A Dissertation on

"CLINICAL SPECTRUM OF HIRAYAMA DISEASE IN TERTIARY CARE HOSPITAL"

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CERTIFICATE

This is to certify that the dissertation entitled "**CLINICAL SPECTRUM OF HIRAYAMA DISEASE IN TERTIARY CARE HOSPITAL"** is a genuine work done by **Dr. S SARAVANAN** for the partial fulfillment of the requirements for D.M., (Neurology), Examination of **The Tamil Nadu Dr. M.G.R. Medical University** to be held in August 2013, under the able guidance and supervision of **Prof. Dr. S GOBINATHAN M.D., D.M.(Neurology),** Professor and Head, Department Of Neurology, Government Stanley Medical College and hospital, Chennai.

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DECLARATION

I, **Dr. S SARAVANAN**, Solemnly declare that the dissertation, titled "**CLINICAL SPECTRUM OF HIRAYAMA DISEASE IN TERTIARY CARE HOSPITAL"**, is a bonafide work done by me during the period of January 2011 to January 2013 at Government Stanley Medical College and Hospital, Chennai under the expert supervision of **Prof. Dr. S GOBINATHAN M.D., D.M. (Neurology),** Professor and Head, Department Of Neurology, Government Stanley Medical College and hospital, Chennai.

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CONTENTS

ABBREVIATION

1) HD	: Hirayama disease
2) NCS	: Nerve conduction study
3) CMAP	: Compound muscle action potential
3) MN	: Median nerve
4) UN	: Ulnar nerve
5) MRI	: Magnetic resonance imaging
6) BMA	: Benign monomelic atrophy
7) C	: cervical
8) T	: Thoracic
9) CSF	: Cerebro spinal fluid
10) Lt	: Left
11) Rt	: Right
12) Neck in E	: Neck in extension
13) Neck in F	: Neck in flexion
14) T1W /T2W	: T 1 weighted or T2 weighted imaging on MRI
15) M	: Male
16) F	: Female
17) f mean	: f mean latency
18) SSEP	: Somato sensory evoked potential
19) DTR	: Deep tendon reflex
20) U/l	: Unilateral
21) B/l	: Bilateral
22) SNAP	:Sensory neural action potential

INTRODUCTION

INTRODUCTION

Juvenile muscular atrophy of the unilateral upper limb localized to hand and forearm was first reported independently in 1959 from Tokyo by Keizo Hirayama *et. al*[1] and Takagi, Okabe[2]. Benign monomelic amyotrophy (BMA) is considered a less common form of motor neuron disease of as yet unknown cause. In view of the first such case being reported by Keizo Hirayama, this disease is now being referred to as Hirayama disease.

Focal muscular atrophy of unknown etiology has been reported since 1959 with different names as Juvenile muscular atrophy of unilateral upper extremity (Hirayama *et al*[1]., 1959: Singh *et al*[3]., 1980), Benign focal amyotrophy (Adornato *et al*[4]., 1978), Monomelic amyotrophy (Gourie-devi *et al*[5]., 1981), Sobue disease (Soube *et al*[6]., 1978). Wasted leg syndrome (Prabhakar *et al*[7]., 1981). Benign monomelic atrophy (Choi *et al*[8,9]., 1982: 1987: Cheong *et al*[10]., 1992).

This disease was initially reported from Japan and later there has been numerous case series published predominately from Japan, India, Korea and China. There are numerous case reports published from Brazil, France, Germany, Italy, Spain, Turkey, Poland and Canada [11-15].

Hirayama *et.al* [1,16,17] description of isolated upper limb atrophy was similar to "Tephromalacie Anterieur" reported earlier by Marie and Foix[20] in the year 1912. This previous description was of localized hand muscle wasting which affected the middle aged people and elderly people predominantly, the pathogenic mechanism described for that entity was different and had softening of the anterior horn in the lower cervical cord. Because of the similarity in clinical features a possible pathology of the lower cervical cord in juvenile muscular atrophy of distal upper extremity was thought of by keizo Hirayama and colleagues.

Hirayama disease unlike motor neuron diseases is clinically non progressive after a period of time. Also histopathology of autopsied specimen was being interpreted to be suggestive of anterior horn cell

ischemia in lower cervical spinal cord [1,13]. Nerve conduction studies changes and MRI changes have also been described in literature.

This study is undertaken to study the Clinical features, Nerve conduction changes especially with reference to the ulnar and median f wave conduction in neck flexion and extension, MRI changes in neck extension and flexed position in patients with Hirayama disease attending govt. Stanley hospital Chennai.

HIRAYAMA DISEASE

The clinical features of Hirayama disease were summarized based on previous studies [15-19]. This disease affects people in their teenage or early second decade, it preferentially affects the males (male to female ratio = 20:1). There have been rare case reports of Familial occurrence, six pairs have been reported till date in over 300 case reports from Japan.

Description of patients presenting with similar complaints has been reported differently by authors. Each author had given a different

name to describe the disease they were reporting as the etiology of this disease is largely unknown. This confusion in disease categorization led to the emergence of multiple synonyms for this spectrum of clinical syndromes.

Patients usually present with insidious onset symptoms of weakness in gripping objects with hands, weakness of fine movements of the hand along with tremulousness of the fingers. The muscle weakness preferentially involves the intrinsic hand muscles and forearm muscles. This disease for unknown reasons spares the brachioradialis. The atrophic region extends obliquely over both volar and dorsal surfaces of the forearm which gives the characteristic wasting unique to this disease also described as oblique amyotrophy. This amyotrophy was initially reported to be a unilateral disease, later bilateral occurrence of the disease have been reported in some patients and even among bilateral involvement, it was predominantly observed to be asymmetrical. Weakness develops in both extensor and flexor muscles of the fingers and wrist; the finger extensors and wrist flexors are usually predominantly involved. Many patients show worsening of finger weakness on exposure to cold environment (cold paresis). There are no fasciculation at rest, but fascicular twitching of the forearm muscles

(contraction fasciculation) accompanies the tremulous movement of the fingers on weak finger extension (minipolymyoclonous). Muscle streach reflexes of upper and lower limbs are usually normal, although occasionally it may be brisk ad rarely there may be pyramidal signs.

This disease has been predominantly described as a pure motor syndrome. Although a few patients show slight hypoesthesia in a localized hand region, is usually subjective and objective sensory disturbances are rarely observed. This disease doesn't cause bowel or bladder disturbances, cranial nerve dysfunction or autonomic disturbances.

The clinical course of the disease is usually indolent marked by the initial progressive course followed by a spontaneous remission within 2 to 5 years from onset in most patients.

The etiology of Hirayama disease is elusive. Till now there have been many theories put forth to describe its occurrence, each theory has its own lacunae. The important theories that have been implicated till date are the following.

1) Flexion cervical compressive myelopathy[21,22]
2) Circulatory insufficiency[23,24]
3) Benign form of spinal muscular atrophy[25]

4) Atopy or hyper IgE aemia[26]

5) Ion channel deficiency[27]

The first autopsy was published by Keizo Hirayama et al in 1987 revealed arachnoid mater hypertrophy over the anterior spinal cord, anteroposterior flattening spinal cord with thinning of lower cervical cord at C5-T1 with a predominant lesion in C7-C8 region on both sides. Histological examination revealed atrophy of the anterior horns to about less than 50% of the normal anteroposterior diameter of the anterior horns on both sides of the spinal cord. The lesions showed mild noncavitating necrosis in its center with decreased number of nerve cells in the surrounding region, degenerative features were observed in the other nerve cells, mild astrogliosis without macrophage infiltration. No blood vessel proliferation or amyloid deposits. The blood vessels were largely normal. These changes were highly localized and the remaining spinal cord segments were normal. Based on the Pathologic features of cervical poliomyelopathy in this disease, a possible ischemic etiology was thought to be responsible for these changes. However, the histopathologic features seen in anterior horns and motor neurons was different from those seen in

proven cases of spinal vascular diseases, confounding the understanding of microcirculatory disturbance as a possible pathology.

Neuroradiologists after having noted no significant abnormality in routine cervical MRI, following the report of possible ischemic changes in histopathology, studied dynamic changes in the cervical spine with neck flexion in patients of Hirayama disease. The following changes on neck flexion were reported - flattening of the lower cervical spinal cord and dura which was termed as “over-stretch of the cord”, “tight dural canal in flexion”, “forward displacement of the dural sac” or “disproportionate shortening of the dorsal roots”. The above findings were hypothesized to be responsible for the development of localized cord compression. The reason for this localized nature of the disease was thought to be due to differential growth of the vertebrae and the spinal cord along with meninges during the juvenile growth spurt. This differential growth causes anterior cervical cord compression related to flexion movement of the neck. This theory is supported by the observation that the peak age of onset of Hirayama disease occurs 2 to 3 years after the peak age of normal juvenile growth spurt.

These dynamic changes of spinal cord flattening and possible compression with forward cord shift were predominantly reported in MRI done during the early stages / years of the disease. Later during the non progressive course of illness, absence of the spinal cord shift anteriorly during neck flexion, also suggested that this disease was probably caused due to dynamic compression of the lower cervical spinal cord.

Billé-Turc *et al*.[28] suggested that Hirayama Disease is not a separate disease by itself and probably represented a syndrome complex characterized by the distinctive clinical features. They also suggested that the clinical, electrophysiological or MRI features doesn't classify Hirayama disease as being a distinctive disease and that these features could also be interpreted as one of the clinical variants of Benign Monomelic Amyotrophy or segmental motor neuron disease. They suggested that this variant can be termed Hirayama's form of Benign Monomelic Amyotrophy.

Several studies on dynamic neck flexion MRI in Hirayama disease have consistently reported the anterior shift of the spinal cord and dura along with their flattening. This lead to an overwhelming faction of

neurologist supporting the mechanical compression [29] theory of lower cervical cord as the most likely contributing factor for the development of Hirayama disease. This along with the reports of several patients having arrest of disease progression following use of a cervical collar to restrain neck movement also supported this theory [30]. However still many neurologists do not support or believe in the compressive myelopathy theory, as features thought to be exclusively seen in neck flexion MRI patients of Hirayama disease was not actually exclusive and features suggestive of cervical spinal cord compression and increase in space behind the posterior dura sleeve were also observed during neck flexion MRI in normal people[31,32].

J Kira *et. al.*[33] observed Hirayama disease cannot be attributed solely to mechanical compression of spinal cord hypothesis due to the following reasons - a sudden increased in the reported cases of Hirayama disease in Japan during 1990, Arrest in disease progression spontaneously occurring in 1 or 2 years from onset, young males being affected most often, few familial case reports and Asians being affected most often[1,6,13,30,32]. Atopy was hypothesized as one of the precipitants the microcirculatory disturbance[34,35] as IgE can cause platelet activation and

aggregation [36], histamine release[37] leading to platelet thrombus formation and arterial spasm causing microcirculatory disturbance. In addition to this, venous stasis occurring due to possible spinal cord compression during neck flexion can precipitate a local IgE mediated platelet response. Repeated episodes of microcirculatory disturbance may lead changes seen in the anterior horn cells, as motor neurons are most susceptible to ischemia in the spinal cord. Atopy outbreak in 1990 in Japan can also explain the sudden increase in Hirayama disease patients during that period. Atopy can also be attributed to familial Hirayama disease as familial atopic tendencies are well documented. Also atopic disorders often seen in younger individuals and males than compared to the aged and females[38] and Asians being more prone to atopy[39] may point to a possible alternate theory to partially understand of the epidemiological features of Hirayama disease.

R. M. Van den Berg-Vos *et.al*.[40] In their attempt to understand the pathogenesis of Hirayama disease proposed a classification of adult patients with sporadic Lower motor neuron disease as follows

(i) Slowly progressive Spinal muscular atrophy

(ii) Distal spinal muscular atrophy

(iii) Segmental distal spinal muscular atrophy

(iv) Segmental proximal spinal muscular atrophy

Hirayama disease was considered a distal or proximal segmental variants of spinal muscular atrophy. They also observed bilateral upper limb involvement described as “man-in-the-barrel” phenomenon together with brisk reflexes in 29% of their patients as also noted by Hirayama. These findings were also observed in Hirayama disease. In addition, involvement of the adjacent lower spinal cord segments, suggests a possibility to consider this Lower motor neuron syndrome a variant of Spinal Muscular Atrophy.

Sawai Setsu *et. al.* [27] studied Hirayama disease patient and age matched controls for conduction properties at normal room temperature and after partially cooling the muscle, to study the difference in conduction characteristics based on variation of surrounding environmental temperature. They observed prolonged strength-duration time constant, dispersion of threshold electrotonus, increased refractoriness of muscles and supernormality in patients at room temperature and after cooling and

in control subjects after cooling. These findings suggested axonal depolarization most likely caused due to dysfunction of the sodium – potassium pump. Based on these findings they proposed that Hirayama disease was caused due to altered axonal excitability of the motor neurons due to abnormally increased persistent sodium currents, and dysfunction of transient sodium and potassium channels. These findings could possibly give partial understanding in the pathogenesis of Hirayama disease and phenomenon of cold paresis.

Laboratory evaluation

Clinically patients have patchy wasting of C7, C8, T1 innervated muscles namely – wrist extensors, wrist flexors, small muscles of hand, hypothenar and some times thenar muscles. There is occasional spread of the involvement to C5 and c6 innervated muscles. There is characteristic sparing of the brachioradialis muscles and conspicuous absence of fasciculation other than minipolymyoclonous.

There are several electrophysiological investigations. Electromyography shows acute and chronic denervation in the atrophied muscles.

1) Motor nerve conduction velocities are normal, except for minimal slowing in ulnar nerve conduction.
2) Amplitude of compound muscle action potentials is reduced in the atrophied muscles.
3) F-wave shows increase in latency, reduced persistence, and a single, high-amplitude wave form – suggestive of denervation / reinnervation. F-wave persistency decreases and f latency increases during flexion of the neck in a progressive phase of the disease.
4) The homonymous muscles of the unaffected side also show denervation in about 90% of patients with unilateral amyotrophy. Non-atrophic muscles on the affected side sometimes show denervation, in 50% of triceps brachii, and in less than 25% of brachioradialis, biceps brachii, and deltoid muscles.
5) Single fiber electromyography shows increased fiber density and jitter in a progressive stage. The fiber density further increases but jitter decreases in a late, non-progressive stage, indicating maturation of reinnervation.
6) Somatosensory evoked potentials may show abnormal conduction through the spinal cord.

7) Transcranial magnetic stimulation studies show prolonged latency and reduced amplitude of motor evoked potentials. These changes are worsened by flexing the neck. Based on this finding cervical collar therapy was suggested to prevent neck flexion so that the changes associated with neck flexion could be avoided.
8) Cold paresis is also studied electrophysiologically. With High frequency Repetitive nerve stimulation test of cooled muscle showing prolonged latency and low amplitude, suggesting impaired conduction through muscle membrane.

Neuropathology

1) Muscle biopsy of the atrophic muscles shows typical neurogenic changes with clusters of small angular fibers and large type groupings indicative of reinnervation
2) Autopsy is quite rare because of the excellent prognosis of the disease compared to the classical motor neuron diseases. The spinal cord showed macroscopically evident antero-posterior flattening at the lower cervical segments. Microscopically, the antero-posterior diameter of the lower cervical anterior horns of both sides was reduced, most severely at C7 and C8 predominantly on the left. The anterior horn lesion was

characterized by a decreased number of both large and small neurons, mild astrogliosis, and central necrosis without cavity formation. The surviving neurons showed various stages of degenerative changes. The white matter, posterior horns, and the intra- and extramedullary vessels being normal.

CSF evaluation and its pressure dynamics

Cerebrospinal fluid shows normal cell content with or without a slight increase in protein (40-60 mg/dl; normal <40 mg/dl). Pressure curve of the Queckenstedt test shows a slightly slow and insufficient rise and fall in the neutral neck position, which is aggravated during neck flexion.

Magnetic resonance imaging.

1) Atrophy or thinning or the spinal cord on sagittal view.

2) Flattening of the cervical cord in anterior to posterior diameter.

3) T2 hyperintesity within the spinal cord at anterior horn cell region.

4) Abnormal curving of the cervical vertebral column.

5) Detachment of the posterior dural sac from the overlying lamina.

6) Extension of dural detachment upto upper thoracic level.

7) Sickle shaped space behind the dural in cervical region with

Prominent flow voids

8) Signal changes noted within the cervical spinal cord.

Treatment options

As yet there is no definitive treatment for Hirayama disease, however there are many experimental case reports available in literature which can be tried for preventing further progress of disease

A) Possible suggested treatment options to prevent progression

1) Medical –

- Antiglutamate drugs- Riluzole

- Cervical soft collar therapy to prevent neck flexion

2) Surgical -

- Lower cervical laminectomy with neck fusion in partial

Extension

- Lower cervical laminectomy with duroplasty

B) Functional surgery- tendon transfer surgery to help gain hand function.

AIM & OBJECTIVES

AIM

1) To study the clinical, nerve conduction and radiological profile of patients diagnosed to have Hirayama disease.

OBJECTIVES

1) To study the clinical profile of Hirayama disease.
2) To study the changes in Nerve conduction study parameters, with respect to median and ulnar f wave study in the neutral position of the neck and flexed position of the neck in patients with Hirayama disease and to compare its significance between the 2 neck position and also with controls.
3) To study the MRI changes in patients with Hirayama disease in neck neutral position and neck flexion position.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Hirayama K [1,13,.16.17.,18,19,29,30,41] described this disease based on the clinical presentation as Juvenile muscular atrophy of distal upper extremity (Hirayama disease) as this disease affected males more often than females during their adolescence and it was characterised by weakness and wasting of muscles of the hand. It usually had a progressive course over 2 to 5 years followed by spontaneous arrest. Based on this spontaneous arrest in clinical progression this disease was proposed by him to be a distinct entity when compared to motor neuron disease, although he does acknowledge in his article that still many neurologists consider this disease to be a variant of neurodegenerative motor neuron disease. He interpreted autopsy report published by him, to be secondary segmental ischemic changes restricted to the anterior horn cell region of the lower cervical cord. Based on this cervical ischemic poliomyelopathy was the proposed pathogenesis. However, several authors disagree that these findings suggest ischemic features and probably degenerative motor neuron disease. Hirayama and his colleagues based on the neuropathology findings prompted further neuroradiologic investigations post

neuropathology findings to support the theory of ischemic cervical myelopathy, neck flexion MRI was done, in which dynamic changes of anterior shift of cervical spinal canal contents was induced by neck flexion. These cervical dynamic changes could not be explained at the present level of understanding. Also the number of patients reported to have this disease in Japan exceeds 300 and from India exceeds 100, an ethnic factor contribution to the causation of this disease was also considered.

Sunil Pradhan[42] evaluated 106 patients in northern India, the author observes that eleven patients, constituting 10% had bilaterally symmetrical Hirayama disease and among them 9 patients had asymmetric onset of symptoms this being concluded as unilateral disease progresses to severe form of bilateral involvement. They also noted the presence of atypical features of localized autonomic dysfunction. MRI of these patients revealed the characteristic features described earlier. This study suggested a paradigm shift in the understanding of this disease as a unilateral or grossly asymmetric disease to that of spectrum of clinical features ranging from unilateral to bilateral disease involvement, in some patients progressing to the severe form of bilateral symmetrical involvement. The

author concluded that the description of the term "brachial monomelic amyotrophy" should be reviewed as this disease is not strictly monomelic.

Gourie-Devi M *et.al.*[43] and Nalini A *et.al.*[44] Evaluated 17 patients diagnosed to have Benign monomelic muscular amyotrophy (Hirayama disease), in south India. Somatosensory evoked potential (SSEP) recordings were made from both median and ulnar nerve. The dynamic changes with respect to recording with a straight neck and flexed neck was studied and compared with healthy age matched controls. The author observed that in SSEP central conduction in cervical region represented by N13 response was abnormal in either or both the nerves in all patients and similar changes were absent in the control group. The author concluded that with neck flexed position, N13 response was dearanged in 82% patients with median nerve SSEP and 100% in ulnar nerve SSEP indicating segmental cervical cord dysfunction in patients with Hirayama disease.

Lyu RK *et. al.*[45] studied the median and ulnar nerve conduction among 46 patients with Hirayama disease, 60 patients with amyotrophic lateral sclerosis and 54 healthy subjects for comparison. The author

observed that the ulnar to median CMAP amplitude ratio was reduced (0.64 ± 0.79) in patients of Hirayama disease when compared with that of patients of Amyotropic lateral sclerosis who had higher (2.15 ± 1.77) and the normal controls (0.89 ± 0.23). Based on these findings, the author concluded that Hirayama disease affected the ulnar nerve segments more severely than median nerve segments this was in contrast to patients with amyotrophic lateral sclerosis where median nerve segments were more affected than the ulnar segments. These observations demonstrate the disease specific differential hand muscle wasting between these two diseases.

Hemant A Sonwalkar *et.al.*[46] evaluated the MRI features in eight patients with Hirayama disease. The author observed that the only consistent finding in his study was of lower cervical cord atrophy. The other findings of asymmetrical atrophy, flattening, loss of normal cervical column curvature, dural changes and contrast enhancement was grossly variable between patients studied. In addition to the above findings, they observed another variable presentation of thoracic epidural changes in few patients. Based on these findings they suggested the use of dynamic post

contrast MRI evaluation as a pivotal investigation in the evaluation of Hirayama disease patients.

Nascimento OJ, *et. al.,*[47] reported 4 cases of Hirayama disease from Brazil. They observed Hirayama disease as predominating in Asia and rarely referred among westerners. They followed up the clinical and electrophysiological alterations described in these patients over 5 years duration. They observed that ENMG suggested LMN pattern of involvement. They also analyzed MRI of cervical region in these patients to evaluate for possible spinal cord compression; however no abnormality was detected in MRI of spine. In view of its clinical, and EMG characteristics, they suggested that Hirayama disease is a clinical variant of motor neuronopathy - benign monomelic amyotrophy (BMA). They concluded that Hirayama disease represented the distal variant, upper limb predominant form of benign monomelic amyotrophy and it should not be considered to be a specific disease entity in itself.

Fu Y *et.,al.,*[48] evaluated 27 cases of Hirayama disease clinically and with MRI in dynamic neck positions. They observed that all of their patients were right handed and were young males, Of them 77.8%

developed initial symptoms before they were 19 years old. Right hand involvement was more common in 20 patients (74%) compared to 7 patients (26%) with the left hand onset. MRI was abnormal in neutral neck position in 16 patients with abnormal cervical curvature and 14 patients having lower cord atrophy and 2 having Intramedullary abnormal high signals. During neck flexion abnormality was noted in all patients with flattening and anterior shift of lower cervical cord with a crescent-shaped high signal area behind the cord which showing gadolinium enhancement and disappeared after the patient returned to a neutral position in one case. They opined dynamic neck flexion MRI are useful diagnosed tool revealing significant changes which would be missed on neutral neck position MRI.

U K Misra *et.al.*[49] studied 8 Hirayama disease patient and 7 controls for simultaneous radiological and neurophysiological correlation. They evaluated the effect of neck position in Hirayama disease during study of 1) F waves – in the median and ulnar nerves especially with reference to latency, F to M amplitude ratio, F persistence, and chronodispersion. 2) Somatosensory evoked potentials (SEPs) - evaluating N9, N13, and N20. 3) Magnetic resonance imaging (MRI) – of cervical

Spinal cord to look for evidence of characteristic features described earlier. They observed that these parameters did not show any significant variation in the two neck positions studied in patients of Hirayama disease compared with controls. There were minimal change in N13 and this too was not attributable to changes observed in the dura. The author concluded that no significant variation of nerve conduction parameters could be observed in neck flexion and it was not related to dynamic MRI changes. The author suggested that mechanisms different from flexion ischemic myelopathy should be explored to understand the occurrence of Hirayama disease.

S. Pradhan[50] , Tokumaru *et. al.*[51] observed in their study that the forward movement of dura mater occurs only in the acute phase of illness and can press the cervical spinal cord but later during the stable phase of the illness, which occurs 1–3 years after the onset of weakness and wasting, this compression is not evident. They concluded that the movement of the spinal cord and dura mater was due to longitudinal stretch occurring with flexion of the neck and their movement being independent and not causing compression of the spinal cord. During this stretch the cervical spinal cord mainly abuts the C5, C6 vertebral body probably causing transient compression of radicular

arteries feeding that region. They also observed that following detachment of the dura the vacant space was filled up with passively dilated venous channels. These engorged veins were considered passive dilatation as there was not evidence of dural congestion was seen in a patient during surgery. They suggested that empty space behind dura had negative pressure that favored enlarged epidural veins. Based on this they concluded that vascular changes in the spinal cord were due to the positional effect of neck flexion and this recurring hemodynamic compromised leads to segmental anterior horn cell degeneration in the watershed region. Dural movement was unlikely to cause pressure over the spinal cord and is not responsible for the development of this disease.

MATERIALS AND METHODS

MATERIALS AND METHODS

Study Design: Retrospective and prospective study

Setting: Govt. Stanley Medical College and hospital, Chennai 600001.

Study population: All patients with clinical suspicion of HD between Jan 2011 to Jan 2013 were included in the study

Inclusion criteria:

1) All patients with hand muscle wasting for whom the etiology could not be ascertained on standard evaluation for secondary motor neuron disease.
2) Weakness and wasting predominantly in one or both upper limbs.
3) Absence of cranial nerve, sphincter or cerebellar deficits.
4) 5 control subjects, age matched, with no neurological illness,

Exclusion criteria

1) Patients with focal upper limb atrophy and weakness due to focal disease of nerve, muscle, bone, or maldevelopmental diseases.
2) Patients of Hansen's disease.
3) Patients diagnosed to have traumatic, infectious, vasculitic and metabolic plexopathy or neuropathy with hand wasting.

Methodology

1) Consent would be taken from subjects and their identity would not be revealed.
2) Review of medical records of patients with a diagnosis of Hirayama disease.
3) Demographic and clinical data of these patients.
4) MRI cervical spine, pre- and postcontrast MRI were done with neck in neutral position (neck extension) and flexed position (maximum flexed position of the neck so as to make the chin touch the sternum) – changes in MRI will be recorded as per the description given below.
5) Nerve conduction study of median and ulnar nerves in neutral position (neck extension) and in flexed position of the neck (maximum flexed position of the neck so as to make the chin touch the sternum). The following parameters would be recorded – compound muscle action

potential, f minimum latency, f maximum latency, f mean, f chronodispersion – for both ulnar and median nerves.

6) In patients with Hirayama disease each affected limb is taken as a single entity for the purpose of statistical analysis.
7) Nerve conduction study of median and ulnar nerves in neck neutral position (neck extension) and neck flexed position (maximum flexed position of the neck so as to make the chin touch the sternum). The following parameters would be recorded – compound muscle action potential, f minimum latency, f maximum latency, f mean, f chronodispersion – for both ulnar and median nerves.
8) Comparison of f mean in median and ulnar nerves of affected limbs with that of controls and also comparison between the f mean in Hirayama disease patients in neck extension and flexed position to look for significance in the variation.

Magnetic resonance imaging

Magnetic resonance imaging will be performed at Govt. Stanley hospital with a 1.5 Tesla MRI scanner (Siemens).

MRI protocol based on available literature was formulated by the radiology and the following imaging protocol was planned to be performed on each patient. Imaging was performed in 2 neck positions

1) Patient lying straight on the scanner with the neck in extension / neutral position.
2) The patient lies straight on the scanner, bending his neck forward as far as possible so as to touch the sternum with his or her chin and the head being supposed in this position with the help of MRI compatible pillows.

In the above mentioned position the following sequences were performed as follows

1) Neck straight - Sagittal SE T1W, TSE T2, Gradient Echo T2.
2) Neck in flexed position - Sagittal SE T1W, TSE T2, Gradient Echo T2, Postcontrast SE T1W was done in the sagittal plane using gadolinium based MR contrast at a dose of 0.5mmol/Kg body weight of the patient as a rapid bolus injection via a venous access.

The images were interpreted by radiologists and they were given the necessary clinical information. The following features were evaluated in patients with Hirayama disease.

1) Atrophy or thinning or the spinal cord on sagittal view.

2) Flattening of the cervical cord in antero posterior diameter.

3) T2 hyperintensity within the spinal cord at anterior horn region.

4) Abnormal curving of the cervical vertebral column.

5) Detachment of the posterior dural sac from the overlying lamina.

6) Crescent shaped space behind the dural in cervical region.

7) Gadolinium enhancement of this space.

8) Intramedullary signal hyperintensity.

The above mentioned features are defined and identified based on similar descriptions in the literature described below.

1) The localized atrophy of the cervical spinal cord was usually seen in the spinal cord adjacent to C4 and C7 vertebrae.
2) Cord atrophy was measured in sagittal T1/ T2 imaging by measuring anterior to posterior spinal cord diameter in the upper cervical, lower cervical and upper thoracic region. Atrophy was said to be present if the lower cervical spinal cord diameter was equal or less the other diameter of the spinal cord measured above or below[(52)].
3) On axial imaging of the spinal cord atrophy of the cord was observed as follows. The normal spinal cord is round to elliptical

in cross section. Unilateral or asymmetrical atrophy of the spinal cord appears like a pear fruit with thinning on one half and rounded configuration on the other side. Bilateral atrophy was characterized the flattening of the postero-lateral aspect of the spinal cord giving a cross sectional configuration of a triangle.

4) Flattening was evaluated on axial MR images. The spinal cord is defined as anterior- posteriorly flattened only if there is no obvious evidence of cord compression with the surround CSF space of equal width all around the spinal cord [(52)].

5) The cervical curvature was evaluated based on the description suggested by Batzdorf and Batzdorff. [(53)]. With the neck in a neutral position in T1 sagittal imaging an imaginary line was drawn from the posterior border of the body of the C2 vertebrae to the level of posterior border of the C7 vertebrae. The intervening vertebrae are normally anterior to the imaginary line. If they touch the imaginary line or cross posterior to it then the normal lordotic curvature of the cervical spine is said to be lost.

6) Detachment of the dura from the overlying lamina is best observed in T2 sagittal and T2 axial imaging of the spinal cord with neck in flexion. More than one-third loss of attachment between the

posterior dural sac and the subjacent lamina was considered significant[52].

7) Normally no T2 signal changes are seen within the spinal cord in T2 sagittal or axial view. Hyperintensity in the area of anterior horn cells of the spinal cord, without any evidence of compression, is considered abnormal cord hyperintensity.
8) On injecting Gadolinium contrast, enhancement in normal individuals. Enhancement of the space behind the detached dural is considered abnormal and is suggestive of vascular channels in this region.

Statistical analysis

Statistical analysis was performed using SPSS 17.0 software. CMAP (compound muscle action potential) and f wave latency of the median and ulnar nerves of the affected limb and control limb were fed into the software and verified the data to be parametric. Mean and standard deviation was derived. The independent variable t test was performed. A probability level less than 0.05 was considered to be significant.

RESULTS

OBSERVATIONS & RESULTS

1) In this study there was a male preponderance in Hirayama disease patients, with 27 (87.1%) of males and 4 (12.9%) of females (fig. 1).

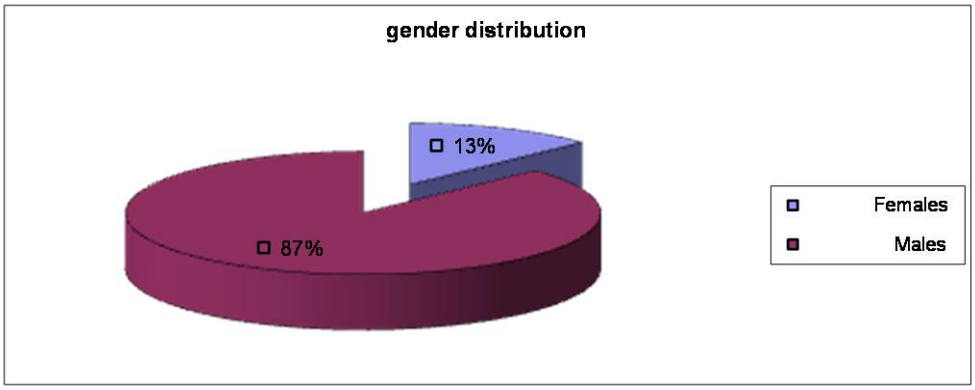

Figure 1: Gender distribution of patients with Hirayama disease

2) Hirayama disease was unilateral in 9 (29%) patient and bilateral in 22 (71%) patients (figure 2). Among females all 4 (100%) patient had bilateral involvement and among males 9 (33.3%) of 27 had unilateral and 18 (67.7%) had bilateral involvement of upper limbs (figure 2).

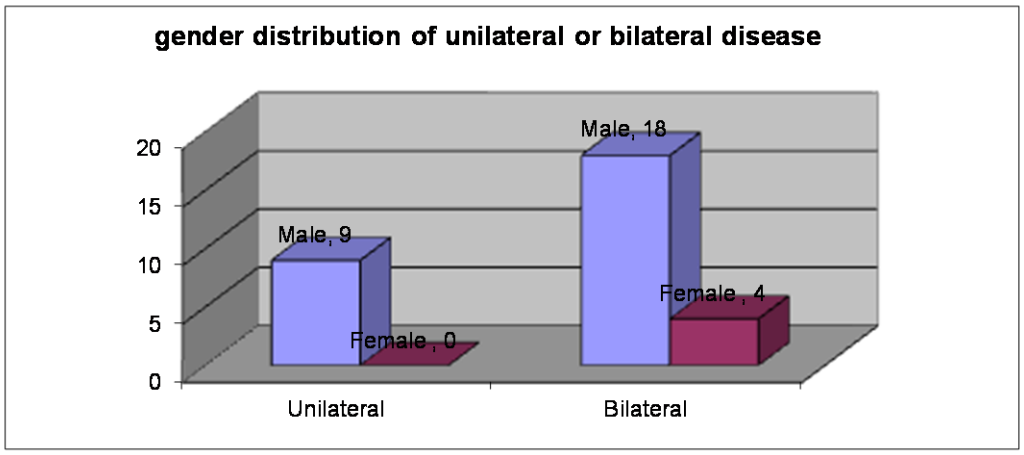

Figure 2: Gender variation of unilateral or bilateral disease involvement

3) All patients were right handed people. Among 9 patients with unilateral disease, 5 (55.6%) had right upper limb affected and 4 (44.4%) had left upper limb involvement (figure 3).

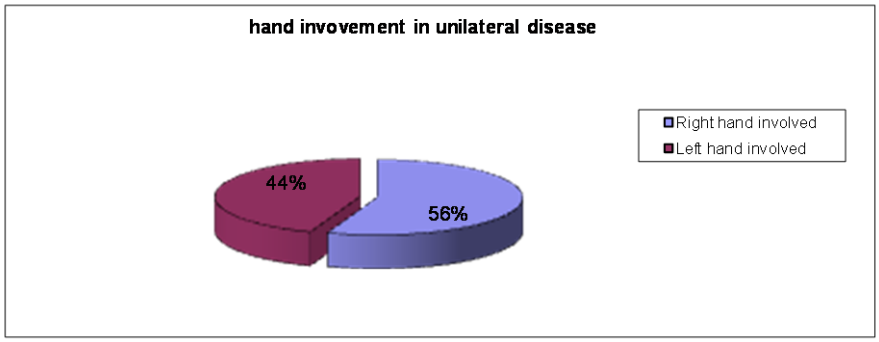

Figure 3: Hand involved in unilateral disease

4) Among 22 patients with bilateral disease, right upper limb was more affected than left in 12 (54.5%), left upper limb was more affected than right in 8 (36.4%) and bilateral equal affected upper limb was seen in 2 (9%) patients (figure 4).

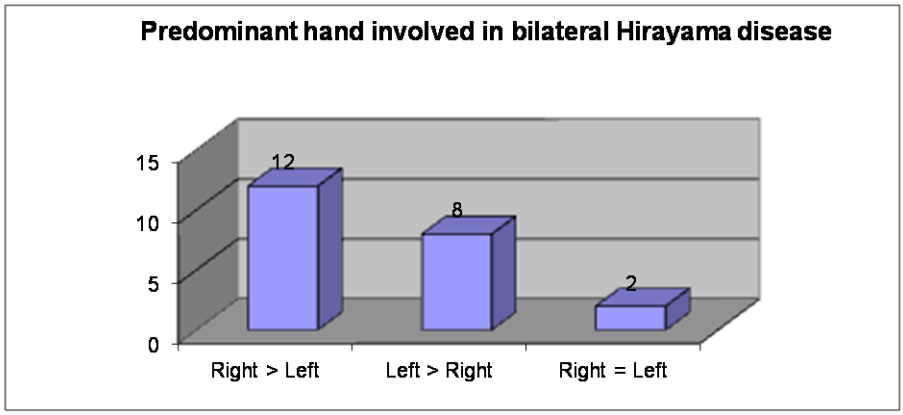

Figure 4: Predominant Hand involvement in bilateral disease

5) Among the 31 patients studied (table 1), 27 patients had right hand involvement and 26 patients had left hand involvement. Although bilateral the hand involvement in this disease is asymmetrical Predominant right hand involvement was seen in 17 (55%) patients (5 with unilateral and 12 with bilateral disease) compared to predominant left hand involvement 12 (39%) and 2 (6%) patients had bilateral equal involvement of hand.

Table 1: Overall Predominant hand involved in Hirayama disease

Predominant hand affected	No of patients	Percentage
Right hand affected	17	55%
Left hand affected	12	39%
Both had equally affected	2	6%

6) The age of the patients (figure 5) in this study ranged from 15 years to 30 years with a mean age of 21.5 years.

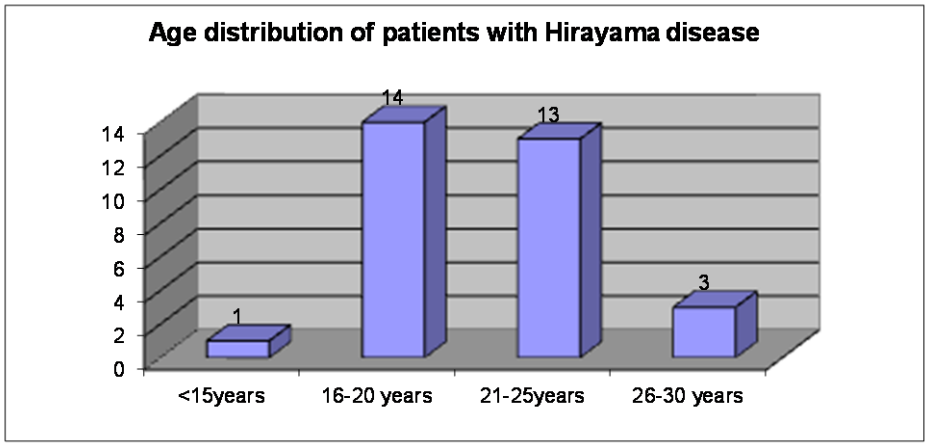

Figure 5: Age distribution of Hirayama disease patients

7) The duration of disease (figure 6) in the patients studied varied from 3 months (0.25 years) to 108 months (9 years) with an average duration of 31.7 months (2.65 years).

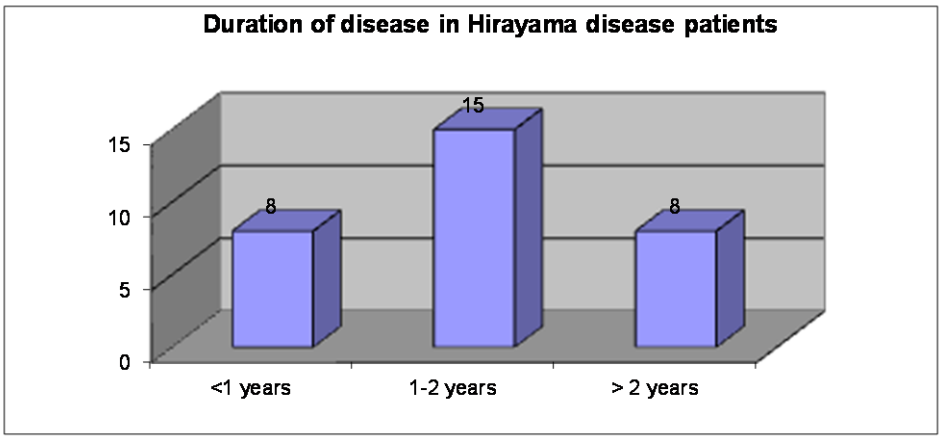

Figure 6: Duration of disease in patients with Hirayama disease.

8) Age at onset of first symptom (figure 7) in the study population varied from 11 years of age to 27 years of age with the average age of disease onset being 18.9 years. 26 (84%) patients had onset of disease between the age of 15 to 25 years.

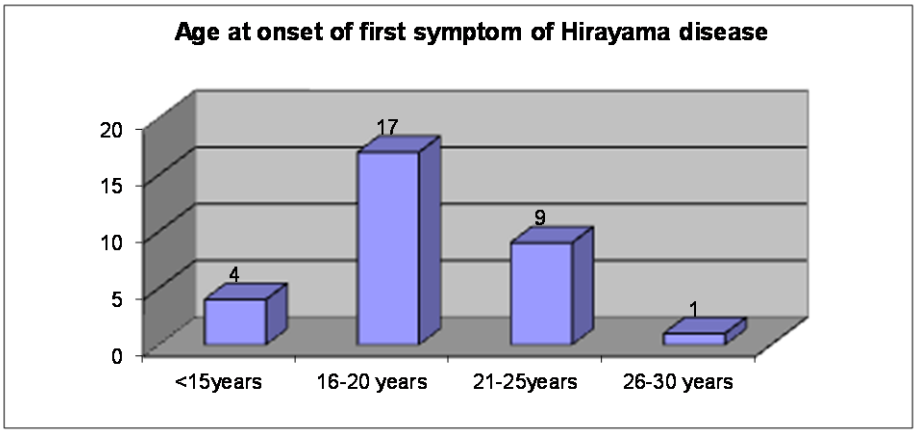

Figure 7: Age at first symptom of Hirayama disease

9) A history of acute worsening of weakness on overnight exposure to cold environment was present in 8 (25%) patients (figure 8), all of them had unilateral disease and had disease duration of 3 months to 18 months. This pattern may suggest that cold paresis is a feature of early stage of the disease than compared to later stages.

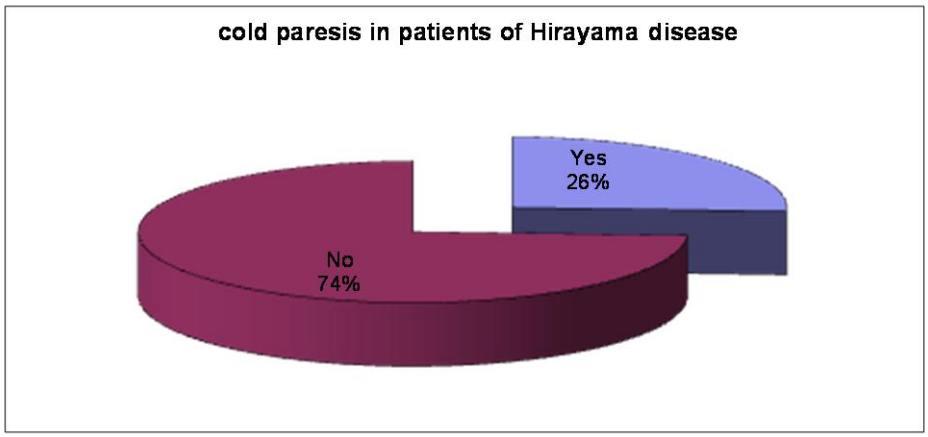

Figure 8: Clinical history of cold paresis in Hirayama disease patients

10) All patients had wasting, weakness, tremulousness of distal upper limbs. In addition, 11(35%) patients (Figure 9) had proximal involvement.

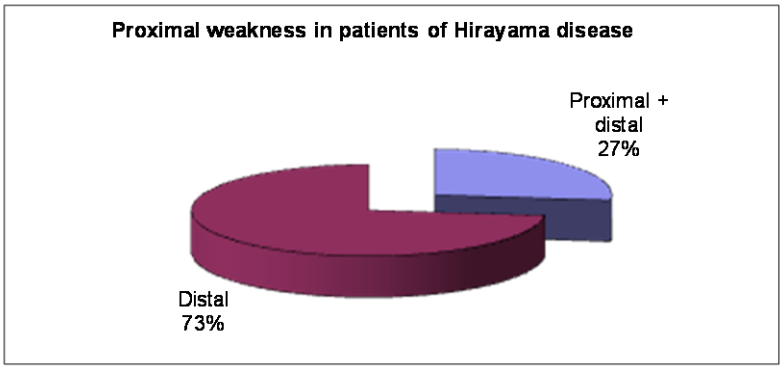

Figure 9- Patients of Hirayama disease with proximal involvement

11) All patients had moderate to severe involvement of C8, T1 myotomes, 27(87%) patients had involvement of C7 myotome and 11 (35%) patients had C5, C6 myotome involvement (figure 10).

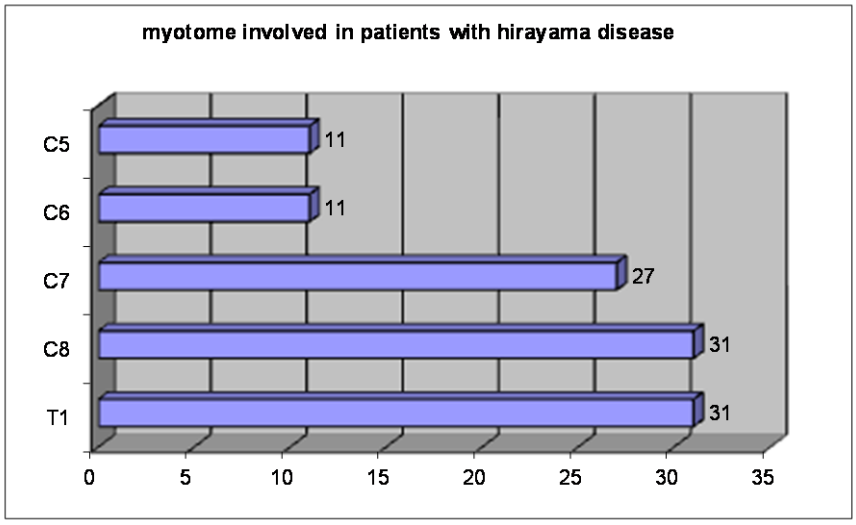

Figure 10: spinal segment involvement in Hirayama disease patients

12) Brisk deep tendon reflexes were observed in 11 (35%) patient in the lower limbs and the rest 20 (65%) had normal DTR (figure11).

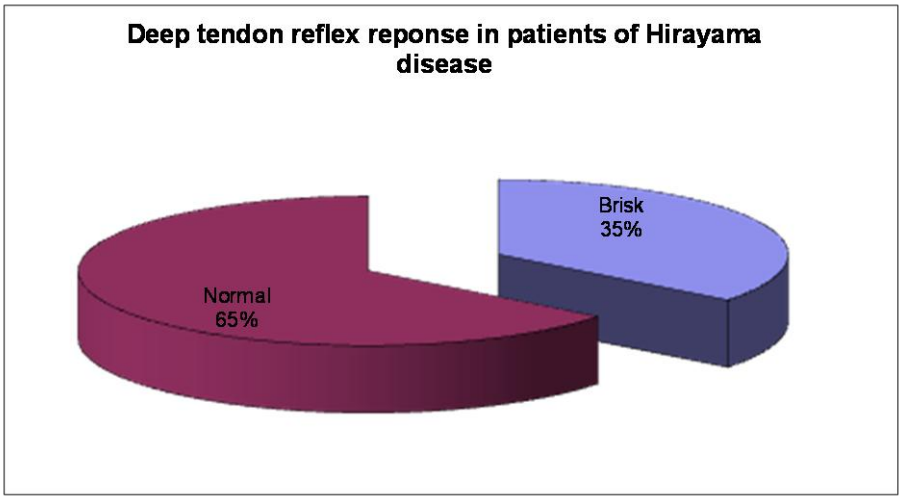

Figure 11: DTR response in Hirayama disease patients

13) Transient benumbed sensation of the affected limb over the dorsum of the hand lasting few days to week with spontaneous recovery was seen in 6 (19%) patients. 5 Of them had unilateral disease and this sensory disturbance was associated with cold paresis. Sensory nerve action potential was normal.

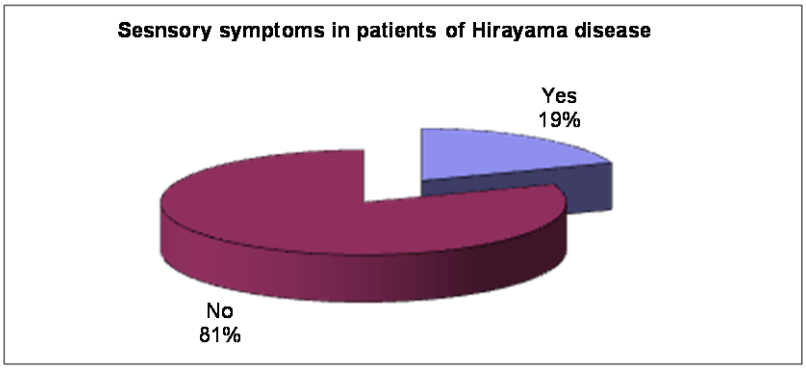

Figure 12: Sensory symptoms in patients of Hirayama disease

14) Fasciculation over deltoid, biceps or triceps was seen in 8 (26%) patient (figure 13), they had bilateral disease and disease duration of more than 24 months. This feature may be suggestive of active denervation during the early proximal disease innervation.

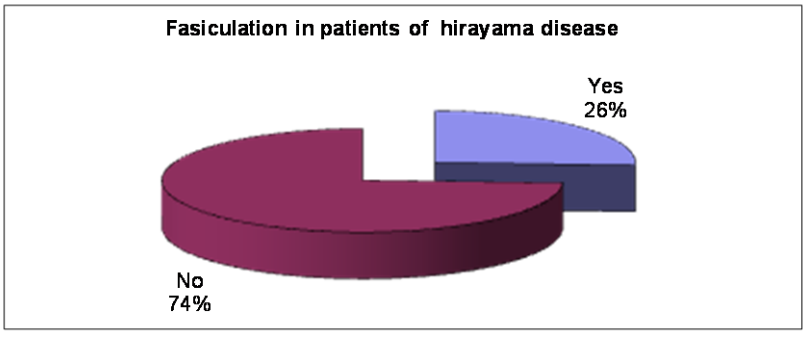

Figure 13: Clinically evident fasciculation in Hirayama disease patient

15) 11 (35%) patients had weakness of deltoid and biceps muscles. Triceps was weak in 27(87%). All patients had wrist flexion weaker than wrist extension. All patients had severe weakness of FDP compared to FDS.

16) All patients had wasting of the intrinsic muscles (figure 14) of the hand which was asymmetric or patchy, which was characteristically evident on inspection of an outstretched hand revealing each finger in different planes suggesting an imbalance in muscle strength causing fingers to project in different planes. Regarding forearm wasting, there was evident wasting of the medial aspect of the forearm with flexor digitorum profundus more weak compared to flexor digitorum superficialis especially of the 4^{th} and 5^{th} digit. Lateral forearm was spared with normal preserved bulk of brachioradialis in all patients.

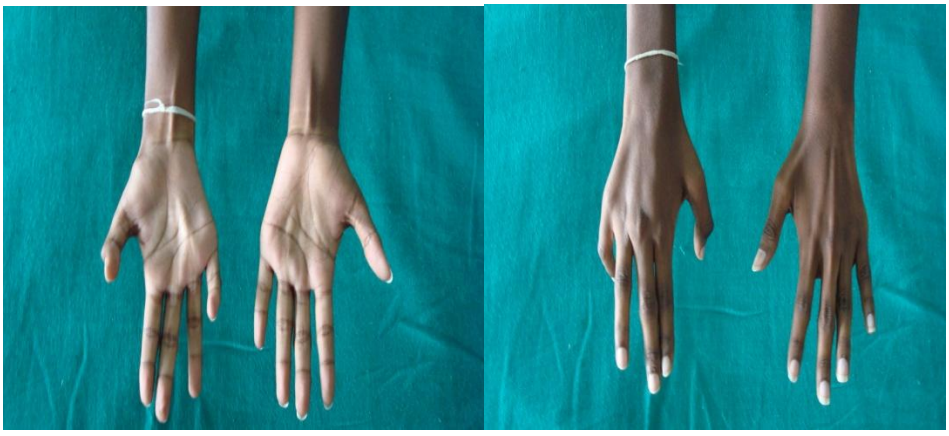

Figure 14: Bilateral Hirayama disease – hand muscle wasting

17) On MRI sagittal images, all 31 patients had straightening of the cervical spine from C3 to C6 vertebra MRI (figure 15-image A & B) with loss of cervical lordosis in neck neutral position.

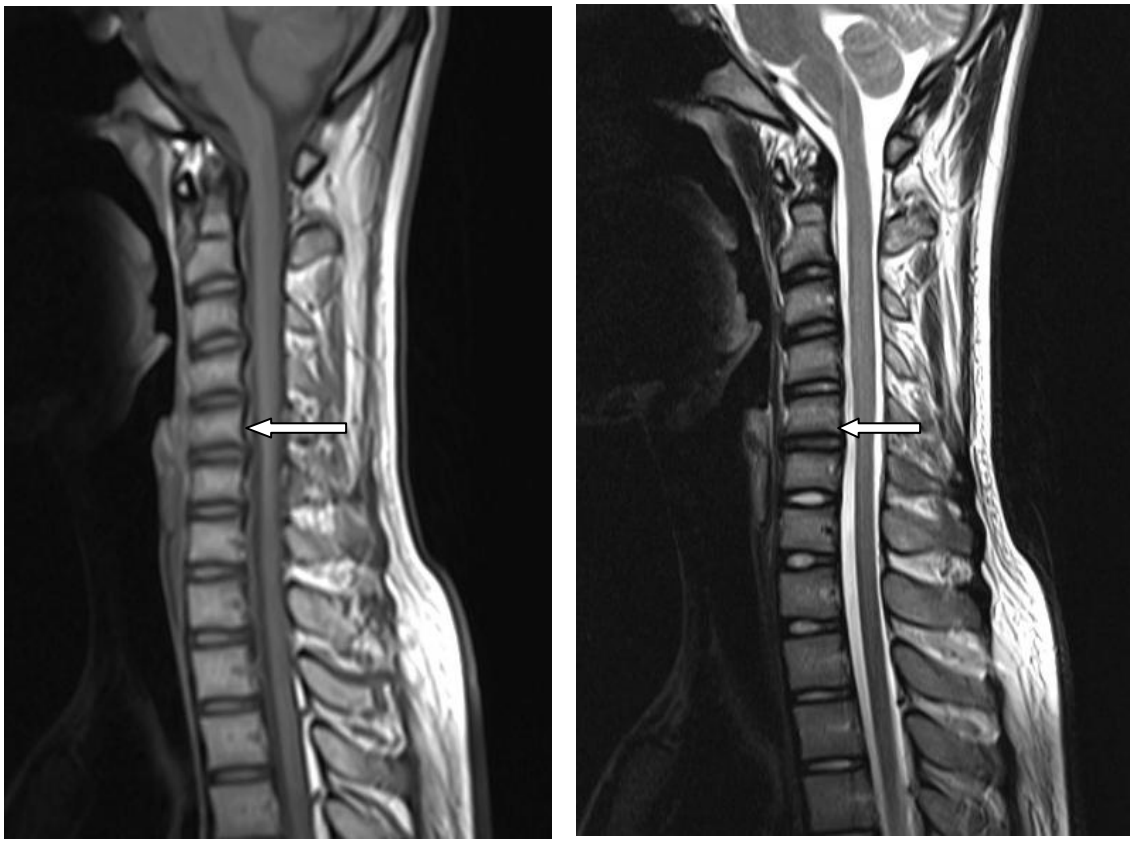

Image A Image B

Figure 15: T1W (image A) & T2W (image B) MRI showing loss of cervical lordosis

18) Lower cervical cord atrophy (figure 16) on MRI sagittal image was seen in 25 (80.6%) patients, remaining 6 (19.4%) patients who did not have lower cervical cord atrophy on sagittal plane had unilateral disease.

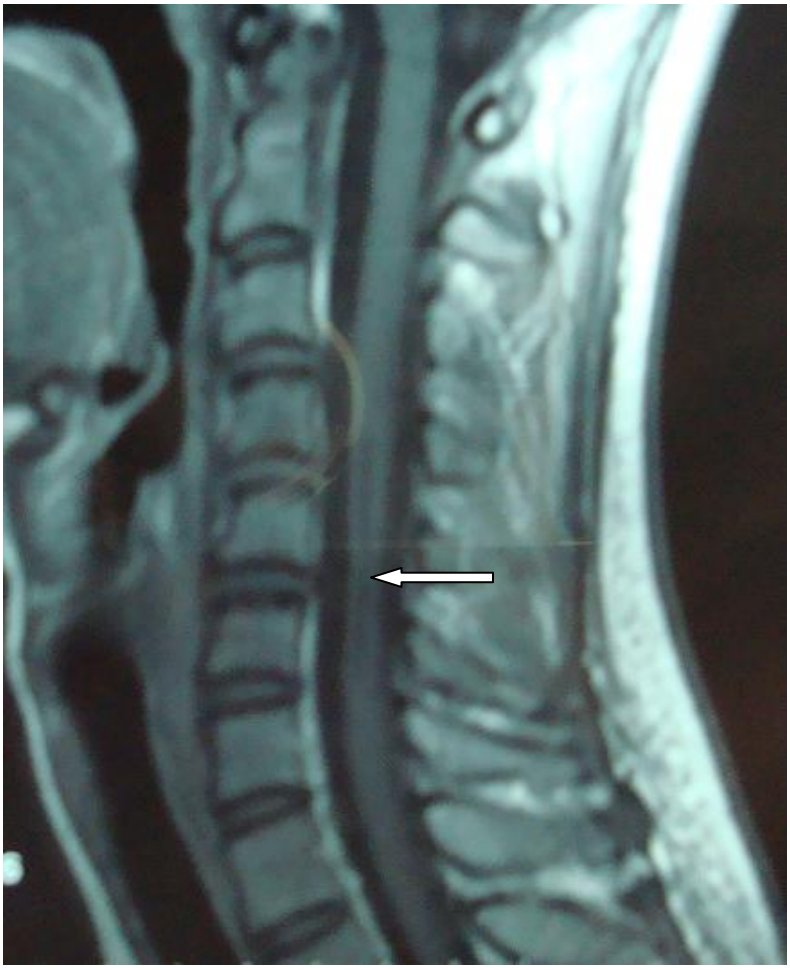

Figure 16: Atrophy of cervical cord at the level of C4 to C7 vertebral level.

19) Intramedullary hyperintensity on MRI T2W sagittal (figure 17) and axial sections were seen in 5 (16.1%) patients of them all 5 were having bilateral disease of more than 5 years duration.

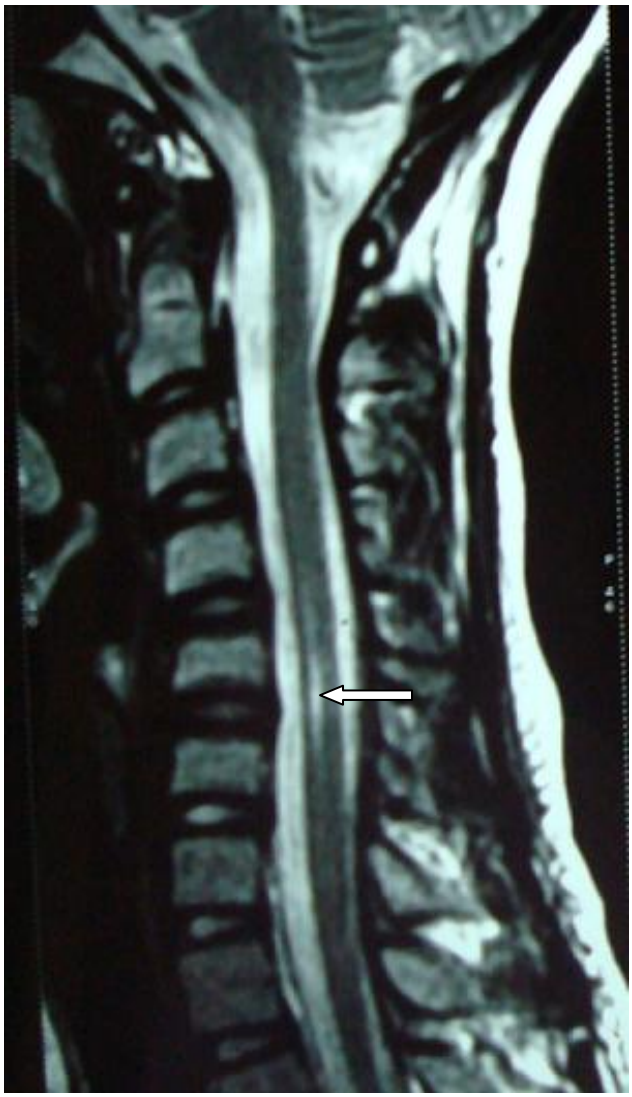

Figure 17: T2 Sagittal MRI shows intramedually T2 hyperintensity within the lower cervical spinal cord.

20) In MRI T2W gradient spin axial view of cervical spinal cord, 2 (6.5%) patients had a normal elliptical shape (figure 18 A) of the cord; they had unilateral disease of less than 1 year duration. 22 (70.9%) patients had triangular (figure 18 B) cross section of spinal cord suggestive of symmetric bilateral cord atrophy corresponding with the bilateral nature of their disease. 7 (22.6%) patients had pear shaped cord cross section suggesting asymmetric cord atrophy (figure 18 C) corresponding with unilateral disease, with atrophy of the cord towards the affected limb side.

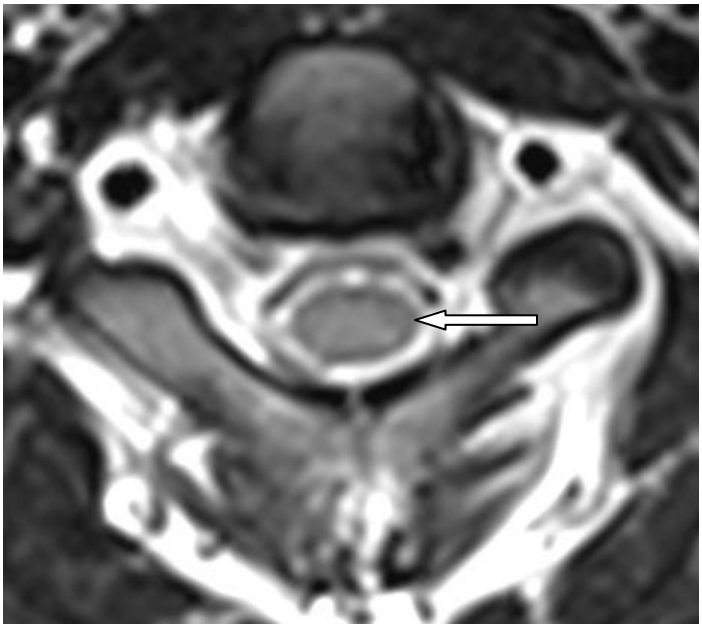

Figure 18 A: Normal elliptical axial T2W cervical spinal cord.

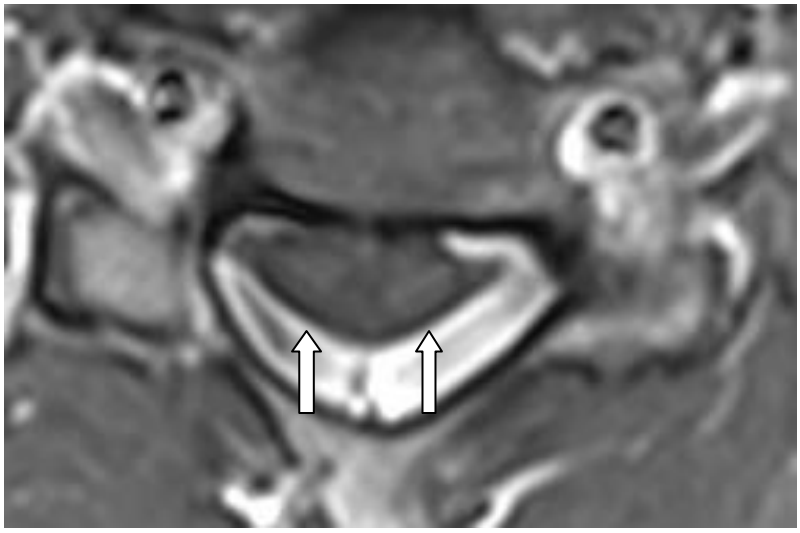

Figure 18 B: Triangular cervical cord atrophy evident on T2W Axial MRI

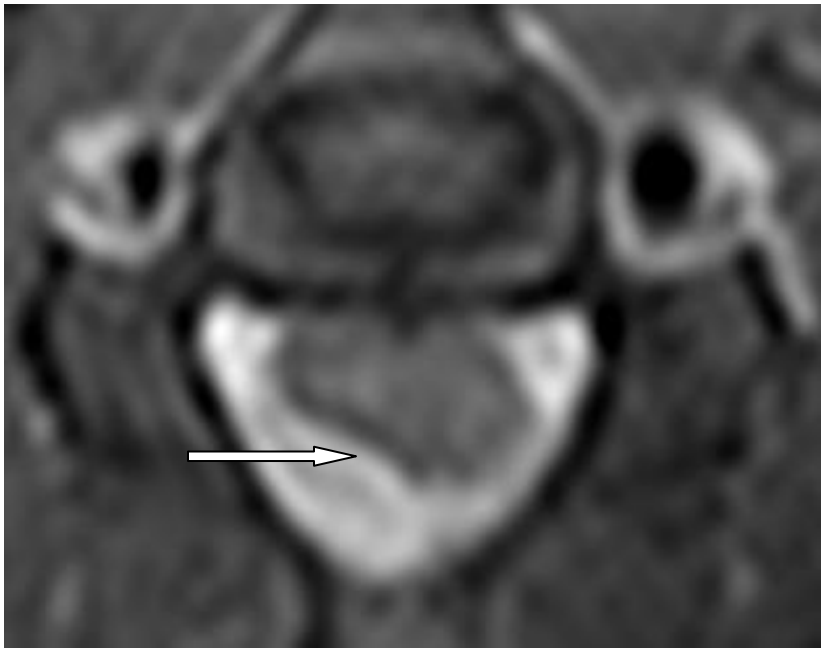

Figure 18 C: Asymmetric cord atrophy - pear shaped on axial T2W MRI

21) On sagittal MRI T2W imaging in neck flexion, anterior displacement of the lower cervical cord (figure 19) was seen in 27 patients (87.1%) and absent in 4 patients (12.9%).

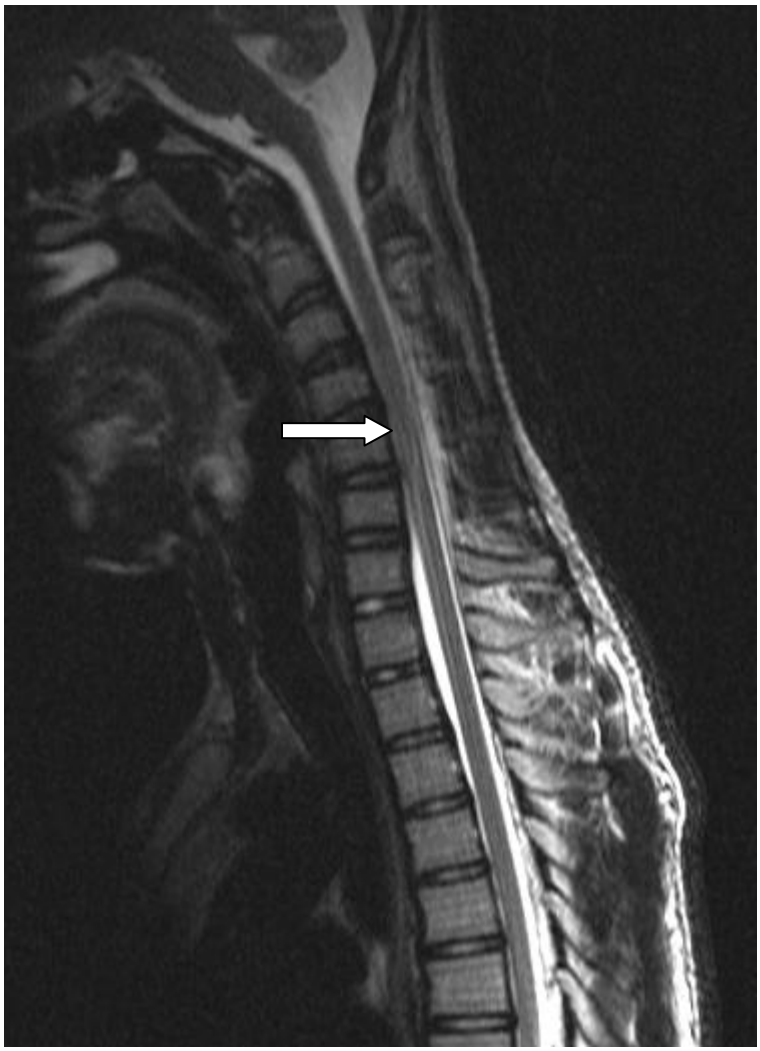

Figure 19: Anterior displacement of cervical cord on neck flexion

22) On Sagittal MRI T1W images in neck flexion position, anterior buckling of the posterior lower cervical dura (Figure 20- image A) with flow voids in the post dural space was seen in 27 patients (87.1%) of them 2 had extension of the post dural space upto T4 to T6 vertebrae (Figure 20- Image B). 4 patients did not have anterior buckling of the posterior lower cervical dura.

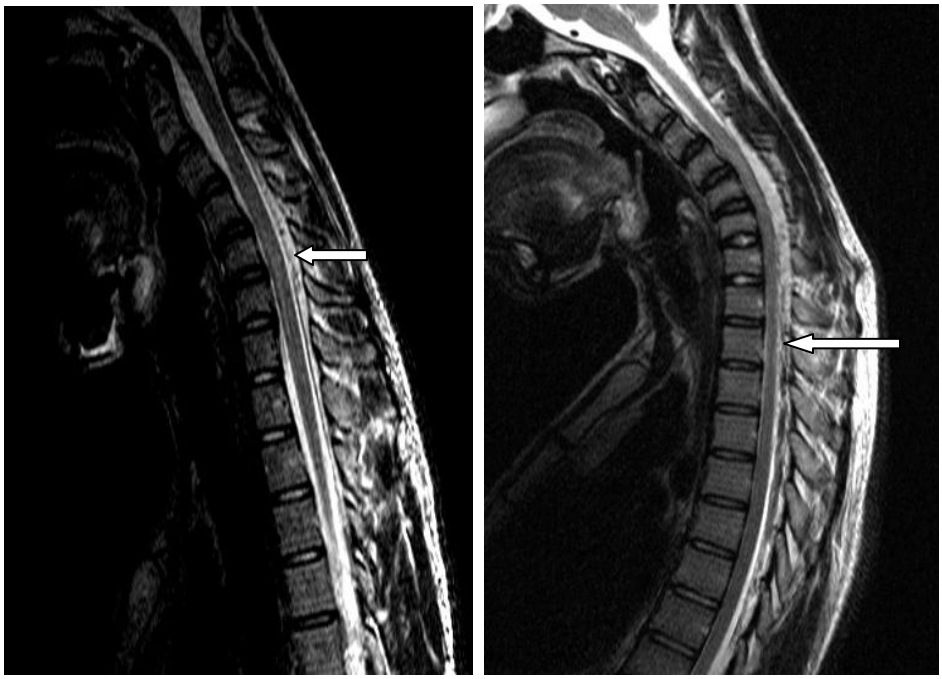

Image A Image B

Figure 20: T2W sagittal imaging in neck flexion

Image A – anterior buckling of posterior dura.

Image B - dural detachment upto T6 vertebrae

23) MRI T1W sagittal sections in neck flexion (figure 21- image A) with contrast, showed contrast enhancement (Figure 21- image B) of post dural flow voids were seen in 27 patients. 4 patients who did not have anterior buckling of the posterior dura did not show any change with contrast injection.

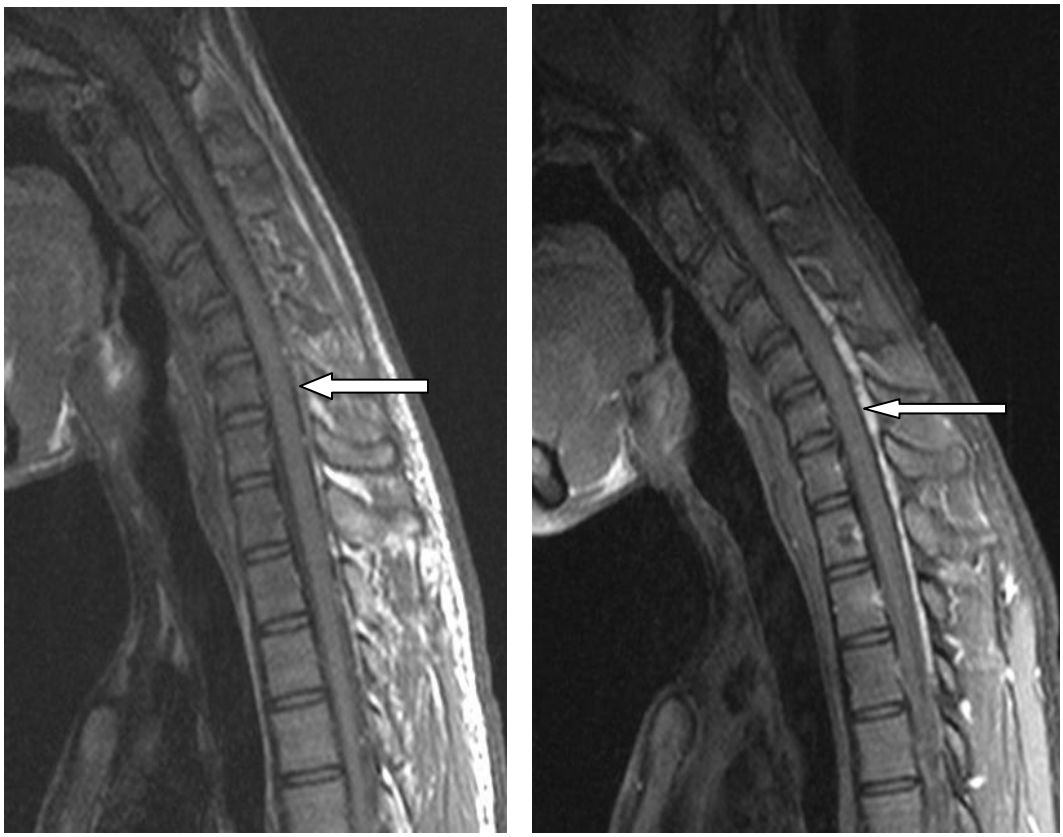

Image A Image B

Figure 21: T1W sagittal neck flexion images

Image A: apparently normal looking T1W image

Image B: Post contrast enhancement behind dura.

24) The median distal latency was normal in all patients, there was significant reduction in CMAP amplitude of median nerve (p=0.001) on comparison of Hirayama disease patients with that of normal controls (table 2). In 3 patients, 2 had unilateral median nerve being not stimulatable and 1 had bilateral non stimulatable median nerve.

Table 2: Comparison of CMAP of median nerve in patients with Hirayama disease and normal controls

	Coding	N	Mean	Std. Deviation	Std. Error Mean	Independent sample t test
CMAP - Median	Disease	49	9.8061	4.99335	0.71334	p=0.001
	Normal	10	16.6400	3.75742	1.18820	

25) The Ulnar nerve distal latency was normal in all patients, there was significant reduction in CMAP amplitude of ulnar nerve (p=0.001) on comparison of Hirayama disease patients with that of normal controls(table 3). 2 patients had bilaterally not stimulatable ulnar nerve.

Table 3: Comparison of CMAP of Ulnar nerve in patients with Hirayama disease and normal controls

	Coding	N	Mean	Std. Deviation	Std. Error Mean	Independent sample t test
CMAP-Ulnar	Disease	49	4.7122	3.78773	0.54110	p=0.001
	Normal	10	11.9000	1.65999	0.52493	

26) The f latency of median nerve (table 4) and ulnar (table 5) nerve of controls did not show any significant change on comparison of neck extension values with neck flexion values. Median nerve (p=0.293) and ulnar nerve (p = 0.293)

Table 4: Comparison of median f latency in normal controls in neck extension / neutral position and flexion position

Normal Controls	Coding	N	Mean	Std. Deviation	Std. Error Mean	Independent sample t test
f latency Median	Extension	10	26.1790	0.96791	0.30608	p=0.293
	Flexion	10	26.7820	1.46843	0.46436	

Table 5: Comparison of ulnar f latency in normal controls in neck extension / neutral position and flexion position

Normal controls	Coding	N	Mean	Std. Deviation	Std. Error Mean	Independent sample t test
f latency Ulnar	Extension	10	25.7180	1.51738	0.47984	p=0.718
	Flexion	10	26.0320	2.24718	0.71062	

27) In 31 patients there were 53 affected limbs (22 bilateral diseases & 9 unilateral diseases). Of the 53 limbs, median nerve was not stimulatable in neck extension position in 4 limbs (49 limbs stimulatable for median nerve in extension) and in neck flexion positions in 10 limbs

(43 limbs stimulatable for median nerve in flexion). The non stimulatable limbs were excluded from statistics.

28) There was no significant difference of f wave latency of median nerve (table 6) in patients of Hirayama disease and controls with the neck in flexion studies with p = 0.089.

Table 6: Comparison of Median f latency in Hirayama disease and normal controls in neck flexion position

Neck flexion	Coding	N	Mean	Std. Deviation	Std. Error Mean	Independent sample t test
f latency median	Disease	43	30.4695	6.63251	1.01145	p=0.089
	Normal	10	26.7820	1.46843	0.46436	

29) There was a significant change in f wave latency of median nerve (table 7) in patients with Hirayama disease with the neck in extension / neutral position p = 0.001.

Table 7: Comparison of median f latency in Hirayama disease and normal controls in neck neutral position

Neck neutral	Coding	N	Mean	Std. Deviation	Std. Error Mean	Independent sample t test
f latency Median	Disease	49	30.2118	1.30416	0.18631	p=0.001
	Normal	10	26.1790	0.96791	0.30608	

30) There was no significant change in f latency of median nerve (table 8) in patients of Hirayama disease on comparison of values in neck extension and neck flexion (p = 0.791).

Table 8: Comparison of Median f latency in Hirayama disease in neck extension / neutral position and flexion position

Hirayama disease	Coding	N	Mean	Std. Deviation	Std. Error Mean	Independent sample t test
f latency Median	Extension	49	30.2118	1.30416	0.18631	
	Flexion	43	30.4695	6.63251	1.01145	p=0.791

31) Among 31 patients there was 53 affected limbs (22 bilateral and 9 unilateral) in them ulnar nerve was not stimulatable in 4 limbs in neck neutral/extension position & were excluded leaving 49 limbs for analysis & 12 were not stimulatable in flexion leaving 41 for analysis.

32) Ulnar nerve f latency was significant different(table 9) in patients of HD & controls with neck in neutral position / extension, p = 0.001.

Table 9: Comparison of Ulnar f latency in Hirayama disease and normal controls in neck neutral position

Neck neutral	Coding	N	Mean	Std. Deviation	Std. Error Mean	Independent sample t test
f latency Ulnar	Disease	49	31.2400	1.36212	0.19459	
	Normal	10	25.7180	1.51738	0.47984	p=0.001

33) There was a significant increase in f wave latency of ulnar nerve (table 10) in patients with Hirayama disease than compared to controls with neck in flexion (p = .001).

Table 10: Comparison of Ulnar f latency in Hirayama disease and normal controls in neck flexion position

Neck flexion	Coding	N	Mean	Std. Deviation	Std. Error Mean	Independent sample t test
f latency Ulnar	Disease	41	33.4399	.92482	0.14443	p=0.001
	Normal	10	26.0320	2.24718	0.71062	

34) There was a significant change in f wave latency of ulnar nerve (table 11) in patients with Hirayama disease with the neck in flexion compared to in extension / neutral position (p = 0.001).

Table 11: Comparison of ulnar f latency in Hirayama disease in neck extension / neutral position and flexion position

Hirayama disease	Coding	N	Mean	Std. Deviation	Std. Error Mean	Independent sample t test
f latency Ulnar	Extension	49	31.2400	1.36212	0.19459	p=0.001
	Flexion	41	33.4399	0.92482	0.14443	

DISCUSSION

DISCUSSION

Hirayama disease is a disease predominantly affecting the males. In this study too there was a male preponderance of with 87% patients compared to 13 % of female patients. This disease affects individuals in the age group of 2nd to 3rd decade, in our study the age of disease onset varied from 11 to 27 years with an average age of disease onset of 18.9 years. These observations in our study are consistent with the data reported from other studies[30.54]. Although there is no definitive explanation available at present to account for this disproportionately high male preponderance of cases and onset of disease in the 2nd decade of life, however there are some proposed indirect evidence for this clustering as follows.

The average pubertal spurt in growth occurs in the early to mid teenage, and this growth spurt is more in males compared to females. Also it is interesting to note that the growth spurt precedes the onset of Hirayama disease onset by 4 to 6 years. It is hypothesized based on these findings that the male preponderance could result from the rapid increase in the height of boys[54,55] leading on to disproportionate growth of the

vertebral column and the contents of the spinal canal during puberty leads to the development of microcirculatory disturbance in lower cervical spinal cord during neck flexion [56,57,58,59,61]. This mechanism also supports one of the proposed explanations for the pathogenesis of cervical flexion myelopathy producing Hirayama disease. The differential growth rates between males and females have been previously proposed by Thoma *et.al*[60,61]. Also the disproportionate dural shortening accentuated during growth spurts in juveniles explains the adolescent onset of Hirayama disease [60,61].

In this study 19 patients were students, 10 patients were manual laborer or auto driver, 2 patients were housewife. The preponderance of cases in students could be explained by 2 major reasons. The first, this being a disease of late 2nd to early 3rd decade, the age when most are in their student life. The other factor that can be proposed is that students while reading from book have a tendency to keep the neck flexed and study, both these factors the age and neck flexor are already explained above for the development of Hirayama disease.

Hashimoto *et. al.,* [62] have reported that strenuous exercise of the arms was a frequent association with their patients. Biondi *et. al.,* [63] reported that repeated subclinical cervical trauma is a cause of chronic microcirculatory disturbances. Therefore, strenuous physical activity over a long duration could be a risk factor for Hirayama disease. This explanation can be applied for development of Hirayama disease in manual laborers and auto driver.

These patients predominantly present with insidious onset slowly progressing wasting and weakness of the hand and forearm associated with tremulousness of the fingers of the affected limb. In our study 8 (25.1%) patients had acute worsening of weakness in the background of slowly progressing weakness, especially with exposure to cold. This phenomenon of cold paresis is thought to occur due to sodium potassium ion channel dysfunction on exposure to cold. Sawai Setsu *et. al* [27] have studied this phenomenon and proposed that increased persistent sodium channel function and reduced transient sodium channel and potassium channel function in motor axon neurons leads to axonal dysfunction and if persistent can lead to neuronal damage. In this study all 8 patients with cold paresis had disease duration ranging from 3 to 18 months. This

pattern suggests that cold paresis is a feature of the early stage of Hirayama disease and it indicates ongoing neuronal dysfunction and probably damage which could be preventable if appropriate treatment strategies are applied at this stage of disease.

Predominant right hand involvement was seen in 17 (55%) patients (5 with unilateral and 12 with bilateral disease) compared to predominant left hand involvement 12 (39%) and bilaterally equal involvement of hand in 2 (6.5%). These observations too might support the hypothesis that strenuous physical activity could have a role in causation of Hirayama disease as all the patients in this study were right handed.

In this study bilateral involvement of upper limb was seen in 18(67.7%) patients. Though initially Hirayama disease was thought to be a unilateral disease, later studies have demonstrated asymmetric bilateral involvement. Proximal upper limb wasting was present in 11 (35.5%) patients and 8 had fasciculation in proximal arm, 2 years after onset of illness, suggestive active progressive disease involving the proximal upper limb later in the course of Hirayama disease.

Nerve conduction study of patients with Hirayama disease reveals reduced CMAP in median and ulnar nerve in patients with atrophy of the muscle supplied by these nerves. Severely atrophic muscles were not stimulatable in few patients.

In this study there was a significant difference in f wave latency of median and ulnar nerve in patients and controls, and also significant prolongation in f wave latency in ulnar nerve on neck flexion compared to neck extension with a variation in f latency of up to 6 milliseconds in patients with Hirayama disease. However in normal control this variation was usually less than 1 millisecond. This phenomenon was not observed in ulnar nerve conduction in normal controls. With regards to median nerve conduction there was no significant variation in either patients with Hirayama disease or normal controls in neck flexion or extension. Similar f wave changes were reported by WANG Xin-ning *et. al.*,[54]. However, Misra *et. al.*, [49] and Ammendola *et. al.*, [64] have reported the effect of neck flexion in Hirayama disease on changes in N13 and f wave parameters. They concluded based on their study that there was no

significant difference in these parameters in standard conditions and neck flexion.

This variation of f latency can be explained based on the dynamic flexion myelopathy theory, as during neck flexion there would be compression of the lower cervical cord in the region of C8, T1 (which corresponds more with ulnar nerve distribution than median nerve) causing microcirculatory disturbance in the region supplying the anterior horn cell region and probably leading to conduction disturbance.

On MRI sagittal view in neutral position there was loss of cervical lordosis and straightening of cervical vertebral column in all patients. In neck flexed position, anterior shift of spinal cord abutting the vertebral column was also seen in 27 patients, which was not evident on neck extended view. No specific correlation between duration, severity of disease, unilateral / bilateral disease or anterior shifting of the spinal cord.

Hirayama K[30], Tokumaru Y *et.al.*[29] and tang *et.al.*[65] have reported similar findings in their study and have recommended cervical collar therapy for preventing progression of cervical flexion myelopathy.

However Robberecht W *et.al.*[31] and Schröder R *et.al.*[32] have reported compression and an anterior shift of lower cervical cord and posterior dura along with increased epidural space in normal subjects in neck flexion.

In Sagittal view of cervical spinal cord, lower cervical atrophy, characterized by loss of cervical widening or thinning of the cord in the lower cervical region compared to upper cervical or upper thoracic spinal cord diameter was seen in 25 patients and most of them had bilateral disease. Patients who did not have evident spinal cord atrophy on the sagittal view had unilateral disease. In patients with early disease of < 6 months duration cervical spinal cord atrophy on axial view was not seen (in 2 patients) in the rest, patients with unilateral disease had asymmetric spinal cord atrophy resembling a pear fruit with the narrow side towards the affected side and the wider side towards the normal hand, patients with bilateral atrophy had triangular atrophy of the spinal cord on axial section. Shinomiya *et.al.*,[66] proposed that "posterior epidural ligament factor" for asymmetric cord atrophy. They proposed presence of two kinds of ligaments between ligamentum flavum and posterior dural sac. One being fine and the other being large. The large ligament resists against separation

of posterior dura. Abnormal and unequal distribution of these ligaments may lead to asymmetric spinal cord compression.

On MRI in neck flexion there is a evident anterior shift of posterior dura in 27 patients in this study, as a consequence of this there was cresentic epidural space seen containing flow voids, which enhance on contrast administration, suggesting engorged venous channels in the epidural space. These findings support the microcirculatory disturbance theory due to venous congestion and also compressive flexion myelopathy

The above findings on MRI have been reproduced on several studies from India and abroad by Pradhan S *et.al.*[56], Hassan KM *et.al.*[61], Kikuchi S *et.al.*[58], Mukai E *et.al.*[59], Biondi A *et.al.*[63], Ammendola A *et.al.*[64] . Based on these findings it is not clear if these dynamic changes are the "cause" for the development of compressive segmental damage or the "effect" occurring secondary to secondary to primary segmental motor neuronopathy.

SUMMARY

SUMMARY OF RESULTS

- Males are predominantly affected with M : F = 7 : 1
- 70% of patients have bilateral involvement.
- 55% of patients have predominant right hand involvement.
- Average age at onset of first symptom is 18.9 years.
- Overnight exposure to cold environment induced worsening of weakness was seen in 25 % of patients. This phenomenon is seen in patients with disease duration of less than 18 months.
- In this study 19 % patients had transient sensory disturbance usually associated with phenomenon of cold paresis.
- Hirayama disease predominantly involves distal upper limbs, but in this study 35% of patients additionally had proximal upper limb involvement.
- In this study brisk DTR was observed in 35% of patients.
- Proximal muscle fasciculation was present in 25% of patients.
- Ulnar nerve F latency is prolonged and is accentuated significantly in neck flexion.
- Median F latency is also prolonged but is not significantly accentuated on neck flexion.

CONCLUSION

CONCLUSION

In this study, in addition to the features originally described by Kiezo Hirayama, atypical features such as bilateral involvement, proximal muscle wasting, sensory symptoms, fasciculation and brisk DTR were observed.

This study also concludes that in Hirayama disease ulnar nerve conduction studies of mild prolongation of the f wave latency which is accentuated on neck flexion will characterize this disease. This feature can be used as a monitoring parameter and also to objectively record progress during therapy.

MRI of the cervical spine in Hirayama disease patients with neck in neutral position is often reported as normal. It is an essential tool to rule out secondary treatable causes of compressive or non compressive myelopathy. Dynamic neck flexion MRI highlights the characteristic features of Hirayama disease.

In this study despite the smaller sample size it can be concluded that the presence of atypical features, predominant right hand involvement in young males, ulnar f wave changes and MRI changes are characteristic features and not pathology of the disease.

The pathogenesis of Hirayama disease is still an enigma wrapped in a mystery with a possibility of segmental neuronal damage due to mechanical disturbance of integuments, vascular compromise and / or degenerative processes. Hence decompressive procedures are debated. To facilitate preservation of hand function and quick rehabilitation, cervical collar application may be of immense help to patients with` Hirayama disease.

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MASTER CHART

MASTER CHART – PATIENTS WITH HIRAYAMA DISEASE – PART 1

sl. No.	Name	Neuro no.	Age	Gender	Occupation	Handedness	Disease Duration (months)	age of onset (years)	cold paresis	Unilateral / bilateral	Right	Left	R / L
1	Karthik	2103/11	18	Male	Student	Right	6	17.5	yes	Unilateral	No	yes	Left
2	Balaji	2963/11	30	Male	auto driver	Right	96	22	no	Bilateral	Yes	yes	left > right
3	Devi	1850/11	25	Female	house wife	Right	24	23	no	Bilateral	Yes	yes	right > left
4	Augustine	6190/10	22	Male	Student	Right	24	20	yes	Bilateral	Yes	yes	right > left
5	Babu	7124/10	18	Male	Student	Right	24	16	no	Bilateral	Yes	yes	left > right
6	Rajesh	1368/11	20	Male	Student	Right	3	19.75	yes	Unilateral	Yes	no	Right
7	Karthikeyan	6839/10	21	Male	Student	Right	24	19	no	Bilateral	Yes	yes	right > left
8	Arthi surya	512/11	20	Female	Student	Right	108	11	no	Bilateral	Yes	yes	right > left
9	Karthik	3178/11	19	Male	Student	Right	18	17.5	no	Unilateral	Yes	no	Right
10	Vivek	6780/10	15	Male	Student	Right	12	14	no	Bilateral	Yes	yes	right > left
11	Suman	2124/11	18	Male	Student	Right	24	27	no	Unilateral	Yes	no	Right
12	Ramamurthy	4219/11	26	Male	labrour	Right	60	21	no	Bilateral	Yes	yes	left > right
13	Alagappan	3195/11	22	Male	auto driver	Right	6	21.5	yes	Unilateral	No	yes	Left
14	Manikandan	1290/12	19	Male	labrour	Right	36	16	no	Bilateral	Yes	yes	right = left
15	Suresh kumar	2197/11	23	Male	student	Right	18	21.5	no	Bilateral	Yes	yes	left > right
16	Ramachandran	1570/12	24	Male	auto driver	Right	24	22	no	Bilateral	Yes	yes	right > left
17	Jagdish	342/12	19	Male	student	Right	6	18.5	yes	Unilateral	No	yes	Left
18	Ansari	3212/12	28	Male	auto driver	Right	96	20	no	Bilateral	Yes	yes	left > right
19	Usha	2892/11	22	Female	house wife	Right	24	20	no	Bilateral	Yes	yes	right > left
20	Giri	6512/12	21	Male	student	Right	24	19	yes	Bilateral	Yes	yes	right > left
21	Arulraj	4589/12	18	Male	student	Right	24	16	no	Bilateral	Yes	yes	left > right
22	Vijaykumar	2168/12	20	Male	student	Right	12	19	yes	Unilateral	Yes	no	Right
23	Raja	5400/11	21	Male	student	Right	24	19	no	Bilateral	Yes	yes	right > left
24	Meena	7810/11	20	Female	student	Right	60	15	no	Bilateral	Yes	yes	right > left
25	Arjunan	1637/12	16	Male	student	Right	12	15	no	Bilateral	Yes	yes	right > left
26	Durairaj	5423/12	19	Male	student	Right	24	17	no	Unilateral	Yes	no	Right
27	Darshan	1275/11	25	Male	labrour	Right	42	21.5	no	Bilateral	Yes	yes	left > right
28	Moorthy	3164/12	21	Male	auto driver	Right	9	20.25	yes	Unilateral	No	yes	Left
29	Dinesh	1260/12	19	Male	labrour	Right	36	16	no	Bilateral	Yes	yes	right = left
30	Ram kumar	6410/12	21	Male	student	Right	24	19	no	Bilateral	Yes	yes	left > right
31	Chandran	2174/12	23	Male	auto driver	Right	24	21	no	Bilateral	Yes	yes	right > left

MASTER CHART – PATIENTS WITH HIRAYAMA DISEASE – PART 2

sl. No.	Weakness	Wasting	Distal	proximal	Tremulousness	Fasciculation	Deltoid	Biceps	Brachio-Radialis	triceps	FDS	FDP
1	Yes	Yes	Yes	Yes	yes	Yes	Mild	Moderate	Normal	moderate	moderare	moderate
2	Yes	Yes	Yes	Yes	yes	Yes	Mild	Mild	Normal	moderate	normal	moderate
3	Yes	Yes	Yes	Yes	yes	Yes	Mild	Mild	Normal	normal	normal	mild
4	Yes	Yes	Yes	No	yes	No	Normal	Normal	Normal	moderate	normal	mild
5	Yes	Yes	Yes	No	yes	No	Normal	Normal	Normal	moderate	normal	mild
6	Yes	Yes	Yes	No	yes	No	Normal	Normal	Normal	Mild	normal	mild
7	Yes	Yes	Yes	No	yes	No	Normal	Normal	Normal	moderate	normal	mild
8	Yes	Yes	Yes	Yes	yes	Yes	moderate	Moderate	Normal	moderate	mild	mild
9	Yes	Yes	Yes	Yes	yes	Yes	moderate	Moderate	Normal	moderate	moderate	moderate
10	yes	Yes	Yes	No	yes	No	Normal	Normal	Normal	moderate	normal	mild
11	yes	Yes	Yes	No	yes	No	Normal	Normal	Normal	moderate	normal	mild
12	yes	Yes	Yes	Yes	yes	Yes	moderate	Moderate	Normal	moderate	moderate	moderate
13	yes	Yes	Yes	No	yes	Yes	Normal	Normal	Normal	normal	normal	mild
14	yes	Yes	Yes	No	yes	No	Normal	Normal	Normal	moderate	moderate	severe
15	yes	Yes	Yes	No	yes	No	Normal	Normal	Normal	moderate	mild	moderate
16	yes	Yes	Yes	No	Yes	No	Normal	Normal	Normal	moderate	mild	moderate
17	yes	Yes	Yes	Yes	Yes	Yes	Mild	Moderate	Normal	moderate	moderare	moderate
18	yes	Yes	Yes	Yes	Yes	Yes	Mild	Mild	Normal	moderate	normal	moderate
19	yes	Yes	Yes	Yes	Yes	Yes	Mild	Mild	Normal	normal	normal	mild
20	yes	Yes	Yes	No	Yes	No	Normal	Normal	Normal	moderate	normal	mild
21	yes	Yes	Yes	No	Yes	No	Normal	Normal	Normal	moderate	normal	mild
22	yes	Yes	Yes	No	Yes	No	Normal	Normal	Normal	Mild	normal	mild
23	yes	Yes	Yes	No	Yes	No	Normal	Normal	Normal	moderate	normal	mild
24	yes	Yes	Yes	Yes	Yes	Yes	moderate	Moderate	Normal	moderate	mild	mild
25	yes	Yes	Yes	No	Yes	No	Normal	Normal	Normal	moderate	normal	mild
26	yes	Yes	Yes	No	Yes	No	Normal	Normal	Normal	moderate	normal	mild
27	yes	Yes	Yes	Yes	Yes	Yes	moderate	Moderate	Normal	moderate	moderate	moderate
28	yes	Yes	Yes	No	Yes	Yes	Normal	Normal	Normal	normal	normal	mild
29	yes	Yes	Yes	No	Yes	No	Normal	Normal	Normal	moderate	moderate	severe
30	yes	Yes	Yes	No	Yes	No	Normal	Normal	Normal	moderate	mild	moderate
31	yes	Yes	Yes	No	Yes	No	Normal	Normal	Normal	moderate	mild	moderate

MASTER CHART – PATIENTS WITH HIRAYAMA DISEASE – PART 3

Sl. No.	Wrist extensor / flexor	Intrinsic muscles of hand	C5	C6	C7	C8	T1	DTR	Sensory Sympt	Straight C3-C6	Sagittal cord atrophy	Cervical cord signal change	Cervical cord cross section	Ant. Shift of cord	space behind dura	contrast enhancement
1	WF > WE	Severe	1	1	2	3	3	Brisk	Yes	yes	No	No	pear	yes	yes	Yes
2	WF > WE	Severe	1	1	2	2	2	Brisk	No	yes	yes	Yes	Triangular	yes	yes	Yes
3	WF > WE	Severe	1	1	0	3	3	normal	No	yes	yes	No	Triangular	yes	yes	Yes
4	WF > WE	Severe	0	0	2	3	3	normal	Yes	yes	yes	No	Triangular	yes	yes	Yes
5	WF > WE	severe	0	0	2	3	3	normal	No	yes	yes	No	Triangular	yes	yes	Yes
6	WF > WE	severe	0	0	2	3	3	normal	Yes	yes	No	No	Normal	yes	yes	Yes
7	WF > WE	severe	0	0	3	3	3	Brisk	No	yes	yes	No	Triangular	no	no	No
8	WF > WE	severe	2	0	2	3	3	normal	No	yes	yes	Yes	Triangular	yes	yes	Yes
9	WF > WE	severe	2	0	2	3	3	normal	Yes	yes	yes	No	pear	yes	yes-upto T4	Yes
10	WF > WE	severe	0	0	2	3	3	Brisk	No	yes	yes	No	Triangular	yes	yes	Yes
11	WF > WE	severe	0	0	2	3	3	normal	No	yes	yes	No	pear	yes	yes	Yes
12	WF > WE	severe	2	0	2	3	3	normal	No	yes	yes	Yes	Triangular	yes	yes- upto T6	Yes
13	WF > WE	severe	0	0	0	3	3	normal	No	yes	No	No	pear	No	no	No
14	WF > WE	severe	0	0	2	3	3	Brisk	No	yes	yes	No	Triangular	yes	yes	Yes
15	WF > WE	severe	0	0	2	3	3	normal	No	yes	yes	No	Triangular	yes	yes	Yes
16	WF > WE	severe	0	0	2	3	3	normal	No	yes	yes	No	Triangular	yes	yes	Yes
17	WF > WE	severe	1	1	2	3	3	Brisk	Yes	yes	No	No	pear	yes	yes	Yes
18	WF > WE	severe	1	1	2	2	2	Brisk	No	yes	yes	Yes	Triangular	yes	yes	Yes
19	WF > WE	severe	1	1	0	3	3	normal	No	yes	yes	No	Triangular	yes	yes	Yes
20	WF > WE	severe	0	0	2	3	3	normal	Yes	yes	yes	No	Triangular	yes	yes	Yes
21	WF > WE	severe	0	0	2	3	3	normal	No	yes	yes	No	Triangular	yes	yes	Yes
22	WF > WE	severe	0	0	2	3	3	normal	Yes	yes	No	No	Normal	yes	yes	Yes
23	WF > WE	severe	0	0	3	3	3	Brisk	No	yes	yes	No	Triangular	no	no	No
24	WF > WE	severe	2	0	2	3	3	normal	No	yes	yes	No	Triangular	yes	yes	Yes
25	WF > WE	severe	0	0	2	3	3	Brisk	No	yes	yes	No	Triangular	yes	yes	Yes
26	WF > WE	severe	0	0	2	3	3	normal	No	yes	yes	No	pear	yes	yes	Yes
27	WF > WE	severe	2	0	2	3	3	normal	No	yes	yes	Yes	Triangular	yes	yes	Yes
28	WF > WE	severe	0	0	0	3	3	normal	No	yes	No	No	pear	no	no	No
29	WF > WE	severe	0	0	2	3	3	Brisk	No	yes	yes	No	Triangular	yes	yes	Yes
30	WF > WE	severe	0	0	2	3	3	normal	No	yes	yes	No	Triangular	yes	yes	Yes
31	WF > WE	severe	0	0	2	3	3	normal	No	yes	yes	No	Triangular	yes	yes	Yes

MASTER CHART – PATIENTS WITH HIRAYAMA DISEASE – PART 4

sl. No.	Rt M CMAP	Rt U CMAP	Rt M E f min	Rt M E f max	Rt M E f mean	Rt M E f disp	Rt U E f min	Rt U E f max	Rt U E f mean	Rt U E f disp	Rt M F f min	Rt M F f max	Rt M F f mean	Rt M F f disp	Rt U F f min	Rt U F f max	Rt U F f mean	Rt U F f disp
1	16.2	3.4	29.12	31.34	30.23	2.22	28.34	30.22	29.28	1.88	29.54	31.84	30.69	2.3	29.23	31.95	30.59	2.72
2	10.2	5.8	28.16	30.49	29.33	2.33	28.82	30.93	29.88	2.11	30.24	34.2	32.22	3.96	30.38	34.22	32.3	3.84
3	4.2	2.1	29.82	32.68	31.25	2.86	30.2	33.32	31.76	3.12	31.58	34.94	33.26	3.36	32.86	35.7	34.28	2.84
4	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
5	21.8	12.5	28.17	30.75	29.46	2.58	28.33	29.79	29.06	1.46	NS	NS	NS	NS	30.42	33.29	31.86	2.87
6	11.2	3.12	28.72	29.98	29.35	1.26	29.78	32.1	30.94	2.32	29.34	30.56	29.95	1.21	31.24	34.86	33.05	3.62
7	5.1	2.4	28.79	32.21	30.5	3.42	29.73	32.84	31.26	3.11	31.16	35.12	33.14	3.96	32.25	35.84	34.05	3.59
8	5.8	2.7	29.54	33.12	31.33	3.58	30.24	33.65	31.95	3.41	31.68	35.4	33.54	3.72	32.42	35.96	34.19	3.54
9	12.1	2.86	29.34	32.1	30.72	2.76	28.82	32.94	30.88	4.12	29.56	32.9	31.23	3.56	29.57	34.34	31.95	4.77
10	4.9	1.9	28.39	31.98	30.66	3.59	29.68	33.12	31.4	3.44	32.1	35.92	34.01	3.82	31.58	35.46	33.52	3.88
11	10.8	2.3	26.04	27.5	26.7	1.46	28.66	31.24	29.95	2.58	25.42	27.08	26.25	1.66	NS	NS	NS	NS
12	12.2	6.2	29.1	31.38	30.24	2.28	29.14	31.04	30.1	1.9	31.24	34.68	32.96	3.44	31.12	34.26	32.69	3.14
13	14.1	4.7	28.54	30.83	29.69	2.29	31.67	33.75	32.71	2.08	28.33	31.04	29.63	2.71	32.29	33.54	32.92	1.29
14	5.6	1.5	29.24	30.82	30.04	1.58	30.38	33.46	31.92	3.08	31.34	34.96	33.15	3.62	31.96	36.24	34.1	4.28
15	25.3	16.9	26.46	30.84	28.65	4.38	27.92	31.88	29.9	3.96	27.71	31.88	29.79	4.17	29.17	33.96	31.56	4.79
16	11	7.5	28.26	31.88	30.08	3.62	29.66	32.69	31.18	3.03	29.86	34.92	32.39	5.06	31.64	35.28	33.46	3.64
17	16.2	3.4	29.12	31.34	30.23	2.22	28.34	30.22	29.28	1.88	29.54	31.84	30.69	2.3	29.23	31.95	30.59	2.72
18	10.2	5.8	28.16	30.49	29.33	2.33	28.82	30.93	29.88	2.11	30.24	34.2	32.22	3.96	30.38	34.22	32.3	3.84
19	4.2	2.1	29.82	32.68	31.25	2.86	30.2	33.32	31.76	3.12	31.58	34.94	33.26	3.36	32.86	35.7	34.28	2.84
20	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
21	21.8	12.5	28.17	30.75	29.46	2.58	28.33	29.79	29.06	1.46	NS	NS	NS	NS	30.42	33.29	31.86	2.87
22	11.2	3.12	28.72	29.98	29.35	1.26	29.78	32.1	30.94	2.32	29.34	30.56	29.95	1.21	31.24	34.86	33.05	3.62
23	5.1	2.4	28.79	32.21	30.5	3.42	29.73	32.84	31.26	3.11	31.16	35.12	33.14	3.96	32.25	35.84	34.05	3.59
24	5.8	2.7	29.54	33.12	31.33	3.58	30.24	33.65	31.95	3.41	31.68	35.4	33.54	3.72	32.42	35.96	34.19	3.54
25	4.9	1.9	28.39	31.98	30.66	3.59	29.68	33.12	31.4	3.44	32.1	35.92	34.01	3.82	31.58	35.46	33.52	3.88
26	10.8	2.3	26.04	27.5	26.7	1.46	28.66	31.24	29.95	2.58	25.42	27.08	26.25	1.66	NS	NS	NS	NS
27	12.2	6.2	29.1	31.38	30.24	2.28	29.14	31.04	30.1	1.9	31.24	34.68	32.96	3.44	31.12	34.26	32.69	3.14
28	14.1	4.7	28.54	30.83	29.69	2.29	31.67	33.75	32.71	2.08	28.33	31.04	29.63	2.71	32.29	33.54	32.92	1.29
29	5.6	1.5	29.24	30.82	30.04	1.58	30.38	33.46	31.92	3.08	31.34	34.96	33.15	3.62	31.96	36.24	34.1	4.28
30	25.3	16.9	26.46	30.84	28.65	4.38	27.92	31.88	29.9	3.96	27.71	31.88	29.79	4.17	29.17	33.96	31.56	4.79
31	11	7.5	28.26	31.88	30.08	3.62	29.66	32.69	31.18	3.03	29.86	34.92	32.39	5.06	31.64	35.28	33.46	3.64

MASTER CHART – PATIENTS WITH HIRAYAMA DISEASE – PART 5

sl. No.	Lt M CMAP	Lt U CMAP	Lt M E f min	Lt M E f max	Lt M E f mean	Lt M E f disp	Lt U E f min	Lt U E f max	Lt U E f mean	Lt U E f disp	Lt M F f min	Lt M F f max	Lt M F f mean	Lt M F f disp	Lt U F f min	Lt U F f max	Lt U F f mean	Lt U F f disp
1	14.2	4.5	29.84	32.88	31.36	3.04	30.24	34.46	32.35	4.22	31.21	33.25	32.23	2.04	31.11	35.68	33.95	4.57
2	10.2	2.8	27.49	30.94	29.22	3.45	29.4	31.29	30.35	1.89	29.48	32.82	31.15	3.34	30.96	34.42	32.69	3.46
3	6.2	2.5	29.59	32.63	31.11	3.04	30.28	32.93	31.6	2.65	31.2	35.38	33.29	4.18	32.34	35.86	34.1	3.62
4	7.5	NS	31.43	36.42	33.93	4.99	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
5	NS	1.8	NS	NS	NS	NS	32.92	39.17	36.04	6.25	NS	NS	NS	NS	NS	NS	NS	NS
6	14.2	11.8	26.71	28.2	27.46	1.49	26.58	28.47	27.53	1.89	27.49	28.95	28.22	1.46	29.32	30.84	30.08	1.52
7	8.2	3.6	28.3	32.14	30.22	3.84	29.3	32.5	30.9	3.2	29.8	34.1	31.95	4.3	31.82	36.4	34.11	4.58
8	6.9	2.8	29.49	32.84	31.66	3.35	30.28	33.42	31.85	3.14	30.8	34.76	32.78	3.96	32.4	36.92	34.66	2.52
9	15.6	13	27.12	28.98	28.05	1.86	27.88	29.87	28.88	1.99	27.24	28.56	27.9	1.32	28.94	31.1	28.52	2.16
10	7.9	3.5	28.98	32.26	30.62	3.28	29.51	32.85	31.18	3.34	31.28	35.32	33.3	4.04	31.6	35.12	33.36	3.52
11	16.4	12.7	25.21	26.42	25.83	1.12	27.29	30.21	28.75	2.92	24	26.83	25.42	2.83	26.67	28.33	27.5	1.66
12	9.4	3.6	27.94	30.78	29.36	2.84	30.24	33.21	31.73	2.97	29.96	33.29	31.63	3.33	31.82	36.24	34.03	4.42
13	12.2	9.5	28.96	31.46	30.21	2.5	30.83	34.38	32.61	3.55	26.46	29.38	27.92	2.92	NS	NS	NS	NS
14	5.2	1.2	29.2	31.92	30.56	2.71	30.38	33.24	31.81	2.86	30.62	35.24	32.93	4.62	32.28	37.34	34.81	5.06
15	11.3	9.1	26.88	31.67	29.27	4.79	27.71	31.04	29.38	3.33	NS	NS	NS	NS	NS	NS	NS	NS
16	6.9	4.2	28.46	30.98	29.72	2.52	29.74	31.93	30.84	2.19	30.18	33.48	31.83	3.3	31.26	34.28	32.77	3.02
17	14.2	4.5	29.84	32.88	31.36	3.04	30.24	34.46	32.35	4.22	31.21	33.25	2.04	32.23	31.11	35.68	33.95	4.57
18	10.2	2.8	27.49	30.94	29.22	3.45	29.4	31.29	30.35	1.89	29.48	32.82	31.15	3.34	30.96	34.42	32.69	3.46
19	6.2	2.5	29.59	32.63	31.11	3.04	30.28	32.93	31.6	2.65	31.2	35.38	33.29	4.18	32.34	35.86	34.1	3.62
20	7.5	NS	31.43	36.42	33.93	4.99	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
21	NS	1.8	NS	NS	NS	NS	32.92	39.17	36.04	6.25	NS	NS	NS	NS	NS	NS	NS	NS
22	14.2	11.8	26.71	28.2	27.46	1.49	26.58	28.47	27.53	1.89	27.49	28.95	28.22	1.46	29.32	30.84	30.08	1.52
23	8.2	3.6	28.3	32.14	30.22	3.84	29.3	32.5	30.9	3.2	29.8	34.1	31.95	4.3	31.82	36.4	34.11	4.58
24	6.9	2.8	29.49	32.84	31.66	3.35	30.28	33.42	31.85	3.14	30.8	34.76	32.78	3.96	32.4	36.92	34.66	2.52
25	7.9	3.5	28.98	32.26	30.62	3.28	29.51	32.85	31.18	3.34	31.28	35.32	33.3	4.04	31.6	35.12	33.36	3.52
26	16.4	12.7	25.21	26.42	25.83	1.12	27.29	30.21	28.75	2.92	24	26.83	25.42	2.83	26.67	28.33	27.5	1.66
27	9.4	3.6	27.94	30.78	29.36	2.84	30.24	33.21	31.73	2.97	29.96	33.29	31.63	3.33	31.82	36.24	34.03	4.42
28	12.2	9.5	28.96	31.46	30.21	2.5	30.83	34.38	32.61	3.55	26.46	29.38	27.92	2.92	NA	NS	NS	NS
29	5.2	1.2	29.2	31.92	30.56	2.71	30.38	33.24	31.81	2.86	30.62	35.24	32.93	4.62	32.28	37.34	34.81	5.06
30	11.3	9.1	26.88	31.67	29.27	4.79	27.71	31.04	29.38	3.33	NS	NS	NS	NS	NS	NS	NS	NS
31	6.9	4.2	28.46	30.98	29.72	2.52	29.74	31.93	30.84	2.19	30.18	33.48	31.83	3.3	31.26	34.28	32.77	3.02

NERVE CONDUCTION VALUES IN CONTROL SUBJECTS

sl. No.	Media CMAP	Ulnar CMAP	M E f min	M E f max	M E f mean	M E f disp	U E f min	U E f max	U E f mean	U E f disp	M F f min	M F f max	M F f mean	M F f disp	U F f min	U F f max	U F f mean	U F f disp
1	14.1	11.2	26.67	28.33	27.5	1.66	27.71	29.58	28.65	1.87	28.33	30.21	29.27	1.88	27.7	29.58	28.5	1.88
2	14.3	8.3	25	28.96	26.98	3.96	24.38	27.5	25.94	3.12	23.96	28.13	26.04	4.17	25	28.33	26.67	3.33
3	25.5	12.4	23.96	27.29	25.63	3.33	23.13	26.46	24.79	3.33	24.17	26.04	25.1	1.87	23.96	25.42	21.25	1.46
4	14.4	11.4	23.71	26.71	25.21	3	22.5	25	23.75	2.5	23.54	26.46	25	2.92	22.92	26.04	24.48	3.12
5	13.6	13.6	25	27.29	26.15	2.29	22.61	25.32	23.75	2.71	25	26.25	25.6	1.25	22.71	24.17	23.44	1.46
6	14.9	12.4	24.94	27.93	26.44	2.99	24.69	28.49	26.59	3.8	25.78	29.24	27.51	3.46	25.82	29.12	27.47	3.3
7	15.2	11.2	23.24	25.42	24.33	2.18	24.84	27.62	26.23	2.78	25.12	26.98	26.1	1.86	25.6	28.98	27.29	3.38
8	20.4	14.2	24.66	27.25	25.96	2.59	23.76	25.37	24.57	1.58	26.2	28.52	27.36	2.32	25.21	28.59	26.9	3.4
9	18.2	13.1	25.29	27.28	26.29	1.99	25.38	27.24	26.31	1.86	25.99	28.21	27.1	2.22	26.21	28.22	27.22	2
10	15.8	11.2	26.2	28.4	27.3	2.2	25.4	27.8	26.6	2.4	27.6	29.88	28.74	2.28	26.64	27.48	27.1	0.84

Abbreviations and Codes

1) M = median nerve
2) U = Ulnar nerve
3) CMAP – compound muscle action potential
4) E = value recorded with neck in extension / neutral postion
5) F = value recorded with neck in flexion
6) f = f wave latency
7) disp =Chronodispersion
8) NS = not stimulatable
9) DTR = deep tendon reflex
10) Min = minimum latency
11) Max = maximum latency
12) WF = wrist flexor
13) WE = Wrist extensor

PROFORMA

PROFORMA

Name: Neuro no. :

Age: Gender:

Occupation: Handedness:

Disease duration (months): Age of onset (years):

Iimb involvement: Distal – Y/N Proximal – Y/N

Unilateral: Y/N Right / Left

Bilateral: Y/N Right > Left / Left > Right / Right = Left

Weakness: Y/ N Wasting: Y/N

Tremulousness: Y/N

Fasciculation: Y/N

Cold paresis: Y/N

Muscle involvement

Deltoid: Y/N

Biceps: Y/N

Brachioradialis: Y/N

Triceps: Y/N

FDS: Y/N

FDP: Y/N

Wrist extensor: Y/N

Wrist Flexor: Y/N

Wrist : Extensor > Flexor Flexor > Extensor

Intrinsic hand muscle: Y/N

Myotome involved

C5: Y/N

C6: Y/N

C7: Y/N

C8: Y/N

T1: Y/N

Deep tendon reflexes: Normal / Absent / Sluggish / Brisk

Sensory: Y/N

Nerve conduction study

Median nerve				
	Right		Left	
Neck position	Extension	Flexion	Extension	Flexion
CMAP				
F minimum				
F mximum				
F mean latency				
Chronodispersion				
SNAP				

Ulnar nerve				
	Right		Left	
Neck position	Extension	Flexion	Extension	Flexion
CMAP				
F minimum				
F mximum				
F mean latency				
Chronodispersion				
SNAP				

MRI findings

Straightening of C3 – C6 spine: Y/N

Lower cervical cord atrophy
- Sagittal view in neck extension- Y/N
- Axial view - Normal elliptical / Pear shaped / Triangular

Anterior shift of cord on neck flexion: Y/N

Anterior buckling of posterior dural sac: Y/N

Cresentic space posterior to dura in neck flexion: Y/N

Flow voids in cresentic space in neck flexion: Y/N

Contrast enhancement of flow voids: Y/N

ANNEXURES

INSTITUTIONAL ETHICAL COMMITTEE,
STANLEY MEDICAL COLLEGE, CHENNAI-1

Title of the Work : Clinical Spectrum of Hirayama disease in tertiary Care Hospital

Principal Investigator : Dr. S. Saravanan

Designation : PG in DM (Neuro)

Department : Department of Neurology
Government Stanley Medical College,
Chennai-1

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 07.02.2013 at the Council Hall, Stanley Medical College, Chennai-1 at 2PM

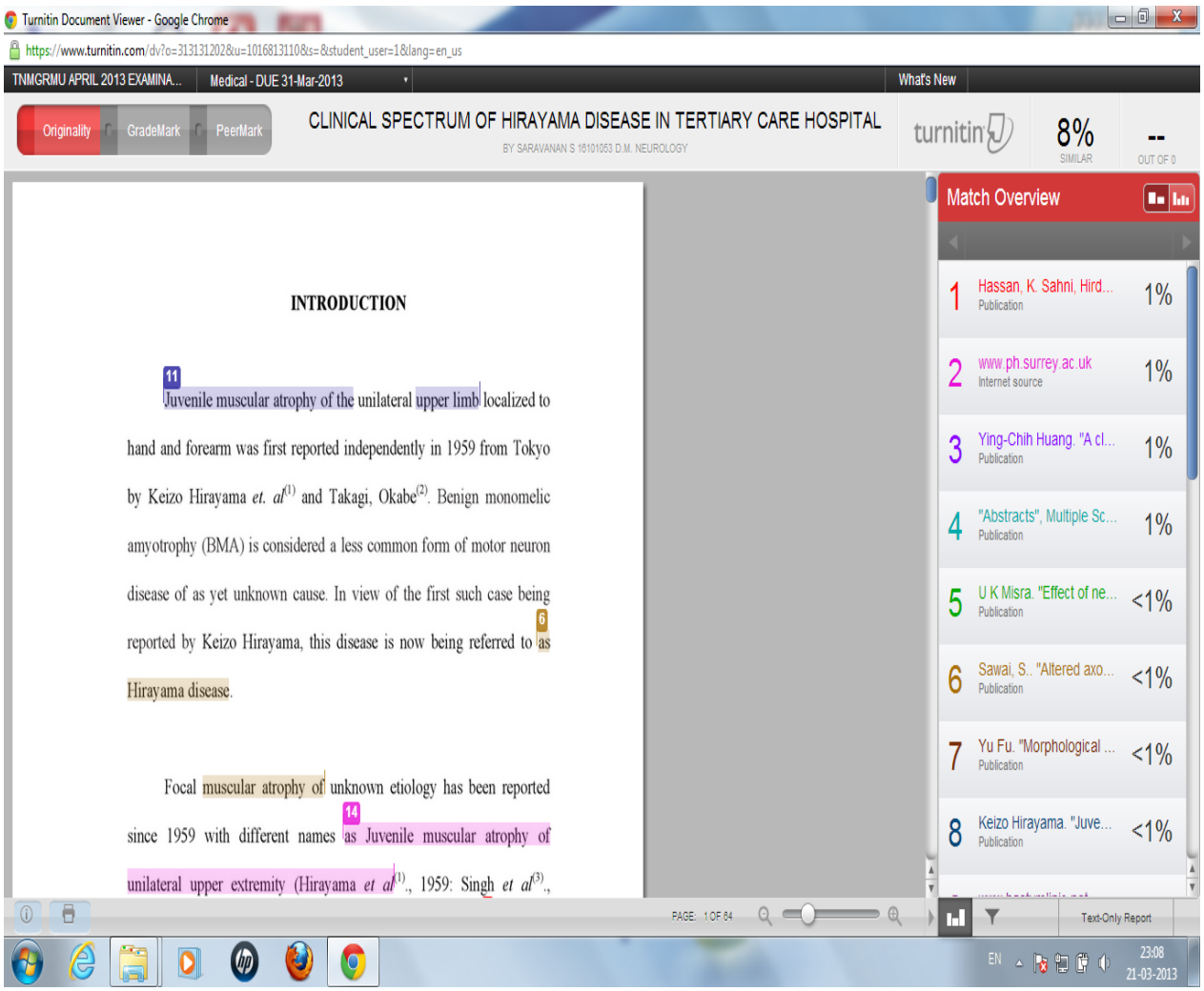
The members of the Committee, the secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal investigator and their team are directed to adhere to the guidelines given below:

1. You should inform the IEC in case of changes in study procedure, site investigator investigation or guide or any other changes.
2. You should not deviate from the area of the work for which you applied for ethical clearance.
3. You should inform the IEC immediately, in case of any adverse events or serious adverse reaction.
4. You should abide to the rules and regulation of the institution(s).
5. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work.
6. You should submit the summary of the work to the ethical committee on completion of the work.

19/2/13

MEMBER SECRETARY,
IEC, SMC, CHENNAI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CLINICAL SPECTRUM OF HIRAYAMA DISEASE IN TERTIARY CARE HOSPITAL
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INTRODUCTION
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Juvenile muscular atrophy of the unilateral upper limb localized to hand and forearm was first reported independently in 1959 from Tokyo by Keizo Hirayama et. al(1) and Takagi, Okabe(2). Benign monomelic amyotrophy (BMA) is considered a less common form of motor neuron disease of as yet unknown cause. In view of the first such case being reported by Keizo Hirayama, this disease is now being referred to 6 as Hirayama disease.
Focal muscular atrophy of unknown etiology has been reported since 1959 with different names 14 as Juvenile muscular atrophy of unilateral upper extremity (Hirayama et al(1)., 1959: Singh et al(3).,
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நோயாளிகளின் தகவல் குறியீடு

1) ஹிறாயாமா நோய் பொதுவாக 15 இல் இருந்து 25 வயது வரை உள்ள ஆண்களை மிகவும் அதிகமாக பாதிக்கும்
2) ஹிறாயாமா நோய் என்பது முதுகு தண்டுவட நோய். இந்த நோய் பொதுவாக கை தசைகளை பாதிக்கும்.
3) இந்த நோயில் கை பிடிப்பு தன்மை குறைந்துவிடும், கை நடுக்கம் இருக்கும், தசைகள் சுருங்கி வலு இழந்துவிடும்.
4) இந்த நோயில் வலியோ அல்லது உணர்ச்சியற்ற தன்மையோ இருக்காது.
5) இந்த நோயின் காரணங்களை கண்டறியும், சிறந்த சிகிச்சைகள் குறித்தும் உலகளாவிய ஆராய்ச்சிகள் மேற்கொள்ளப்பட்டு வருகிறது.

சுய ஒப்புதல் படிவம்

பங்கு பெறுபவரின் பெயர் :
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முகவரி :

தொலைபேசி எண் :

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1) எனக்கு ஹிறாயாமா எனப்படும் முதுகு தண்டுவட நோய் இருக்கிறது என்று தெரிவிக்கபட்டுள்ளது.
2) இந்த நோய் குறித்து ஆய்வில் (Study of clinical spectrum of Hirayama disease in a referral hospital in south India) பங்குகொள்ள நான் முழுமனதோடுஒப்புக் கொள்கிறேன் .
3) இந்த மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது . என்னுடைய சந்தேகங்களை கேட்கவும் அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டது .
4) இந்த ஆய்விற்கு தேவைபடும் பரிசோதனைகளை (எம் .ஆர் .ஐ ஸ்கேன், நரம்பு மின் பரிசோதனை) செய்து கொள்ள நான் முழு மனதுடன் சம்மதிக்கிறேன்.
5) இந்த ஆய்வின் முடிவுகள் மற்ற நோயாளிகளுக்கு சிகிச்சை அளிக்கவும் பிற்காலத்தில் உதவியாக இருக்கும் என்பதும் எனக்கு தெரிவிக்கப்பட்டது.
6) இந்த ஆய்வின் முடிவுகளை அறிவியல் சார்ந்த மருத்துவ இதழ்கள் பிரசுரிக்கவும் நான் சம்மதிக்கிறேன்.

பங்கேற்பவரின் கையொப்பம் /
கட்டைவிரல் ரேகை :

ஆய்வாளரின் கையொப்பம் :

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தேதி :