC etal: changes in the balance between motor cortical exitation and inhibition in focal, task specific dystonia. J neurol Neurosurg Psychiatry 59: 493-498, 1995.

BIBLIOGRAPHY

9. Tolosa SE, Marti MJ: Adult onset idiopathic torsion dystonias, in watts RL, Koller wc eds, Movement disorders: Neurologic principles and practice, Mc Graw Hill 1997, chap 31, pp. 429-441.

10. Zweig RM, Hedreen jC, Delong RM, Whitehouse PJ, Price DL: Primary dystonias : A review of the pathology and suggestions for new directions of study. Adv neurol vol. 50 pp 123-132.

11. Dee Yebenes JG, Pernaute RS, Tabernero C. Symptomatic dystonias, in Movement disorders: Neurologic principles and practice, Mc Graw kill 1977, chap 33pp 455-475.

12. Madhusudanan M, Gracykutty M, Cherian M. Athetosis - dystonia in intramedullary lesion of spinal cord. Acta Neurol Scand 1995, 92; 308-312

13. Obeso JA, Gimenez-Roldan S. Clinico pathological correlation in symptomatic dystonia. Adv Neurol Vol 50 pp 113-122.

14. Bressman SB, Fahn S. Childhood dystonia, in movement disorders; Neurologic principles and practice, Mc Graw Hill 1997, chap 30 PP 419-428.

15. Eldridge R. The torsion dystonias : literature review and genetic and clinical studies. Neurology 20 (2) 1-78, 1970.

16. Pauls DL, Korcyzn AD. Complex segregation analysis of dystonia pedigrees suggests autosamal dominant inheritance. Neurology 40: 1107 - 1110, 1990.

17. Bressman SB, Deleon D, Brin MF, Risch N, Shale H, Burke RE, Greene PE, Fahn S. Inheritance of idiopathic torsion dystonia among Ashkenazi Jews. Adv. Neurol. Vol 50 pp 45-56.

18. Wilhelmoren KC, Weeks DE, Nyggard TG et al. Genetic mapping of "lubag" (X-linked dystonia - Parkinsonism) in a Filipino kindred to the pericentromeric region of the X-chromosome. Ann Neurol 29: 124-131, 1991.

19. Duane D D. Spasmodic torticollis. Adv. Neurol 49, 135-150, 1988.

20. Jankovic j, Orman J. Blepharospasm : Demographic and clinical survey of 250 patieents. Ann ophthalmol 16: 371-376, 1984.

21. Jankovic J, Leder. S, Warner D, Schwartz K. Cervical dystonia: clinical findings and associated movement disorders. Neurology 41; 1088-1091, 1991.

22. Louis E, Lynch T, Bressman SB, et al: Gender differences in Dopa resparsive dystonia. Neurology, 44, 368-369, 1994.

23. Bressman SB et al. Clinical Genetic spectrum of primary dystonia Adv. Neurol Vol 78 pp 71-91, 1998.

24. J.Jankovic & S.Fahn. Dystonic disorders. In J.jankovic, E. Tolsa ed., Parkinson's discase and movement disorders. edition 3. William & Wilkins 1998.

Appendix I

PROFORMA

A retrospective study of the aetiological profile and clinicoanatomical correlations of dystonic disorders seen during 10 years in a tertiary referral centre

Participants : Jacob George, Asha Kishore, K. Radhakrishnan

Name : _____

Address : _____

_____

_____

Occupation : _____

CARD - 1

Column	Code	Item
	_____	SCTIMST Number
	_____	Study number
	_____	Age
	_____	Gender
	_____	Age at onset of symptoms
	___	Mode of onset
	__	Acute (1=Yes, 0=No)
	_	insidious (1=Yes, 0=No)

Site of onset of symptoms (1=Yes, 0=No)

..... Neck

..... Face

..... upper limb

..... Lower limb

..... Trunk

Course of disease (1=Yes, 0=No)

..... Static

..... Progressive

Firs symptom (1=Yes, 0=No)

..... dystonia

..... Other neurological symptoms

(Specify :.....)

Precipitating factors identified (1=yES, 0=No)

..... Writing

..... Typing

..... Playing musical instruments

..... Skilled activities

..... Other actions

..... Stress

..... Fatigue

..... Exercise

..... Excitement

..... Others

Specify :_____

Relieving factors (1Yes, 0=No)

..... Sensory tricks

..... Alcohol

..... Relaxation

..... Drugs

Aetiologic histories (1Yes, 0=No)

..... Prenatal problems

..... Encephalitis

..... Measles

..... Trauma

Specify : _____

..... Toxin exposure

Specify : _____

..... Drug exposure

Specify : _____

Fluctuations (1Yes, 0=No)

..... Paroxysmal

..... Diurnal

..... Nil

Family history

..... Family history of dystonia (1Yes, 0=No)

..... Number of siblings affected

..... Consanguinity among parents (1Yes, 0=No)

..... Degree of consanguinity (1=1^0, 2=2^0, 3=3^0)

..... Members other than siblings with dystonia

..... Relation of affected members to index case (1=Parents, 2=1^0 rlatives, 3=2^0 relatives; 4=3^0 relatives)

..... Family history of tremor

..... No of siblings with tremor

..... Family history of other movement disorders.

Pattern of inheritance (1Yes, 0=No)

..... AD

..... AR

..... Maternal inheritance

..... X-linked

..... Sporadic

CARD - 2

Muscles involved (1Yes, 0=No)

..... Blepharospasm

..... Facial dyskinesias

..... Hemifacial spasm

..... Masticatory muscles

..... Lingual

..... Laryngeal

..... Torticollis

..... Retrocollis

..... Anterocollis

..... Upper limb dystonia

..... Truncal dystonia

..... Striatal foot

Neurological Examination (1Yes, 0=No)

..... Dmentia

..... Limb apraxia

..... Seizures

..... Oculomotor apraxia

..... Visual disturbances

..... Ataxia

..... Weakness

..... Spastcity

..... Amyotrophy

..... Areflexia

..... Sensory deficit

..... Bradykinesia

..... Cogwheel rigidity

..... Dysautonomia

..... Skeletal anomalies

..... Tremore

Specify : _____

Severity of dystonia (1Yes, 0=No)

..... Task specific dystonia

..... Action induced dystonia

..... Overflow dystonia

..... At rest dystonia

..... Fixed postures

..... contracture

Evidence for Psychogenic dystonia (1=Yes, 0=No)

..... Inconsistent weakness

..... Inconsistent sensory loss

..... Psychiatric disturbances

..... Response to placebo\suggestions

..... None

CARD - 3

Investigations (0=negative or norma; 1=positive or abnormal; 2=Net done)

..... Slit lamp examination for K.f. ring

..... Serum copper

..... Serum ceruloplasmin

..... Serum lactate

..... Serum pyruvate

..... Serum uric acid

..... Acanthocytes

..... Urinary aminogram

..... CSF lactate

..... CSF antimeasles antibody

..... Hexosaminidase

..... Aryi sulfatase

..... Liver function tests

..... Urine homocytine

CT scan (0=not; 1=done, normal; 2=done, abnormal)

Sescribe site of lesion : _____

Nature of lesion : _____

MRI (0=not; 1=done, normal; 2=done, abnormal)

Describe site oflesion : _____

Nature of lesion : _____

NCV/EMG (0=not; 1=done, normal; 2=done, abnormal)

Describe : _____

Tissue biopsy (0=not; 1=done, normal; 2=done, abnormal)

Describe : _____

..... Response to levodopa (0=Absent; 1=Present)

CARD - 4

Classification of Dystonia (1=Yes, 0=No)

by age

..... Childhood (0=12 years)

..... Adolescent (13-20 years)

..... Adult (>20 years)

by distribution

..... Focal

..... Segmental

..... Multifocal

..... Generalised

..... Hemidystonia

by severity

..... Task specific

..... Action induced

..... Overflow

..... At rest

..... Fixed postures

by aetiology

..... Idiopathic

Specify : _____ (Familial/Sporadic)

..... Secondary

Specify

Clinical evidence : _____

_____

Radiologic evidence : _____

_____

Laboratory evidence : _____

_____

Combined evidence : _____

_____