MAGNETIC RESONANCE IMAGING FINDINGS AND CLINICAL CHARACTERISTICS OF PATIENTS WITH DEGENERATIVE CERVICAL MYELOPATHY AT MOI TEACHING AND REFERRAL HOSPITAL

BY

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Research thesis submitted to Moi University, School of Medicine in partial fulfillment of the requirements for an award of the degree of Master of Medicine in Radiology and Imaging.

DECLARATION

DECLARATION BY THE CANDIDATE

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DEDICATION

I dedicate this work to all the patients suffering from neurological dysfunction due to degenerative pathology of the cervical spine.

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LIST OF ABBREVIATIONS

CCSS	Congenital Cervical Spinal canal Stenosis
CD-ROM	Compact Disc Read Only Memory
CSF	Cerebral Spinal Fluid
DCM	Degenerative Cervical Myelopathy
DICOM	Digital Imaging and Communications in Medicine
IREC	Institutional Research and Ethics Committee
LFH	Ligamentum flavum
MRI	Magnetic Resonance Imaging
MTRH	Moi Teaching and Referral Hospital
OPLL	Ossification of Posterior Longitudinal Ligament
PLLH	Posterior Longitudinal Ligament Hypertrophy

DEFINITION OF KEY TERMS

Cervical spine: the portion of the spinal column at the neck region involving the first seven vertebrae.

Clinical characteristics: the age, gender and presenting myelopathy-related neurological symptoms of patients with degenerative cervical myelopathy.

Congenital cervical spinal canal stenosis: developmental abnormality due to inborn narrow cervical spine vertebral foramen based on a Spinal Cord Occupation Ratio of ≥70%.

Degenerative changes: progressive age-related structural changes of body tissues that result from wear and tear that occur over a period of time.

Isolated Disc Pathology: intervertebral disc bulge causing cervical spinal cord compression at a single level which is not associated with any other degenerative pathology at any other level.

Ligamentum flavum hypertrophy: thickening of the ligamentum flavum secondary to accumulation of granulation tissue attributed to chronic inflammation.

Myelopathy: neurological dysfunction due to extrinsic spinal cord compression caused by a spectrum of age-related cervical spinal column degenerative changes.

Posterior longitudinal ligament hypertrophy: enlargement of posterior longitudinal ligament, which may be contiguous across multiple levels, caused by accumulation of granulation tissue secondary to chronic inflammation.

Spinal cord compression: flattening, indentation, torsion, or circumferential narrowing of the spinal cord due to extrinsic compression by surrounding tissues.

Spinal Cord Occupation Ratio: percentage of the cervical vertebral foramen occupied by the spinal cord at non-pathological segments immediately above and below the level of maximum cord compression.

Spondylolisthesis: anterior or posterior displacement of a cervical vertebra relative to the one beneath it.

Spondylosis: multilevel osteoarthritic changes of the cervical vertebral column which include bulging of intervertebral discs and vertebral body osteophytes

ABSTRACT

Background: Degenerative Cervical Myelopathy (DCM) is a progressive neurological disorder attributed to extrinsic cervical spinal cord compression by age-related spinal column structural changes. DCM is a unifying diagnostic term for all degenerative pathology that compress the cervical spinal cord which include spondylosis and ligamentous aberrations. It has subtle onset, progressive course and varied clinical presentation. It can be clinically determined but accurately diagnosed using Magnetic Resonance Imaging (MRI) which is a noninvasive non- ionizing imaging modality of choice. Despite being the commonest cause of non-traumatic cervical spinal cord injury among adults contributing up to 23.6% cervical myelopathy globally, there is paucity of literature of this disease in Africa.

Objective: To describe the cervical spine MRI findings of patients with DCM in relation to their clinical characteristics at Moi Teaching and Referral Hospital (MTRH).

Methods: A cross-sectional study was carried out in the Radiology and Imaging department of MTRH between January and December 2017. Fifty seven patients with degenerative cervical myelopathy-related neurological symptoms and cervical MRI findings who met the eligibility criteria were recruited. Informed consent was sought before data was collected using structured questionnaires. Data was analyzed using Stata/ MP Version 13. Categorical variables were summarized as frequencies and percentages while continuous variables as mean, median and standard deviation. Associations between categorical variables were assessed using Fisher exact test. A p-values of less than 0.05 was considered statistically significant. Results were presented using tables and charts

Results: The mean age of the participants was 51.7 years (±13.3) and the male to female ratio was 1:1.4. Cervical spondylosis was the commonest cause of DCM. The most frequent location for both maximum cord compression (43.7 %) and spinal cord hyperintense foci as seen on T2 Weighted Image (T2WI) (36.8%) was at C5-C6 level. All patients with congenitally narrow cervical vertebral canal, based on a Spinal Cord Occupation Ratio (SCOR) of ≥70%, had spinal cord T2WI hyperintense foci. There was a statistically significant association between presence of spinal cord T2WI hyperintense foci and neurological symptoms of more than one year (81%, p= 0.0007).

Conclusion: Spondylosis was the commonest cause of DCM. C5-C6 level was the most frequently location for maximum cord compression. Patients with inborn narrow cervical vertebral canal and those who reported of neurological symptoms lasting for more than one year were more likely to have T2WI hyperintense foci within their spinal cord.

Recommendations: High index of suspicion of spondylosis and C5-C6 cervical spine level involvement in patients suspected with DCM. Assessment of vertebral canal caliber in patients with degenerative cervical spine pathology.

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CHAPTER ONE: INTRODUCTION

1.1 Background

Degenerative cervical myelopathy is a chronic progressive neurological condition caused by extrinsic cervical spinal cord compression by age-related degenerative changes of the spinal axis (Martin et al., 2018). Its pathogenesis can be categorized into cervical spondylosis and ligamentous aberrations. Cervical spondylosis is an umbrella term used to describe various osteoarthritic changes of vertebral column such as intervertebral disc herniation, vertebral body osteophytosis, facet joint arthropathy and hypermobility or listhesis of the vertebral segments (Yamaguchi, Mitsuhara, Abiko, Takeda, & Kurisu, 2017). On the other hand, nonosteoarthritic degeneration include ligamentous pathologies such as ossification or hypertrophy of the posterior longitudinal ligament and/or ligamentum flavum (L.A. Tetreault et al., 2013).

The aforementioned cervical spine degenerative pathology are distinct diagnostic entities that result from compensatory structural changes that aim at maintaining the stability of an aging cervical spine. Unfortunately, these changes may inadvertently cause progressive spinal canal stenosis and eventually spinal cord injury through static or dynamic compression leading to DCM (Nouri, Tetreault, Singh, Karadimas, & Fehlings, 2015). These degenerative pathology differ with respect to diagnostic methodology, global prevalence, management strategies, and prognosis (Nouri, Tetreault, Singh, et al., 2015).

DCM may present as subclinical cord stenosis or may have a progressive course with periods of quiescent disease accompanied by intermittent episodes of neurologic decline. It may also be result in neurologic sequelae attributed to low-energy impact trauma (Darren R. et al 2011). The onset of symptoms is usually after the age of 40 years, often between 50 and 70 years (Tracy & Bartleson, 2010). Men are more often

affected and tend to present with more severe disease compared to women (Nouri, Martin, Tetreault, et al., 2016).

Environmental or occupational risk factors that may lead to early development of DCM include smoking, trauma, prolong abnormal posture, carrying heavy loads on the head and contact sports such as rugby (Nouri, Tetreault, Singh, et al., 2015). Some of the congenital anomalies that predispose to degenerative cervical myelopathy include congenital spinal canal stenosis, Klippel-Feil syndrome and Down syndrome (Yamaguchi et al., 2017)

Certain lifestyles in Africa and other developing nations may pose additional risk for early development of vertebral degenerative changes, for instance, frequent carrying of domestic items on the head (Belachew, Schaller, & Guta, 2007). Heavy loads carried on the head increases the axial strain on the cervical spine and exacerbates the degenerative process leading to manifestation of DCM early in life (Jäger, Gordon-Harris, Mehring, Goetz, & Mathias, 1997). Furthermore, Belachew et al reported that in sub- Saharan-Africa most patients with cervical spine degenerative pathology were often diagnosed very late in the course of the illness due to lack of access to health facilities, inadequate diagnostic facilities, delays in seeking treatment and inadequate suspicion of this disease on the part of the healthcare providers (Belachew et al., 2007).

Magnetic Resonance Imaging is crucial in diagnosis, prognostication and post-intervention assessment of patients with DCM. The advantages of MRI that make it the ideal imaging modality is its noninvasive, non-ionizing and multiplanar properties. It can clearly demonstrate the spinal cord anatomy and any pathology (Martin et al., 2018). Relevant MRI parameters assessed in diagnosis of DCM include the cervical spine sagittal alignment, the diameter of the functional vertebral canal, caliber and signal intensity of the spinal cord, anatomical location and the type of the compressive

pathology, number of compressed levels, degree of spinal cord compression and presence of cervical column instability (Nouri, Martin, Tetreault, et al., 2016; Nouri, Martin, Tetreault, et al., 2017).

Poor prognostic indicators observed on MRI included mal-alignment, subluxation, multilevel cord compression and presence of spinal cord T2WI hyperintensity (Nouri, Martin, Tetreault, et al., 2016). Notably, MRI features of severe disease have also been observed in asymptomatic individuals (L. Tetreault et al., 2015). Therefore, to achieve superior predictive performance, MRI parameters of prognostic significance should be used in combination with clinical prediction rule based variables such as age, gender, duration of symptoms and baseline severity score rather than using either a clinical or an imaging-based model alone (Nouri, Tetreault, Côté, et al., 2015).

1.2 Statement of the Problem

Cervical spine degenerative pathology that cause extrinsic cord compression are highly interrelated and often manifest concomitantly. The precise pathology that contribute to neurological dysfunction vary from one patient to another (Yamaguchi et al., 2017). Furthermore, diagnosis of DCM is frequently challenging, particularly in mild cases, because of it often presents with subtle, intermittent and highly variable subjective symptoms. Delay in diagnosis of this disease may also occur since these symptoms are non-specific and often overlap with those of other neurological conditions (Lebl et al., 2011).

Magnetic Resonance Imaging is crucial in diagnosis, prognostication and post-therapeutic follow up of patients with DCM. (Nouri, Martin, Tetreault, et al., 2016). However, MRI poor prognostic indicators of DCM which include cervical spine mal-alignment, multilevel cord compression and presence of T2WI hyperintense foci within

the cord may also be observed in asymptomatic individuals (L. Tetreault et al., 2015). Therefore, these MRI parameters alone have inferior predictive performance when they are not used in combination with clinical-based prediction model based on variables such as age, gender, duration of symptoms and preoperative myelopathy baseline severity score (Nouri, Tetreault, Côté, et al., 2015). This study aims at establishing the cervical spine MRI findings in symptomatic adults with DCM at MTRH and the relationship of these findings with clinical variables of prognostic significance.

1.3 Justification of the Study

Degenerative structural changes of the cervical spine are progressive and cumulative over time hence they are often observed in older individuals (Martin et al., 2018). Advanced in age is therefore one of the significant risk factor in development of degenerative cervical myelopathy (Takamiya et al., 2006). It often presents after the age of 40 years and the peak between 50 and 70 years (Tracy & Bartleson, 2010).

DCM is the commonest cause of non-traumatic cervical spinal cord injury among the adults contributing up to 23.6% globally (Nouri, Martin, Tetreault, et al., 2016). According to the WHO factsheet, the global population of adults over 60 years of age is projected to double from 12% in 2015 to 22% in 2050. This change will be observed particularly in the low and middle income countries, Kenya included (WHO, 2015). As a result of this worldwide increase in the population of the elderly, the incidence of geriatric diseases for which degenerative spinal disorders are among them, are on the increase (Nakashima et al., 2015). Despite these findings, the exact epidemiology of DCM in Africa has not been well established due to paucity of research studies on this disease. Therefore, assessment of all of degenerative cervical spine pathology that cause cervical cord compression is paramount in this region. The results from this

research study will help in filling the knowledge gap and provide base line information that will be used to facilitate comparison with research findings from other parts of the world.

Magnetic Resonance Imaging was the radiological modality of choice in evaluation of DCM in this study because it enables determination of the type of degenerative pathology, detection of any intrinsic spinal cord abnormalities, quantification of the degree of vertebral canal stenosis and spinal cord compression (Martin et al., 2018). It also enables effective distinction between DCM and other mimics such as infections, neoplasms and demyelinating plaque. Furthermore, MRI is a noninvasive and radiation-free imaging tool that provides excellent multi-planar imaging of the spinal cord and surrounding soft tissues (Nouri, Tetreault, Côté, et al., 2015).

1.4 Research Question

What are the cervical spine MRI findings of patients with degenerative cervical myelopathy in relation to their clinical characteristics at MTRH?

1.5 Research Objectives

1.5.1 Broad Objective

To describe the cervical spine MRI findings of patients with degenerative cervical myelopathy in relation to their clinical characteristics at MTRH.

1.5.2 Specific Objectives

1. To find out the clinical characteristics of patients with degenerative cervical myelopathy at MTRH.
2. To describe the cervical spine MRI findings of patients with degenerative cervical myelopathy at MTRH.
3. To determine the relationships between the cervical spine MRI findings and the clinical characteristics of patients with degenerative cervical myelopathy at MTRH.

CHAPTER TWO: LITERATURE REVIEW

2.1 INTRODUCTION

Degenerative cervical myelopathy is a progressive neurological disorder caused by extrinsic spinal cord compression by various age-related structural changes of the spinal column including osteophytes, bulging intervertebral discs, enlarged or ossified spinal ligaments and spondylolisthesis. (Nouri, Tetreault, Côté, et al., 2015). The exact pathophysiology of DCM is multifactorial. The spinal cord injury may result from either static factors that cause stenosis of the cervical vertebral foramen or dynamic factors that result in motion-related repetitive injury to the cervical cord (L. Tetreault et al., 2015).

While often episodic and benign, DCM can be debilitating leading to severe neurologic sequelae. Its clinical presentation is often subtle, intermittent and vary considerably from one individual to another. Clinical variables associated with poor prognosis include male gender, age of sixty years and above, and prolonged duration of the disease (Martin et al., 2018).

Magnetic resonance imaging is an ideal imaging modality for diagnosis of DCM due to its excellent soft tissue characterization, multiplanar capabilities, non-ionizing and non-invasive properties (Martin et al., 2018). It is also helpful in identifying the degenerative changes, cord compression, intrinsic cord abnormalities and other types of spinal column disorders. It can also be used to potentially predict neurological outcome and response to intervention (Nouri, Martin, Tetreault, et al., 2016).

2.1.1 Epidemiology

It is estimated that degenerative cervical myelopathy encompasses 23.6% of non-traumatic cervical cord injuries globally, 59% in Japan, 54% in the United States, 31% in Europe, 22% in Australia, and between 4% and 30% in Africa. The incidence of myelopathy caused by degenerative pathology of the spine in North America is approximately 41 per million while the prevalence is estimated at 605 per million (Nouri, Martin, Tetreault, et al., 2017). It is estimated that the surgical rates for DCM are 4.4 per 100,000 person years, and surgical rates seem to be rising (Yamaguchi et al., 2017).

Environmental and genetic predisposing factors that influence development of degenerative changes of the cervical spinal column result in presentation of the disease in younger individuals (Yamaguchi et al., 2017). These factors include prolonged abnormal posture, smoking, trauma, congenital spinal canal stenosis, Klippel-Feil syndrome and conditions associated with excessive motion or instability of the cervical spine for instance cerebral palsy (Echarri & Forriol, 2002).

Certain occupational activities such as carrying heavy loads on the head impose considerable extra strain on the anterior cervical column hence exposing the intervertebral discs to excess mechanical stress and eventually leading to premature and faster progression of cervical osteoarthritis (Hiratzka, Ching, & Hart, 2011). Jäger et al in a case control study evaluating the relationship between the load carrying on the head and the development of cervical spine degenerative changes in Ghana, found that 89% of the carriers had cervical spondylosis but only in 23% of non-carriers were affected (Jäger et al., 1997). In another radiographic-based study in Bangladesh, a considerably high prevalence of cervical spondylosis (39.8%) was recorded among

coolies younger than 40 years (Mahbub et al., 2006; Patel, Spiker, Daubs, Brodke, & Cannon-Albright, 2012).

In addition, repetitive minor overuse injuries or occasional strong direct axial loading impact on the cervical spine promote osteoarthritic and ligamentous degeneration (Yamaguchi et al., 2017). Petren-Mallmin and Linder in their longitudinal case control study found that young military high-performance aircraft pilots had a higher risk of intervertebral disc premature degeneration due to repetitive stress on their cervical spine (Petren-Mallmin & Linder, 2001). Similarly, Jonasson and colleagues reported that players of contact sports such as American football were more likely to develop neck pain and degeneration of the cervical spine due to sports-related overuse injuries (Jonasson et al., 2011). Furthermore, occupations which require maintaining a particular posture for a long period of time, such as continuous sitting by office workers, have also been associated with increased chances of developing cervical spondylosis (Akinpelu, Odole, & Odejide, 2010)

2.1.2 Anatomy

The cervical spinal cord is located within the vertebral canal of the first seven vertebrae of the spinal column. It extends from the foramen magnum down to the level of the first thoracic vertebrae. The first two vertebra are considered atypical because the atlas (C1) has no vertebral body while the axis (C2) has an odontoid peg extending superiorly from its vertebral body. Moreover, there exist no intervertebral disc or uncovertebral joints between them. The typical vertebra consisting of both the vertebral bodies and posterior vertebral arch are between C3-C7 (Gray, Pick, & Howden, 1901).

The cervical spinal cord is comprised of the eight cervical segments from which a similar number of spinal nerves arise from and exit above the pedicles of the corresponding vertebrae. It is covered by the three layers of meninges (pia, arachnoid

and dura mater) and cerebrospinal fluid within subarachnoid space surrounds it. In the middle, there is a central canal which is continuous with the fourth ventricle superiorly that is surrounded by H-shaped area of grey matter (Gray et al., 1901). The spinal cord white matter composed of long ascending and descending tracts is located outside the grey matter. One of the spinal cord enlargements extending from approximately C4 up to T1 corresponds to the location in the cord that supply the spinal nerves for the upper extremities (Ryan, McNicholas, & Eustace, 2011).

The cervical spinal cord arterial supply arises from single anterior and paired posterior spinal arteries which originate from the two vertebral arteries. The venous drainage is via a plexus of veins anterior and posterior to the cord which drain along the nerve roots to vertebral veins. The extradural space contains loose areolar tissue, ligaments, fat and a plexus of veins. The posterior longitudinal ligament and ligamentum flavum are located posterior and anterior to the cord between C2-C7 level respectively (Gray et al., 1901).

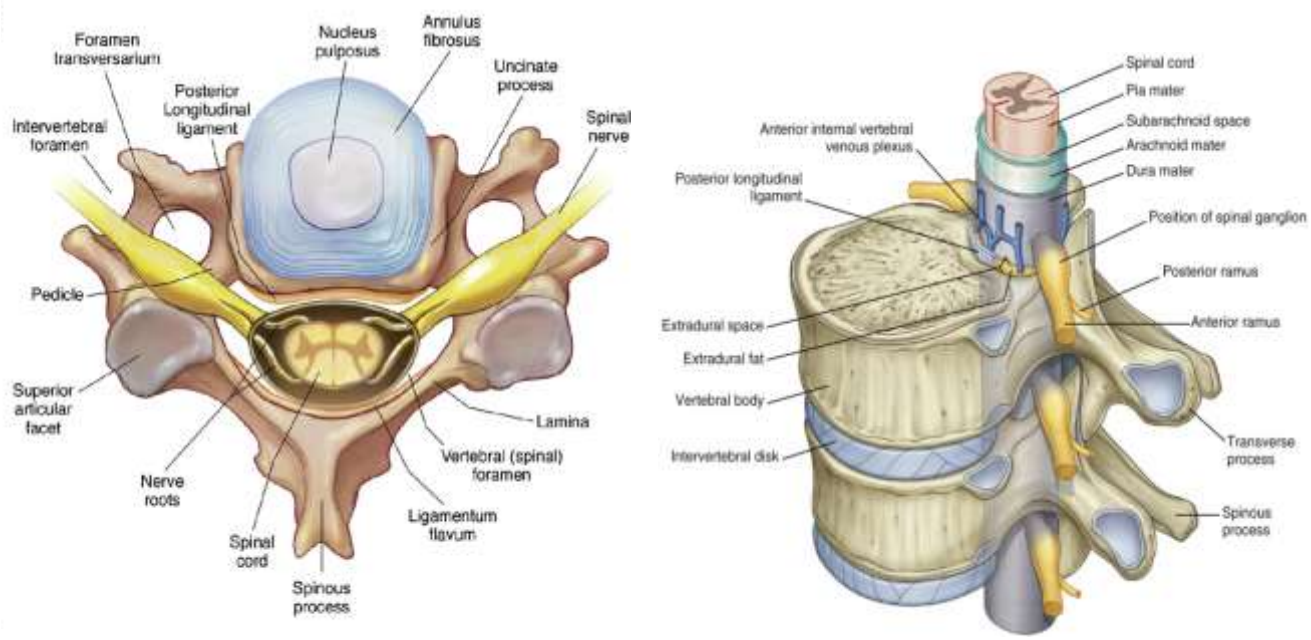


Figure 2.1: Schematic diagrams demonstrating normal cervical spine anatomy (Tracy & Bartleson, 2010)

2.1.3 Pathophysiology

The exact pathophysiology underlying degenerative cervical myelopathy remains uncertain. It is largely attributed to multifactorial extrinsic compressive forces on the spine that cause primary or secondary spinal cord injury (Ellingson, Salamon, & Holly, 2015). Primary degenerative changes are age-dependent processes attributed to the intrinsic axial load of the head transmitted through the anterior column of the spine. Secondary degenerative pathology on the other hand are linked to specific risk factors such as previous trauma, smoking, and metabolic disorders (Jäger et al., 1997)

Repetitive cervical spine motions results in a cascade of degenerative changes that begin with intervertebral discs desiccation and fibrillation leading to altered biomechanics of the anterior spinal column (Martin et al., 2018). Consequently, more axial load is transferred from the discs onto the uncovertebral processes and articular cartilage endplates resulting in development of osteophytes. The role of these bony excrescence is to increase the uncovertebral joints stability and endplate weight-bearing surface (Nouri, Tetreault, Côté, et al., 2015). Other compensatory changes include, hypertrophic bone remodeling of the uncinated processes and facet joints, and hypertrophy or ossification of the posterior longitudinal ligament and ligamentum flavum (L. Tetreault et al., 2015). Progressive increase of these structural changes of the cervical spine may inadvertently cause static extrinsic spinal cord compression. Bulging discs, osteophytes, and hypertrophic posterior longitudinal ligament compress the cord from the ventral side while thickened ligamentum flavum offend the cord dorsally (Figure 2.1) (Mohanty, Massicotte, Fehlings, & Shamji, 2015).

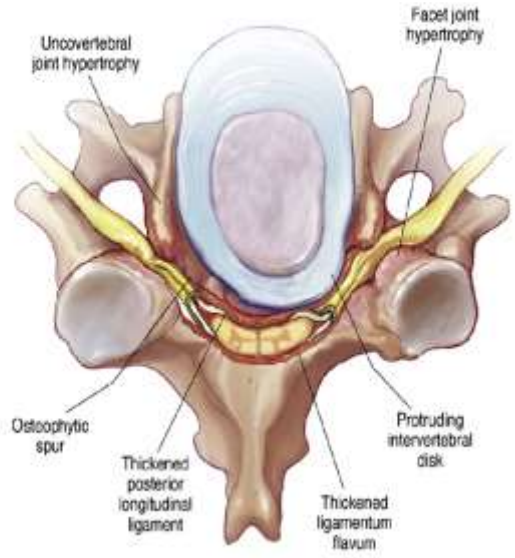


Figure 2.2: Schematic diagrams demonstrating flattened cervical spinal cord due to compression caused by bulging disks, osteophytes, thickened posterior longitudinal ligament and ligamentum flavum (Tracy & Bartleson, 2010)

When these compensatory structural changes surpass their stabilization effect, the affected cervical spine segments becomes unstable and hypermobile resulting in chronic and repetitive insult on the cord (Martin et al., 2018). This dynamic spinal cord injury arises from focal micro-trauma and non-physiological cord excursion attributed to distraction and shear forces caused by both longitudinal tension of the unstable spine. For instance, during neck flexion, the cord can be compressed anteriorly by ventral osteophytic spurs and bulging discs. On the other hand, hyperextension may result in the cord being pinched posteriorly between the posterior margin of the vertebral body and hypertrophied ligamentum flavum (Nouri, Tetreault, Côté, et al., 2015). Dynamic imaging enables diagnosis of movement-dependent instability and the effects of spondylisthesis such as spinal canal stenosis and cord compression which is not evident in neutral position during static MRI (Dean, Gabriel, Cassinelli, Bolesta, & Bohlman, 2009).

Furthermore, these degenerative pathology may also cause disruption of spinal cord microvasculature leading to circulatory disturbance such as ischemia and infarctions (Yamaguchi et al., 2017). Spinal cord ischemia frequently involve gray matter and there is usually minimal white matter involvement (Ramzi, Ribeiro-Vaz, Fomekong, Lecouvet, & Raftopoulos, 2008). Ventral cord compression impairs spinal cord perfusion through disruption of the transverse arterioles arising from the anterior sulcal arteries while posterior cord compression affects the intramedullary branches supplying the central grey matter (Echarri & Forriol, 2002; Ellingson et al., 2015). According to Martin et al, C5 – C6 level is the most susceptible cervical spine level to vascular injury since it is the most common level affected by degenerative pathology (Martin et al., 2018).

2.2 Clinical Characteristics

2.2.1Age

According to an international multicenter study by Nouri et.al, the global average age of symptomatic patients with DCM was 56.4 ± 11.83 years (range 21– 87 years).The mean age of patients from Latin America (54.23 ±10.65 years) and Asia Pacific (53.95 ± 12.20 years) was found to be lower than that from Europe (57.44 ± 11.85 years) and North America (57.33 ± 11.77 years) (Nouri, Martin, Tetreault, et al., 2016). Similarly, Northover et al study reported that the mean age of patients with cervical myelopathy was 63.8 years (range 37–88) (Northover, Wild, Braybrooke, & Blanco, 2012).

African-based studies on the different pathology that constitute DCM have comparable results to the rest of the world. A local study on the cervical spine degenerative disc disease at the Moi Teaching and Referral Hospital recorded a mean age of 56 ± 13 years (range 34-81 years) (Boen, 2014). Similarly, in a radiographic-based study carried out in a Nigerian teaching hospital found that 93.75% of the patients 60 years

and above had spondylosis and there was no case below 19years (Eduwem, 2014). A second study carried out in a Nigerian tertiary health institution revealed that 85% of the cases were over the age of 60 years (Iheukwumere & c Okoye, 2014).

Northover et al study reported that the female patients presented at a younger age compared to their male counterparts (57 years versus 66.5 years of age) (Northover et al., 2012). On the contrary, there was also no significant difference in the age at presentation between the different gender; the mean age of female cases was 55.88 ± 11.73 years while that of the men was 56.33 ± 11.71 years (Nouri, Tetreault, Côté, et al., 2015).

2.2.2 Gender

The prevalence of DCM pathologies have been reported to differ between the genders. The male to female ratio of 3:2 revealed that men were more susceptible to developing this disease than women. The proportion of male participants with this condition in Asia Pacific was the highest at (74.00%), followed by Latin America at (67.50%), Europe at (59.52%), and North America at (58.60%) (Nouri, Martin, Tetreault, et al., 2016). Similarly, Northover et al in their study reported that men presented more frequently with MRI findings of cervical myelopathy than women, with a ratio of males to females of 2.7:1 (Northover et al., 2012). Wilder et al in their study recorded higher rates of radiographic progression of cervical spine osteoarthritis in men compared to women regardless of age (8.9 per 100 person-years of observation versus 8.0 per 100 person-years of observation) (Wilder, Fahlman, & Donnelly, 2011).

On the contrary, Yue et.al in their control study on DCM found that gender was not significant predictor of DCM (Yue, Tan, Tan, Koh, & Tan, 2001). This was similar to findings from Fisher et al. study which reported that the incidence rate for males was equal to that of female and that there were no identifiable difference in the risk factors

in both male and female patients (Fisher, Simpson, & Baskin, 1992). Two radiographic-based studies carried out in Nigeria on cervical spondylosis also reported an almost even male to female ratios. One of the studies that had sought to establish the prevalence of symptomatic cervical spondylosis in a tertiary health institution in Nigeria recorded a male: female ratio of 1.17:1 (Eduwem, 2014). The second study that evaluated cervical spondylosis in a Nigerian teaching hospital reported a male: female ratio of 1.75:1 (Iheukwumere & c Okoye, 2014).

2.2.3 Clinical Presentation

The severity of DCM and its clinical presentation vary considerably between patients depending on the cervical spine level affected and the severity of cord compression. (Nouri, Tetreault, Singh, et al., 2015).The pattern of progression of this condition is typically insidious, highly variable and not well defined. Patients may remain clinically stable, have a slow stepwise deterioration with interposed quiescent periods or may progress rapidly to advanced disease (Lebl, Hughes, Cammisa Jr, & O'Leary, 2011). Certain individuals may have significant degenerative changes of the cervical spine yet are remain asymptomatic(L. Tetreault et al., 2015).

High cervical cord compressive lesions symptoms may typically begin with loss subtle fine motor hand dexterity followed by diffuse weakness and paresthesia in the upper limbs. Lower myelopathy typically present with a syndrome of weakness, spasticity and loss of proprioception in the legs leading to gait disturbance. In severe cases of DCM, quadriparesis and bladder dysfunction may be occur (Ozer, Oktenoglu, Cosar, Sasani, & Sarioglu, 2009; L. A. Tetreault et al., 2013). Furthermore, decreased mobility due to the disease process may significantly affect the patients' quality of life leading to more than one third of them develop mood disorders (Stoffman, Roberts, & King Jr, 2005).

A multicenter study on postoperative patients with DCM revealed that patients from Latin America (37.96 ± 30.92 months) had significantly longer duration of neurological deficits than those from Asia-Pacific (22.04 ± 35.68 months), Europe (24.89 ± 32.48 months) and North America (26.55 ± 42.92 months) (L. Tetreault et al., 2015). According to Belachew et al, patients in sub-Saharan Africa with cervical column degenerative pathology were often diagnosed very late in the course of their illness probably because of inadequate of diagnostic facilities (Belachew et al., 2007).

2.4 Cervical Spine Magnetic Resonance Imaging in DCM

2.4.1 Spectrum of degenerative cervical spine pathology

Degenerative changes in the spine involve a host of specific tissues, including the intervertebral discs, vertebral bodies, spinal ligaments, and the uncovertebral and facet joints (Fehlings, Tetreault, Hsieh, Traynelis, & Wang, 2016). Narrowing of the spinal cord space may result from disc herniation, vertebral bone spurs, hypertrophy or ossification of the ligamentum flavum and the posterior longitudinal ligament, degenerative kyphosis and subluxation (Epstein, 2002).

Degenerative cervical myelopathy often presents with multiple degenerative changes that cause varying degree of spinal compression occurs at a single or multiple levels (Martin et al., 2018). According to Nouri et al multicenter study, degenerative changes affecting three cervical spine segments concurrently was observed a majority of the of patients (30.6%). Moreover, multi-level degenerative pathology was reported in a statistically significant number of the participants (90.4%, $p = 0.008$) probably because the degenerative process is progressive and tends to affect all levels simultaneously (Nouri, Martin, Tetreault, et al., 2016). In addition, Northover et al study reported that majority of patients (44%) who had multilevel cervical degenerative disease had up to three levels affected simultaneously (Northover et al., 2012).

2.4.1.1 Spondylosis

Cervical spine spondylosis is characterized by intervertebral disc herniation and vertebral osteophytes at multiple levels. Spondylosis contributes to more than 90% of spinal cord compression in patients with DCM. It is the most common causes of DCM because the all degenerative processes of the spine typically starts at the level of the intervertebral discs followed by structural changes involving the vertebrae (Martin et al., 2018).

According to Nouri et al. multicenter study, spondylosis was the most common etiology of DCM in North America (75.31%), Europe (92.06%) and in Latin America (80.00%) and the second most common pathology in Asia Pacific (66.67%) (Nouri, Martin, Tetreault, et al., 2016). Similarly, Northover et al found that multi-level disc-osteophyte complexes affected 80.5% of patients with cervical myelopathy (Northover et al., 2012). In another study on conventional radiographic evaluation of cervical spondylosis at Uyo teaching hospital in Nigeria, spondylosis was seen in over 90% of individuals after the age of 40 years but rarely reported before second decade of life (Eduwem, 2014).

2.4.1.2 Ligamentum flavum hypertrophy

Hypertrophy of the ligamentum flavum is a multifactorial disorder that occurs when mechanical stress on the ligament induces an inflammatory response which in turn triggers angiogenesis that leads to scar tissue formation. It is characterized by loss of elastic fibers, increased collagen fibers, calcification, ossification, and chondrometaplasia of the ligament (Hur et al., 2015). According to Al-Jarallah et.al survey in Kuwait, the prevalence of ligamentum hypertrophy of whole spine MRI was 18.6% with 57.7% of the lesions found in the cervical spine (Al-Jarallah, Al-Saeed, Shehab, Dashti, & Sheikh, 2012). A multicenter study on patients with DCM from four

continents reported that the global prevalence of LFH in the cervical spine was 56.8%. It was most was most frequently recorded in Latin America (61.25%) and was least common in North America (18.45%) (Fehlings et al., 2018).

2.4.1.3 Hypertrophy of posterior longitudinal ligament

Hypertrophy of posterior longitudinal ligament is a disorder characterized by thickening of the ligament caused by accumulation of granulation tissue attributed to chronic inflammation. This ligament bridges the posterior margin of cervical vertebral bodies therefore, its enlargement may inadvertently cause direct ventral spinal cord compression. In addition, the degenerative process may also result in the ossification of this ligament leading to rigidity of the affected cervical spine segments and compensatory increase in the mobility of the adjacent segments. Such hypermobile segments are unstable and can result in be a dynamic spinal cord injury (Azuma, Kato, & Taguchi, 2010).

According to Yamaguchi et al, the rates of ethnicity-based prevalence of ossification of posterior longitudinal ligament in United States of America were significantly higher in the Asian Americans (4.8%) compare to the Caucasian Americans (1.3%), Hispanic Americans (1.9%), African Americans (2.1%) or in Native Americans (3.2%) (Yamaguchi et al., 2017). Nouri et al in their multicenter study also found out that cervical myelopathy secondary to ossification of posterior longitudinal ligament was the highest among patients from in Asia Pacific (35.33%) and least common in North America (11.72%) (Nouri, Martin, Tetreault, et al., 2016). The higher risk of this condition among individuals of Asian was probably due to multiple genetic predispositions combined with specific environmental and occupational factors (Fehlings et al., 2018).

2.4.1.4 Degenerative spondylolisthesis

Degenerative spondylolisthesis occurs when a vertebra translates anteriorly or posteriorly relative to the one below it. This pathological condition is attributed to diminished cervical spine mobility in the affected segments leading to increased stress on the adjacent discs and facets so that during flexion and extension excessive stretching of the spinal ligaments occurs resulting in slippage of the vertebra (C. Lee, Woodring, Rogers, & Kim, 1986). According to Dean et al, spondylolisthesis frequently occurs adjacent to relatively stiff spondylotic cervical levels and rarely within spondylotic cervical segments (Dean et al., 2009).

According to a study by Yamaguchi et al, degenerative spondylolisthesis is frequently observed at C4-C5 secondary to reduced cervical flexibility at C5-C6 segment which is the most common level affected by primary spondylosis (Yamaguchi et al., 2017). Jiang and colleagues in their systematic literature review also found that C4-C5 (49.4%) was the most frequently affected site by spondylolisthesis followed by C3-C4 (46%) (Jiang, Jiang, & Dai, 2011).

Similarly, Koakutsu et al in their radiographic-based study on post- operative patients with cervical myelopathy, C4-C5 and C3-C4 slippage was found in 73% and 27% of the cases respectively (Koakutsu et al., 2011). Furthermore, Suzuki et.al evaluation of cervical spondylolisthesis using upright cervical kinetic magnetic resonance imaging found that on the most frequently affected level was C4-C5 (26.4%) followed by C5-C6 (25.5%), C3-C4 (15.5%) and C6-C7 (12.7%) (Suzuki et al., 2013).

2.4.2 Congenital cervical spinal canal stenosis

Congenitally Cervical Spinal canal Stenosis (CCSS) is a developmental disorder attributed to inherently narrow vertebral foramen due to a lower neural arch and flat-shaped spinal canal (Jenkins et al., 2016). It is a significant predisposing factor to

development of DCM because an inborn narrow spinal canal there is limited space available to accommodate the spinal cord therefore, it is more likely to be compressed by less substantial degenerative pathology (Martin et al., 2018). CCSS is also associated with increased segmental mobility which may in turn result in localized increased strain and shear forces to the spinal cord leading to axonal injury (Morishita et al., 2009).

The Spinal Cord Occupation Ratio (SCOR) is one of the parameters used to assess for CCSS in patients with DCM. It describes the proportion of the vertebral canal occupied by the spinal cord at non-pathological segments immediately above and below the level with spinal cord compression. Since C5 segment has been reported to have the narrowest vertebral canal with SCOR of 58.3 (± 4.0%), two standard deviations from this mean (72.3%) is used as the point of reference. Therefore, SCOR ≥70% between C2- C7 is used to identify individuals with CCSS (Nouri, Martin, Mikulis, & Fehlings, 2016).

Nouri et al study reported that the global prevalence of DCM with SCOR ≥70% was 8.4%. They also observed that there was regional variations in the prevalence of congenital stenosis probably due to differences in environmental, occupational and genetic factors. Asia Pacific (11.6%) recording highest prevalence while Europe had the least at (2.3%) (Nouri, Martin, Tetreault, et al., 2016).

Jenkins and colleagues studied 1000 cervical MRIs and reported the overall prevalence of CCSS was 6.8% among American populace (Jenkins et al., 2016). Another study carried out on cadavers estimated that the prevalence of cervical canal stenosis at 4.9% among all adults and 6.8% in those at or above 50 years (M. J. Lee, Cassinelli, & Riew, 2007). Similarly a study by Taitz et al on cervical spines of South African cadavers, reported that the black race despite having less spondylosis compared to the whites

(18.5% versus 44.0%, p=0.02) were more predisposed to developing myelopathy attributed to pathological osteophytes because they had smaller vertebral canal (Taitz, 1999).

2.4.3 Cervical spinal cord compression

Spinal cord compression is a sensitive marker of myelopathy but its specificity is limited since it has been observed in approximately 5% of asymptomatic individuals. The degree of compression of the various spinal cord tracts is an important predictor in the development of neurological symptoms and it also correlates with the severity of pathologic changes (Martin et al., 2018). Spinal cord compression was most frequently observed at C5-C6 probably because it is the most mobile segment of the lower cervical spine. It is from this level that the degree of cervical spine mobility decreases proximally and distally. Furthermore, this level is in close proximity to the relative immobile thoracic spine (Nouri, Martin, Tetreault, et al., 2016) (Northover et al., 2012)

According to Nouri et al, the C5-6 region is the most frequent maximum compressed site (39.7%), and the most common site of MRI degenerative changes. The next most common sites after C5-C6, in descending order of prevalence were C6-C7, C4-C5 and C3-C4. Involvement of the upper segments alone is unlikely to be solely due to cervical spondylosis (Nouri, Martin, Tetreault, et al., 2016). Similarly, Northover et al found that C5-C6 was the most frequently affected level in almost half of their study participants (48.8%) followed by C3-C4 level (Northover et al., 2012).

Eduwem et.al also reported that the most commonly affected level by cervical spondylosis was C5-C6 followed by C4-C5 (11%), C3-C4 (10%) and C6-C7 (7%) in a descending order. C2-C3 was spared by this condition (Eduwem, 2014). A local study on degenerative cervical disc disease at Moi Teaching and Referral Hospital revealed that single most common affected level was C5-C6 (61%), followed in order of

decreasing frequency by C4-C5 (52%), C3-C4 (27%), C6-C7 (18%) and C2-C3 was seen in only one patient (2%) (Boen, 2014).

2.4.4 Increased cervical spinal cord signal intensity on T2WI

Increased intramedullary signal intensity foci within the spinal cord in a conventional T2WI spin echo sequence represent an area of the cord with increased time of relaxation due to increased amount of water content. It provides clear evidence of the location and severity of the spinal cord injury (Nouri, Tetreault, Singh, et al., 2015). It is a sequela of chronic insult to the cord due to reversible damage such as edema or ischemia or irreversible changes including necrosis, myelomalacia, and cavitation (Kato, Yukawa, Suda, Yamagata, & Ueta, 2012).

According to Northover et al, increased T2WI spinal cord signal intensity changes was observed in (72.5%) of patients with cervical myelopathy (Northover et al., 2012). Similarly, the prevalence of T2WI hyperintensity in a global cohort of patients with DCM was 76.5% (Nouri, Martin, Tetreault, et al., 2016). Kato et al. reported that the prevalence of T2 hyperintensity in DCM was estimated at 58–85% globally (Kato et al., 2012).

Foci of increased cervical spinal cord signal intensity was frequently observed at C5-C6 (39.9%) level which coincidentally was also the most common segment with maximum spinal cord compression (88.9%) (Nouri, Martin, Tetreault, et al., 2016). There was also a statistically significant association between presence of T2WI spinal cord hyperintensity changes and CCSS among patients with DCM ($p=0.09$) (Nouri, Tetreault, et al., 2017).

Assessment of the sagittal extension of the T2WI hyperintense lesion is crucial since it is a valuable indicator of disease severity and predictor of post-therapeutic functional outcome. In global multicenter study on the spectrum of DCM pathologies, approximately two thirds of the participants (63.3%) had a single spinal level with a foci of T2WI hyperintensity (Martin et al., 2018). Another study with comparable results carried out on preoperative patients with DCM found that only one segment was involved 73% of all the participants with intramedullary T2WI hyperintensity (Nouri, Martin, Kato, et al., 2017).

According to Nouri et al multicenter study, a quarter of the patients with neurological deficits (25%) had normal spinal signal intensity T2WI spin echo sequence. This may explained by the fact that the neurological dysfunction may have been caused by minor physiological changes that may be so subtle to be detected by conventional MRI techniques. Moreover, spinal cord injury secondary to vascular compromise leading to neurogenic claudication or due to altered cord tension rather than focal cord compression are not visible on T2WI spin echo sequence (Nouri, Martin, Tetreault, et al., 2016) .

2.5 Relationship between Cervical Spine Magnetic Resonance Findings in DCM and Clinical Variables

MRI findings associated with poor outcome included presence of intramedullary spinal cord T2WI hyperintense foci, multilevel cord compression, and cervical column mal-alignment (Nouri, Martin, Tetreault, et al., 2016). On the other hand, poor prognostic demographic factors include male gender, age of sixty years and above and prolonged duration of the disease (Yamaguchi et al., 2017)

2.5.1 Relationship between cervical spine MRI findings in DCM and age

According to Takamiya et al, increase in age is a significant risk factor for development of degenerative cervical myelopathy (odds ratio, 1.07; confidence interval, 1.01-1.14) (Takamiya et al., 2006). Multilevel degenerative cervical spine pathology and spinal cord compression was recorded more frequently in older patients (Mohanty et al., 2015). Yue et al in their control study found that the patients with cervical spinal cord compression (mean age, 56.7 years) were significantly older than subjects in the control group (mean age, 43.3 years) (Yue et al., 2001). The number of levels with cord compression and the degree of canal stenosis at the maximally affected level in patients with degenerative cervical myelopathy was directly proportional to age (Northover et al., 2012). This is because degenerative structural changes are progressive and cumulative over time hence they are likely to lead to cervical spinal cord compression in older individuals (Martin et al., 2018).

Furthermore, more DCM patients with congenital narrow spinal canal were found to be on average, 5.5 years younger than those with normal vertebral foramen($p=0.03$) (Nouri, Tetreault, et al., 2017). Myelopathy tend develop early in life among patients with congenital spinal canal stenosis because the spinal cord is more likely to be

compressed by less substantial degenerative pathology due to limited space available to accommodate it (Martin et al., 2018).

Chronic insult to the cord over a prolong period of time may result in reversible damage such as edema or ischemia or irreversible changes including necrosis, myelomalacia, and cavitation (Kato et al., 2012). On the contrary, Northover et al found that there was no significant association between increased T2WI signal intensity changes and age or number of levels with compressive degenerative pathology (Northover et al., 2012).

2.5.2 Relationship between cervical spine MRI findings in DCM and gender

According to Nouri et al, certain cervical spine degenerative pathology were found to have a gender predilection for instance, more male patients presented with spondylosis (92.3% versus 85.6%, p=0.017) and ligamentum flavum hypertrophy (61.4% versus 49.1%, p=0.012) while single level disc bulge was observed more among the female participants (13.9% versus 6.7%, p=0.013) (Nouri, Martin, Tetreault, et al., 2016).

Less severe canal stenosis at the level of maximum cord compression was also recorded among the female patients compared to their male counterparts (5.9 mm vs 5.6 mm average AP canal diameter). The women also had fewer levels with degenerative pathology compared to men (two versus three levels) (Northover et al., 2012). Milder degenerative changes and lower frequency of T2WI hyperintensity of the cervical spinal cord was also recorded among the female participants (82.4% females versus 66.7% male participants, p= <0.001) (Nouri, Martin, Tetreault, et al., 2016). On the contrary, Northover et al found that there was no significant association between increased T2WI signal intensity changes and gender (Northover et al., 2012)

2.5.3 Relationship between cervical spine MRI findings in DCM and duration of symptoms

According to Bednarik et al, there was no significant association between duration of symptoms and the type of degenerative pathology or number of levels with cervical cord compression (Bednarik et al., 2008). Similarly, Tetreault et al reported no association between duration of the symptoms and the type of degenerative pathology that causing the spinal cord compression, number of cord compressed levels or presence of T2 hyperintensity (L. Tetreault et al., 2015). Comparable duration of symptoms was also recorded among patients with CCSS as those normal cervical vertebral canal (Nouri, Tetreault, et al., 2017).

Longer duration of myelopathy symptoms (24.7 month) was recorded in patients with T2WI cervical spinal cord hyperintensity compared to those with normal signal intensity (17.0 months)(L. Tetreault et al., 2015). Comparable findings were reported by Bednarik et al. who found that prolong neurological symptoms were associated with cervical cord T2WI hyperintensity ($p=0.347$) (Bednarik et al., 2008). According to Tetreault et al however, there was no association between duration of the symptoms and the presence of T2 hyperintensity (L. Tetreault et al., 2015).

CHAPTER THREE: METHODOLOGY

3.1 Study design

A cross-sectional study was carried out between January 2017 and December 2017.

3.2 Study site

The study was carried out at Moi Teaching and Referral Hospital. It is the second national referral facility in Kenya located in Eldoret town. The town is the headquarters of Uasin-Gishu county and is located in Western Kenya about 313 kilometers from Nairobi and lies 0° 31´N 35° 17´E. Uasin-Gishu county has cosmopolitan population and agriculture is its main socioeconomic activity. The catchment area of this hospital includes Rift valley and Western regions of Kenya, parts of Eastern Uganda and South Sudan. This study was conducted in the MRI unit of the Moi Teaching and Referral Hospital radiology and imaging department.

3.3 Study population

The study population included all individuals who presented with myelopathy-related neurological symptoms and demonstrated radiological features of DCM on their cervical spine MRI done at the MTRH radiology and imaging department.

3.4 Sample size

Census study was carried out. A total of 57 patients with myelopathy-related neurological symptoms and a radiological findings of DCM on their MRI of the cervical spine done at the MTRH radiology department were recruited. In the previous year (2016), 72 patients who had undergone cervical spine MRI at the hospital were reported to have various degenerative cervical spine pathology.

3.5 Sampling technique

All patients who underwent cervical spine MRI at the MTRH radiology department and met the eligibility criteria during the study period were recruited to the study.

3.6 Eligibility criteria

3.6.1 Inclusion criteria

- Patients with 18 years and above
- Patients who presented with myelopathy-related neurological symptoms.
- Patient who had radiological findings of degenerative cervical myelopathy based cervical MRI done at MTRH.

3.6.2 Exclusion criteria

- Patients with other cervical spinal cord pathologies such as infective, inflammatory or neoplastic diseases.
- Patients who had previous history of surgery to the cervical spine.
- Patients with previous history of cervical spine trauma.
- Patients with significant spinal deformity or extensive degenerative pathology that prevented measurements of cervical vertebral canal or the cervical spinal cord.
- Patients who declined to give consent to the study

3.7 Procedures

The principal researcher with the help of two trained research assistants screened all patients at the MRI unit of MTRH radiology and imaging department for eligibility to participate in the study based on the aforementioned inclusion and exclusion criteria. Patients were referred for imaging by clinicians in the outpatient, orthopedic, neurosurgical and medical clinics of MTRH and also from other public and private health facilities. Informed consent was then sought from the participants before data was collected using interviewer administered questionnaires. Their demographic details and clinical history of the myelopathy-related neurological symptoms which included

motor and/or sensory dysfunction of the upper extremity, lower limb motor neurological deficits and bowel or urinary sphincter dysfunction were recorded.

Cervical spine MRI in Digital Imaging and Communications in Medicine (DICOM) format were reviewed using DICOM viewer (Clear Canvas Workstation. Ink). Only the index images were taken into consideration for the patients who presented more than once during the study period. Specific MRI parameters assessed included, the type of degenerative pathology, the number of levels with cord compression, level of maximum cord compression, presence of intramedullary cord signal intensity changes and measurements of the cervical cord and canal diameters. The cervical cord compressive degenerative pathology identified included osteophytes, intervertebral disc bulges, degenerative spondylolisthesis, hypertrophy of the ligamentum flavum and posterior longitudinal ligaments. Spinal cord compression was displayed by distortion or flattening of the cord morphology.

Congenital cervical spinal canal stenosis was defined by SCOR of ≥70% between C2-C7 levels. SCOR was obtained by dividing the means of the mid-sagittal cervical spinal cord and canal diameters measured immediately above and below the area of degenerative pathology based on a T2WI spin echo sequence. The average of these measurements obtained at these two levels that did not contribute to spinal cord compression was used to ensure that SCOR was consistent throughout the cervical region by taking into account potential measurement variability and minor differences in caliber between various cervical spine segments. The interface between the hyperintense cerebral spinal fluid and hypointense posterior longitudinal ligament and ligamentum flavum was used to delineate the anterior and posterior borders of the cervical vertebral canal respectively. The upper-most and lower-most measurements were limited to the lower third portion of C2 and the C7-T1 junction respectively.

Reference sites above and below were measured at middle of C3 and C7 vertebra (Figure 3.1).

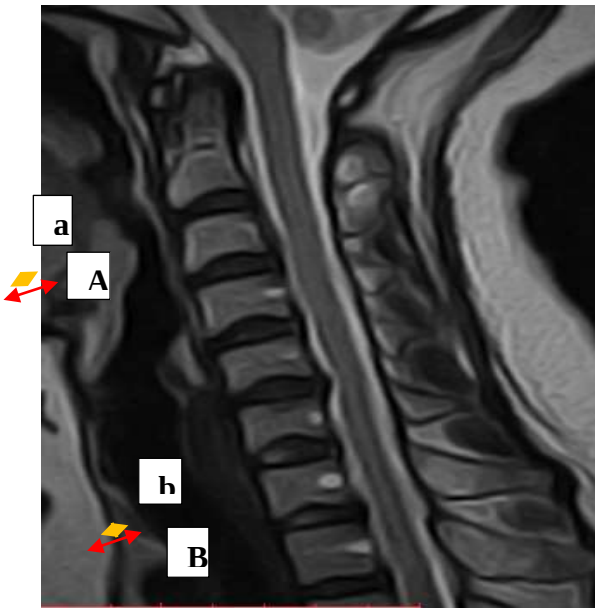


Figure 3.1: Sagittal cervical spine MRI demonstrating dimensions of the cervical vertebral canal and spinal cord used to calculate Spinal Cord Occupation Ratio.

a – Spinal cord diameter above the degenerative pathology

b - Spinal cord diameter below the degenerative pathology

A - Vertebral canal diameter above the degenerative pathology

B - Vertebral canal diameter below the degenerative pathology

SCOR = [(a+b) / (A+B)] x 100

3.8 Study recruitment schema

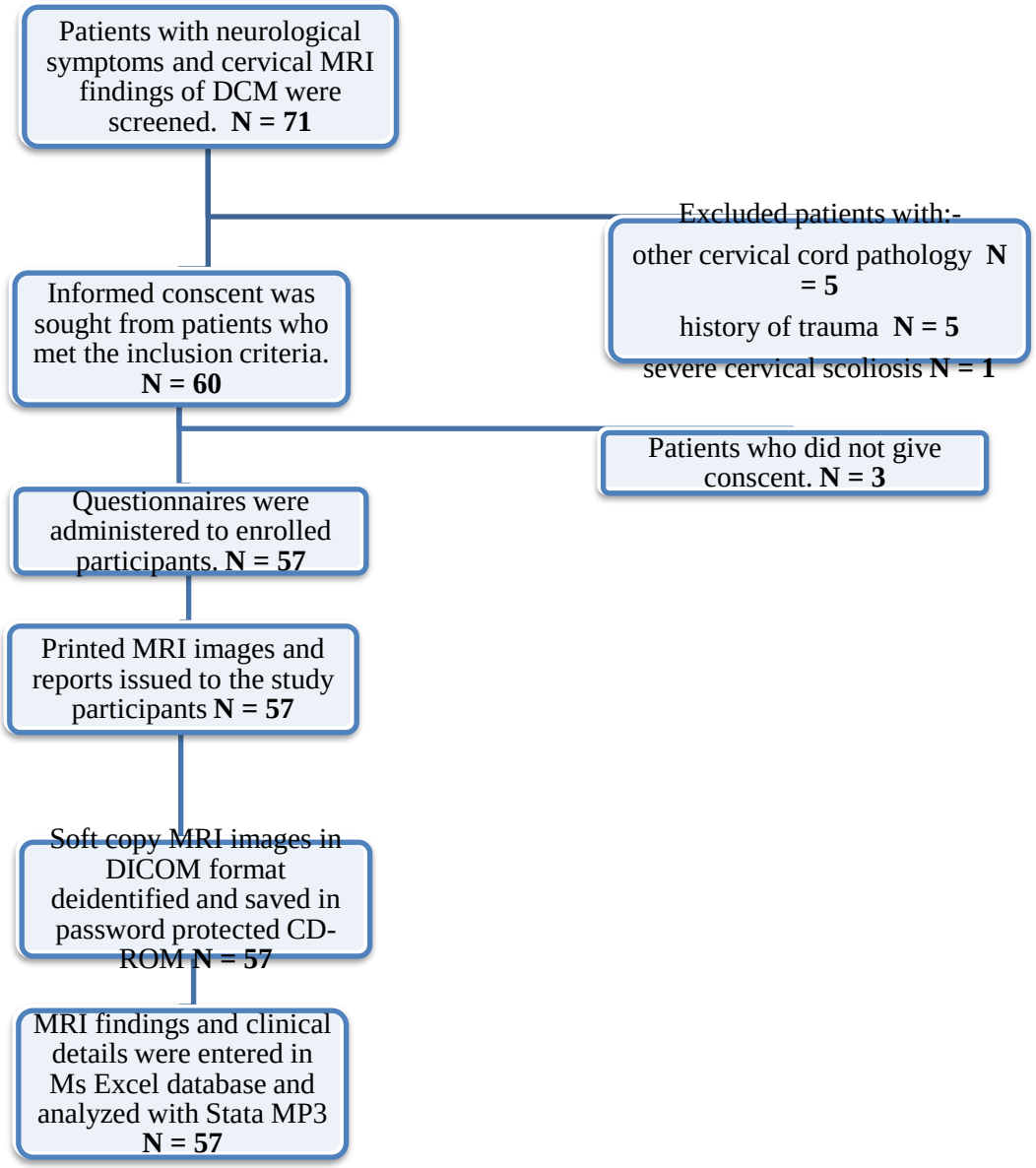


Figure 3.2: Study recruitment schema

3.9 Quality control

All cervical spine MRI were acquired using a 0.36 tesla Magsence 360 machine (Mindray, China) at the MTRH MRI unit using standard MTRH protocol detailed in appendix III. All internal quality controls were maintained throughout the study period. The principle investigator reported all the images and the findings were verified by two consultant radiologists. A third consultant radiologist was sought in situation where there were varying observations. The hard copy images and the printed MRI reports were issued to the participants.

3.10 Data collection and management

Data on the patients' demographic and clinical details were collected using a structured interviewer-administered questionnaire. The MRI findings were recorded in standardized data collection tool. A soft copy of the MRI images in DICOM format were deidentified and saved in CD-ROM. The collected data were then coded and transferred to a Microsoft Excel computer database through double entry method to ensure the accuracy of the data was maintained. Passwords was used to protect access to the data in soft copy while those in hard copy were kept in cabinets under lock and key.

3.11 Ethical considerations

Approval to carry out the study was sought from the Institutional Research and Ethics Committee. Informed consent was sought from the study participants prior to data collection. They were assured of their privacy and the freedom to withdraw from the study at any stage without fear of victimization. All patients received their results and the necessary medical care regardless of their participation in the study. No coercion, incentives or inducement was used to convince patients to participate in the study.

Collected data was only available to the investigator and the supervisors. All patient information were kept confidential.

3.12 Data analysis

Data analysis was performed using Stata MP version 13 statistical package. Categorical variables were summarized as frequencies and the corresponding percentages while continuous variables as mean, median and standard deviation. Fisher exact test was used to assess association between the categorical variables. A p-value of less than 0.05 was considered statistically significant. The results were presented using tables and charts. The findings of this study will be published in relevant journals and presented in conferences.

CHAPTER FOUR: RESULTS

4.1 Clinical Characteristics

4.1.1 Age

The mean age of the participants was 51.7 years (standard deviation = 13.3) and the range was between 30 years and 87 years. Almost half of the respondents, N =29 (51%), were between 40 years and 60 years of age. No patient enrolled to the study was below 30years. The female patients were on average ten years younger (mean age = 47.8 years) than their male counterparts (mean age = 57 years). (Figure 4.1)

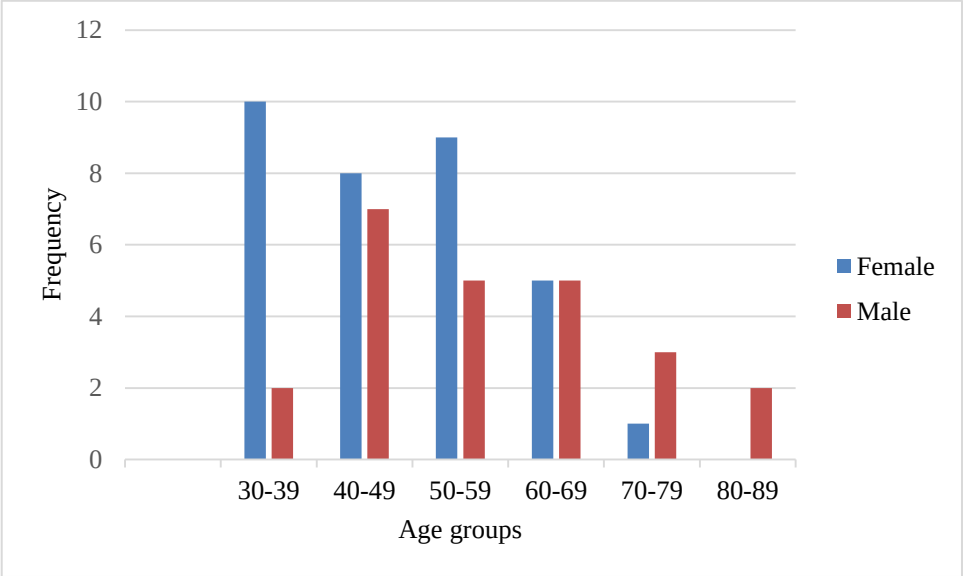


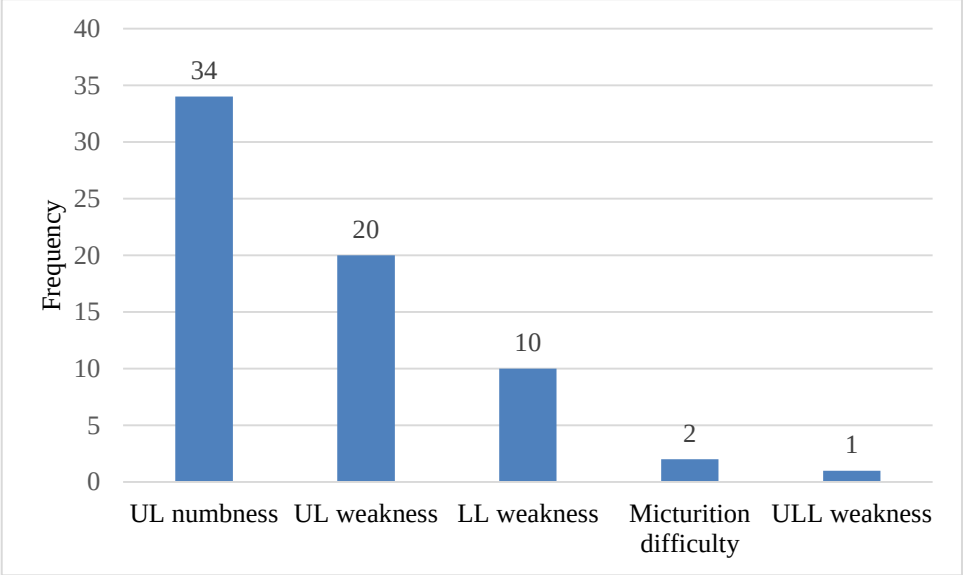
Figure 4.1: Distribution of the study participants by age group

4.1.2 Gender

Of the 57 participants enrolled into the study, slightly more than half of them, N = 33 (58%) were female and the male to female ratio was 1:1.4.

4.1.3 Clinical presentation

Majority of the participants, N= 36 (63.2%) presented with more than one myelopathy –related neurological symptom. The most frequently reported symptom recorded was upper limb paraesthesia, N= 34 (59.6%) while only one patient (1.8%) complained of quadriparesis (Figure 4.2)



Key: UL- upper limb, LL – lower limbs, ULL –upper and lower limbs

Figure 4.2: Distribution of the main presenting symptoms

The average duration of the main neurological symptoms reported was 10.5 months and the range was 1- 48 months. Majority of the participants, N = 24 (42.1%) presented with symptoms lasting less than six months and only nine patients (16.8%) reported symptoms lasting more than two years (Figure 4.3).

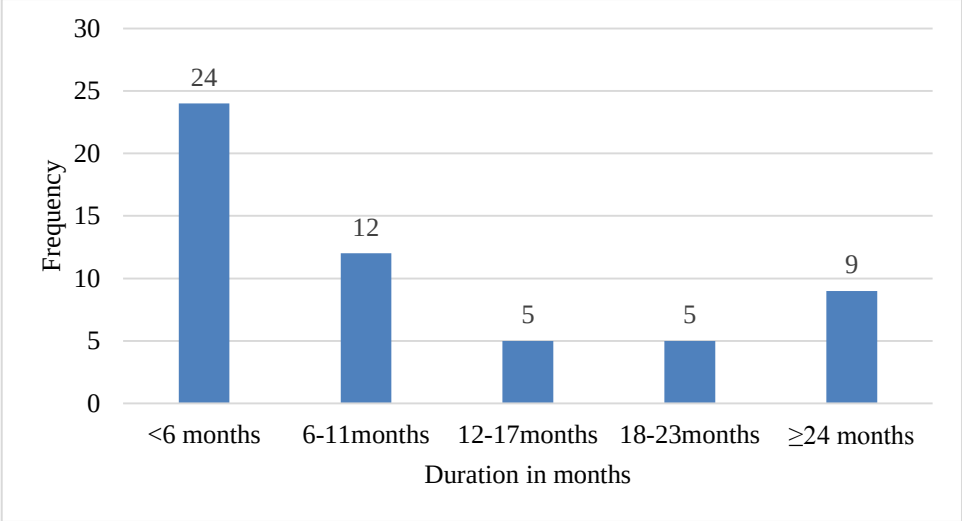


Figure 4.3: Distribution of the duration of main presenting symptoms

4.2 Cervical Spine Magnetic Resonance Imaging Findings in DCM

4.2.1 Spectrum of degenerative cervical spine pathology

The most commonly observed DCM pathology, N=52 (91.2%) was multilevel intervertebral disc bulge and vertebral bone osteophytes collectively referred as cervical spondylosis. This was followed by hypertrophy of the ligamentum flavum N=15 (26.3%) and posterior longitudinal ligament hypertrophy N=10 (17.5%) respectively (Figure 4.4)

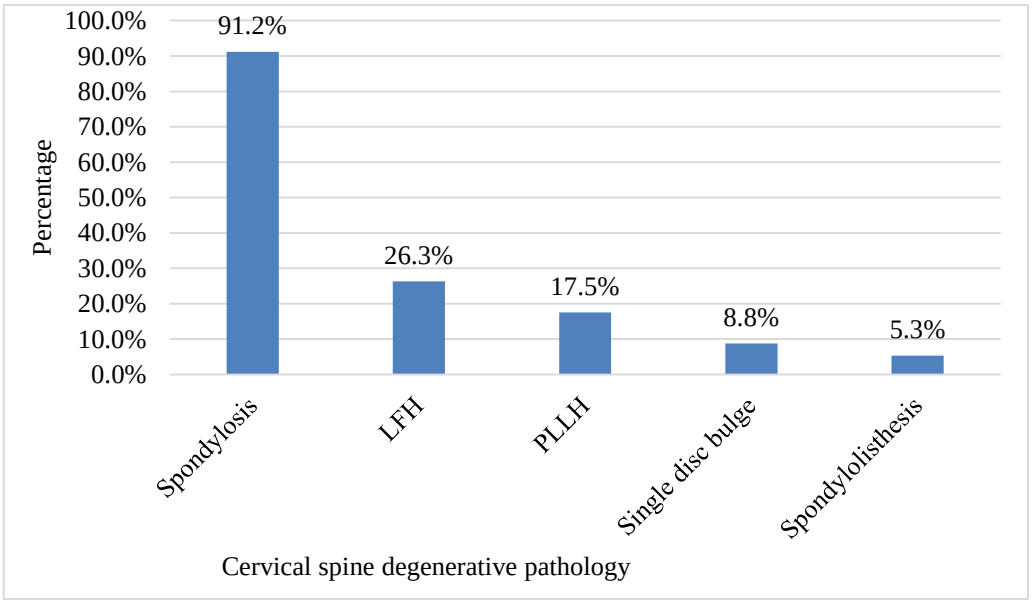


Figure 4.4: Distribution of cervical spine degenerative pathology

The mid-portion of the cervical column, C3-C4, C4-C5 and C5-C6 levels, was most frequently affected by spondylosis, LFH and PLLH. Minority of the patients, N=5 (8.8%) and N=3 (5.2%) had single disc bulge and spondylolisthesis respectively (Table 4.1).

Table 4.1 Frequency table on the cervical spine levels affected by the DCM pathology

Number of patients with DCM pathology	**Cervical spine level**				
	C2-C3	**C3-C4**	**C4-C5**	**C5-C6**	**C6-C7**
Spondylolisthesis (n=3)	0(0%)	0(0%)	1(1.7%)	1(1.7%)	1(1.7%)
Single disc bulge (n=5)	0(0%)	2(3.5%)	0(0%)	3 (5.3%)	0(0%)
Spondylosis (n=52)	3(5.3%)	**28(49.1%)**	**44(77.2%)**	**45(78.9%)**	23(40.4%)
PLLH (n= 10)	1(1.7%)	**8(14.0%)**	**9(15.8%)**	**8(14.0%)**	3(5.3%)
LFH (n= 15)	0(0%)	**10(17.5%)**	**11(19.3%)**	**14(24.6%)**	5(8.8%)

Three cervical spinal levels were most frequently (43.9%) involved concurrently by the degenerative pathology. Only one patient (1.8%) had spinal cord compression on all the five cervical spine levels, from C2 up to C7 level (Figure 4.5).

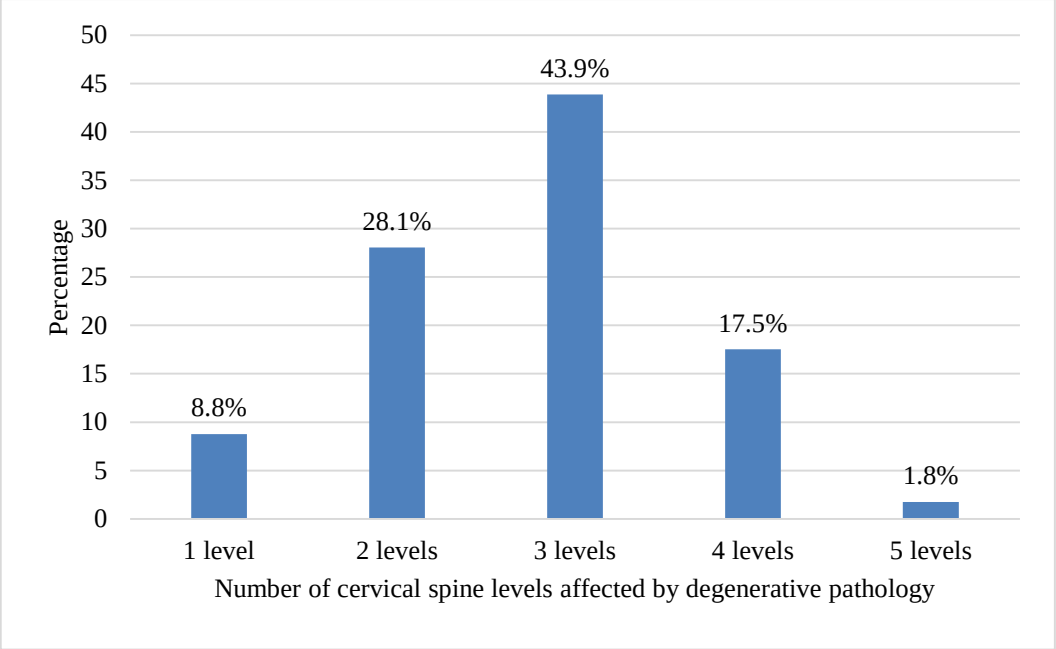


Figure 4.5: Number of cervical spine levels affected by degenerative pathology.

4.2.2 Congenital cervical spinal canal stenosis

Majority of the participants, N= 49 (86%) had normal cervical spinal canal parameters (SCOR<70) with only eight of them having (14%) congenital cervical spinal canal stenosis with (SCOR ≥70). The Spinal Cord Occupation Ratio (SCOR) of all the participants was between 49% and 78% with a mean of 65.02% (standard deviation = 6.16).

4.2.3 Cervical spinal cord compression

The C5-C6 level was the most frequent site of maximum spinal cord compression due of the degenerative pathology in majority of the participants (43.7%) followed by C3-C4 level (24.6%). None of them had spinal cord compression at the C2-C3 level (Figure 4.6)

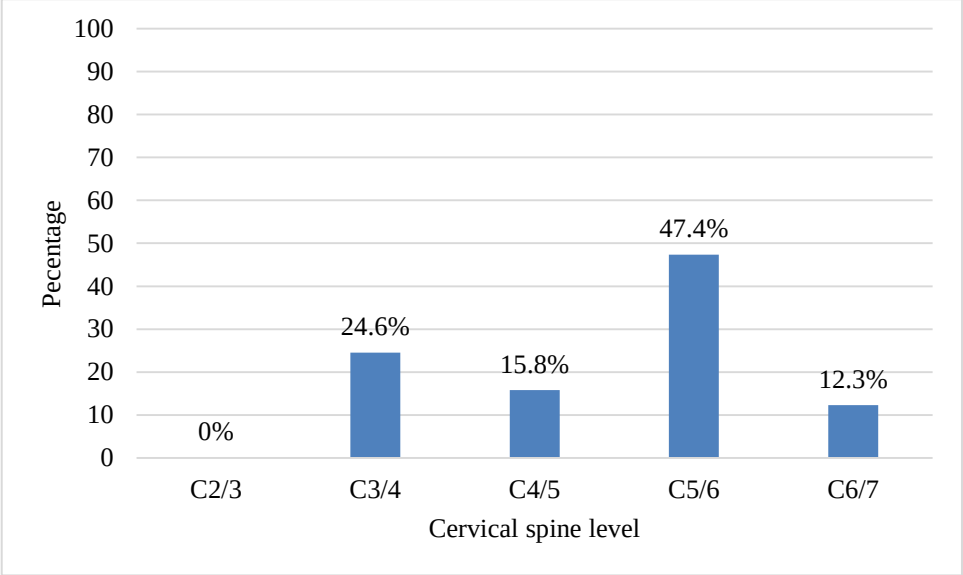


Figure 4.6: Level of maximum cervical spinal cord compression

4.2.4 Increased cervical spinal cord signal intensity on T2WI

Normal cervical spinal cord signal intensity was observed on T2WI in a majority of patients (54.4%). Of the twenty six respondents (45.6%) who had a T2WI hyperintense foci within their cervical spinal cord, C5-C6 (36.8%) was the most commonly involved segment followed by C4-C5 (22.8%). No T2WI cervical cord hyperintensity was observed at C2-C3 segment in any of the participants (Figure 4.7)

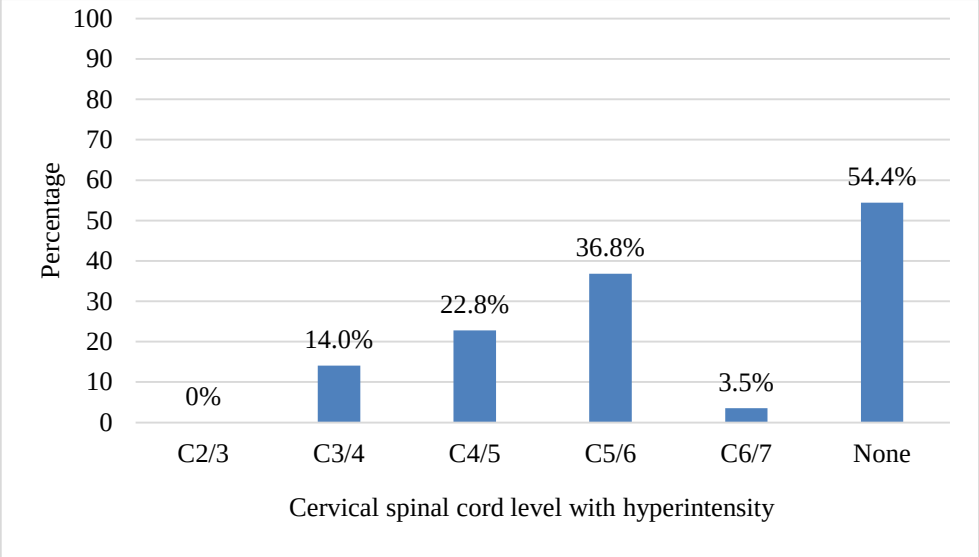


Figure 4.7: Cervical spine segments with T2WI hyperintense region

Involvement of only one cervical spine level was observed in a majority of the patients (23%) with spinal cord T2WI hyperintense foci. No participant had the hyperintense lesion extending beyond three segments. (Figure 4.8)

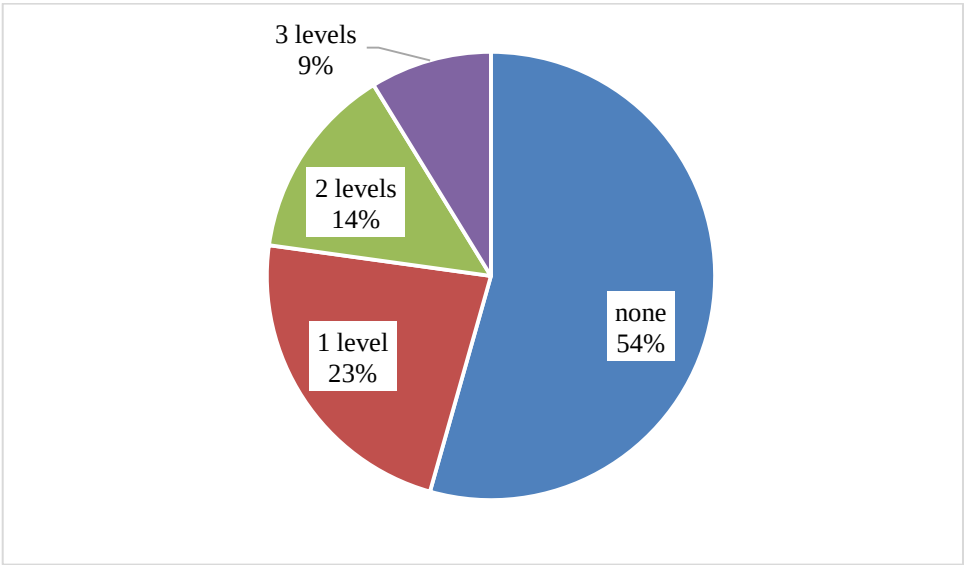


Figure 4.8: Number of cervical spine levels with T2WI hyperintensity

4.2.5 Concurrent degenerative cervical spine pathology occurrence.

Spondylosis which denotes presence of multilevel disc bulges and osteophytes was the most prevalent pathology to be observed together with other DCM conditions followed by ligamentum flavum hypertrophy. Spondylosis was also observed in all patients with CCSS and T2WI cord hyperintense foci. Moreover, foci of increased signal intensity within their spinal cord was observed in all patients with CCSS. No participant had PLLH and spondylolisthesis concurrently (Table 4.2).

Table 4.2 Frequency table on concurrent degenerative cervical spine pathology.

Number of patients with DCM pathology	**DCM pathology and related MRI findings**						
	Spondylolisthesis	Single disc bulge	Spondylosis	PLLH	LFH	CCSS	T2WI hyperintensity
Spondylolisthesis (n= 3)	X	**0**	**3 (100%)**	0	2 (66.7%)	1(33.3%)	1(33.3%)
Single disc bulge (n=5)	0	**X**	0	0	0	0	0
Spondylosis (n= 52)	3(5.8%)	**0**	**X**	10(19.2%)	15(28.8%)	8(15.4%)	26(50%)
PLL H (n = 10)	0	**0**	**10(100%)**	X	6(60%)	2(20%)	5(50%)
LFH (n=15)	2(13.3%)	**0**	**15(100%)**	6(40%)	X	3(20%)	5(33.3%)
CCSS (n=8)	1(12.5%)	**0**	**8(100%)**	2(25%)	3(37.5%)	X	**8(100%)**
T2WI hyper-intensity (n=26)	1 (3.8%)	**0**	**26(100%)**	5(19.2%)	5(19.2%)	8(30.8%)	X

4.3 Relationship between Cervical Spine MRI Findings in DCM and Clinical Variables.

Clinical variables significant in DCM prognostication such as male gender, age of 60 years and above and symptoms of one year and above were compared with specific MRI findings associated with poor outcome including presence of intramedullary spinal cord T2WI hyper intensity, multilevel cord compression, and congenital cervical vertebral canal stenosis (Nouri, Martin, Tetreault, et al., 2016) .

4.3.1 Relationship between cervical spine MRI findings in DCM and age

Multilevel cervical spinal cord compression was observed in all patients with 60 years and above. There was no significant difference in age with respect to presence of CCSS ($p = 0.672$) and spinal cord T2WI hyperintensity ($p = 0.382$) (Table 4.3).

Table 4.3 Frequency table on relationship between cervical spine MRI findings in DCM and age

Patient Characteristics	**Age <60years (N=41)**	**Age≥60years (N=16)**	**Total (N=57)**	**P-value**
Multilevel cord compression	36 (63.2%)	**16 (28.1%)**	52 (91.2%)	0.308
CCSS	5 (8.8%)	3 (5.3%)	8 (14%)	0.672
T2WI hyperintensity	16 (28.1%)	10 (17.5%)	26 (45.6%)	0.382

4.3.2 Relationship between cervical spine MRI findings in DCM and gender

There were more women (N=32, 56.1%) than men with multilevel cervical spinal cord compression but this difference was not statistically significant p=0.151). There was no significant differences between gender with respect to presence of CCSS and spinal cord T2WI hyperintensity (p=0.261) and (p=0.788) respectively (Table 4.4)

Table 4.4 Frequency table on relationship between cervical spine MRI findings in DCM and gender

Patient Characteristics	Male (N=24)	Female(N=33)	Total (N=57)	P-value
Multilevel Cord Compression	20 (35.1%)	32 (56.1%)	52 (91.2%)	0.151
CCSS	5 (8.8%)	3 (5.3%)	8 (14%)	0.261
T2WI hyperintensity	10 (17.5%)	16 (28.1%)	26 (45.6%)	0.788

4.3.3 Relationship between cervical spine MRI findings in DCM and duration of symptoms

All patients who presented with symptoms for 1 year or more than had multilevel cervical spinal cord compression. A statistically significant proportion of them (N=17 (29.8%), p= 0.0007) also had increased T2WI signal intensity within their cervical spinal cord. Duration of symptoms did not have any statistically significant association with presence of CCSS (p =0.697) (Table 4.5)

Table 4.5 Frequency table on relationship between cervical spine MRI findings and duration of symptoms in DCM

Patient Characteristics	< 1year (N=36)	≥1 years (N=21)	Total (N=57)	P-value
Multilevel cord compression	31(54.4%)	**21(36.8%)**	52(91.2%)	0.146
CCSS	6(10.5%)	2(3.5%)	8(14.0%)	0.697
T2WI hyperintensity	9(15.8%)	**17(29.8%)**	26(45.6%)	**0.0007**

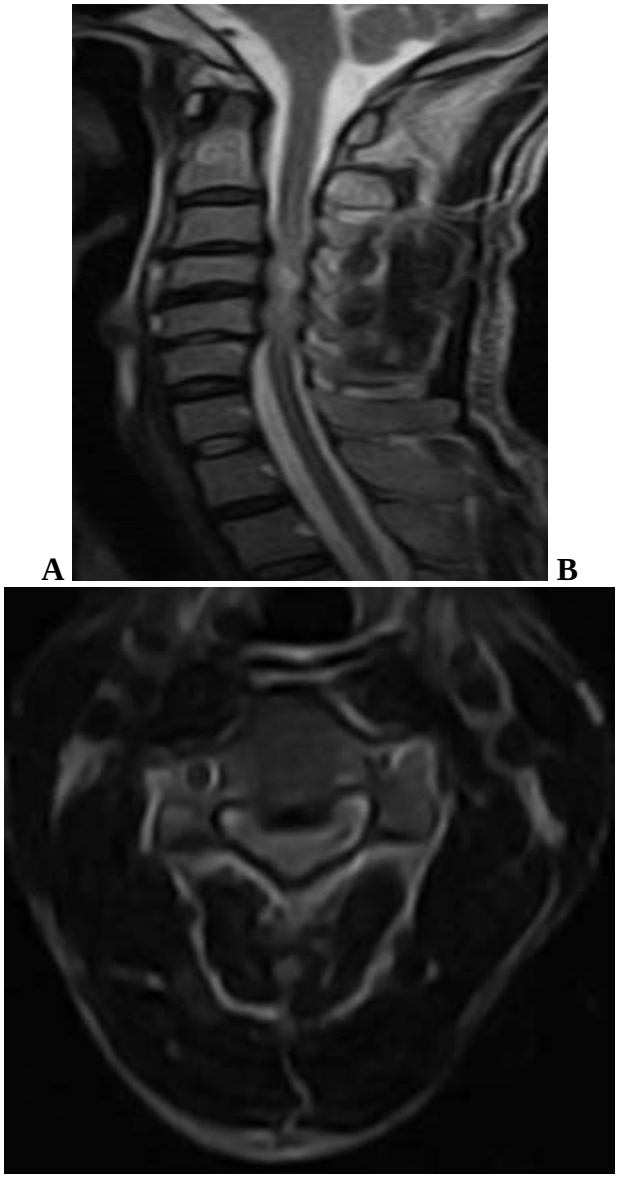


Figure 4.9: T2WI cervical spine MRI of a 59-year-old woman who presented with 1-year history of intermittent neck pain, upper limbs weakness, and numbness of both hands. A. The image on mid-sagittal plane revealed cervical spondylosis at C3/4, C4/5 and C5/6 causing effacement of the surrounding CSF in the subarachnoid space and varying degree of spinal cord compression. Maximum cord compression associated with increased spinal cord T2 signal intensity was observed at C4/5. B. On axial plane at the C4-5 level showed spinal cord deformity and flattening caused by a bulging disc and osteophytic spurring anteriorly associated with spinal cord T2 signal hyperintensity.

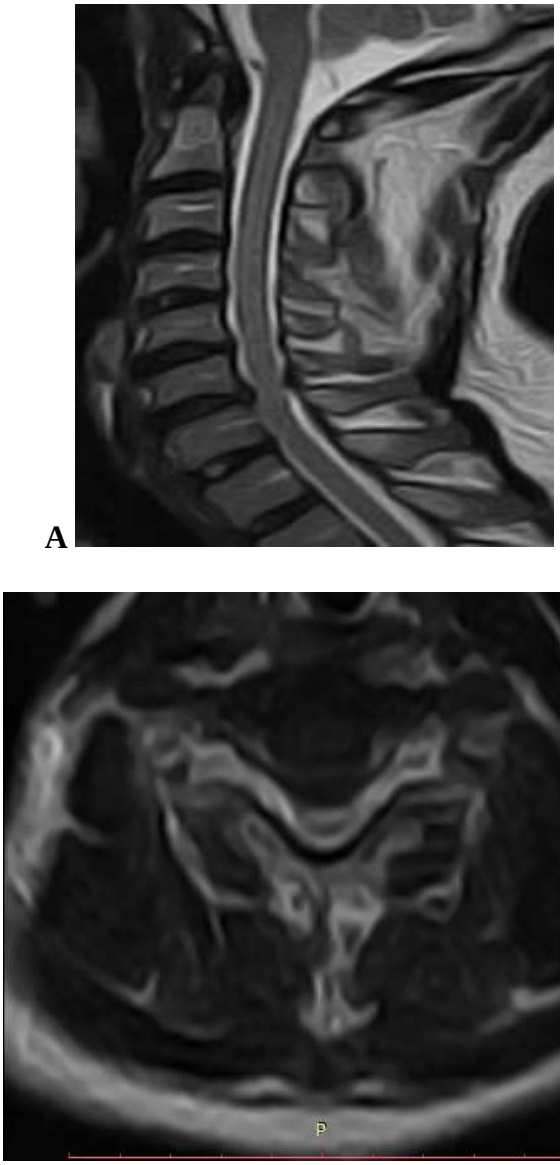


Figure 4.10: T2WI cervical spine MRI of a 49-year-old man who presented with 9-months history of numbness of the right upper limb and axial neck pain. A. Sagittal plane revealed multilevel intervertebral disc desiccation and maximum spinal cord compression at C6/7 caused by posterior disc bulge and LFH at C6/7. There was also subtle posterior disc bulges at C5/6 and C7/T1 and LFH at C5/6. B. Axial plane at C7/T1 level shows posterior disc bulge and LFH causing vertebral canal stenosis and cord compression.

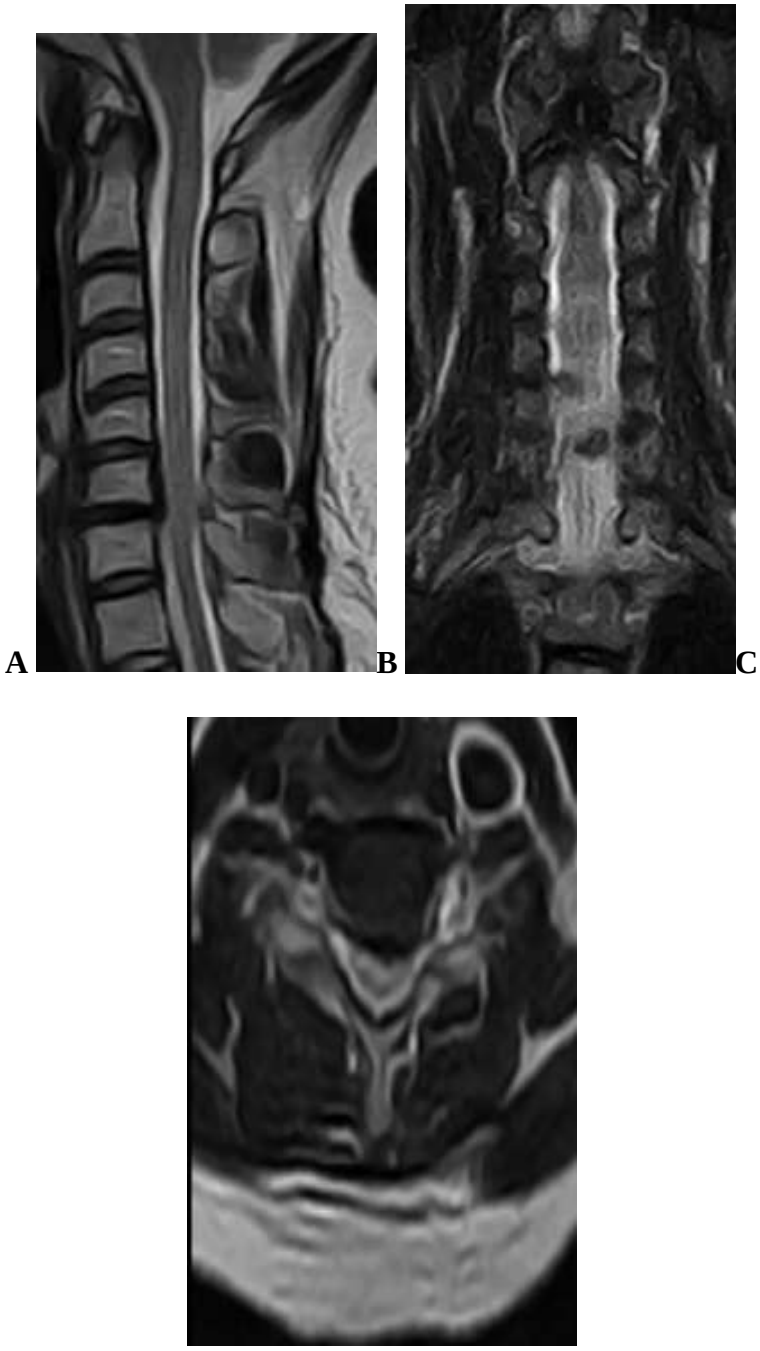


Figure 4.11: T2WI cervical spine MRI of a 48-year-old woman who presented with 6 months history of right upper limb weakness and numbness. A. On sagittal plane, PLH spanning between C5/6 – C6/7 interspaces and posterior disc bulge C5/6 and C6/7 causes cervical canal stenosis and cord compression. B. On coronal plane, reveals the posterior disc bulges compressing the cord on right lateral portion at C5/6 and centrally at C6/7. C. On axial T2WI at the C6 inferior endplate shows osteophytes causing central spinal cord deformity.

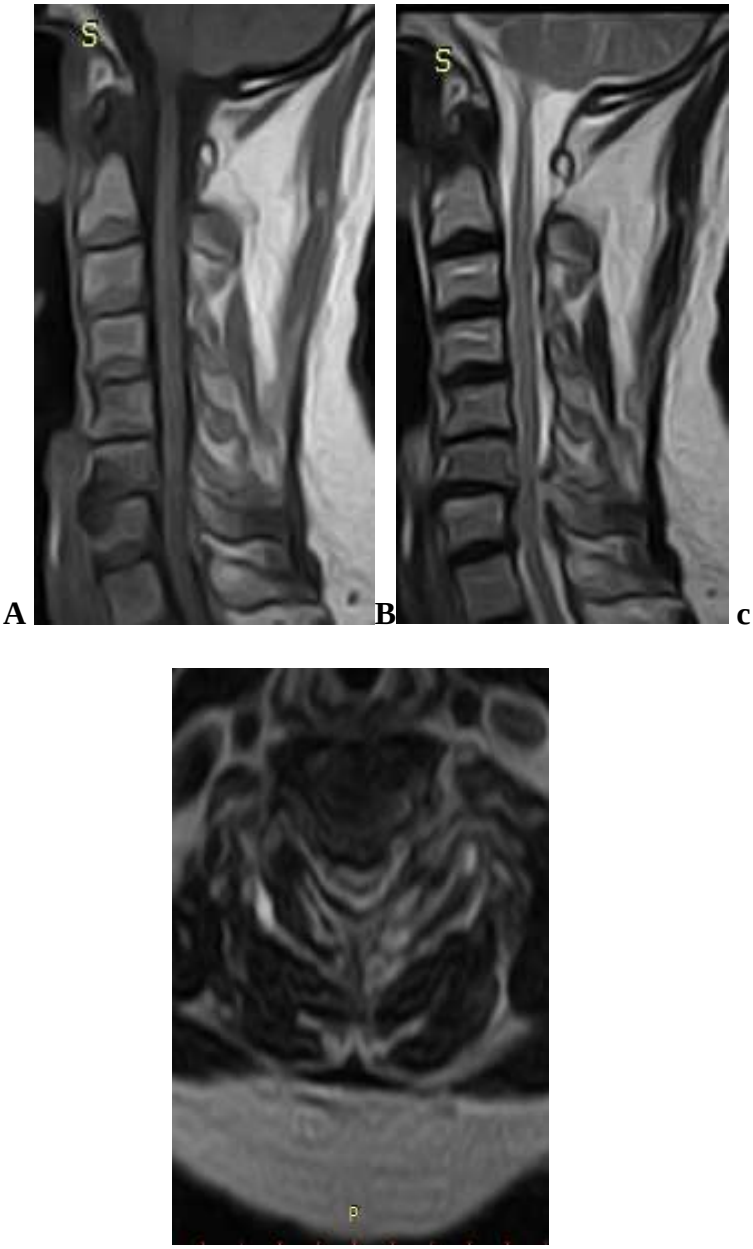


Figure 4.12: Cervical spine MRI of a 64-year-old woman presenting with on and off neck pain and progressive upper limbs weakness for 18 months. A. Sagittal T1WI reveals cervical spine hypolordosis, osteophytic burrs on C4, C5, C6 and C7 vertebral bodies, reduced height of C5/6 intervertebral disc and Modic I changes on C6 inferior endplate and C7 superior endplates. B. Sagittal T2WI reveals subtle posterior disc bulges at C3/4, C4/5, and C7T1 and osteodiscal complex causing cord compression at C6/7. C. Axial T2WI at the level C7 vertebral body, posterior osteophytes causes flattening of the spinal cord.

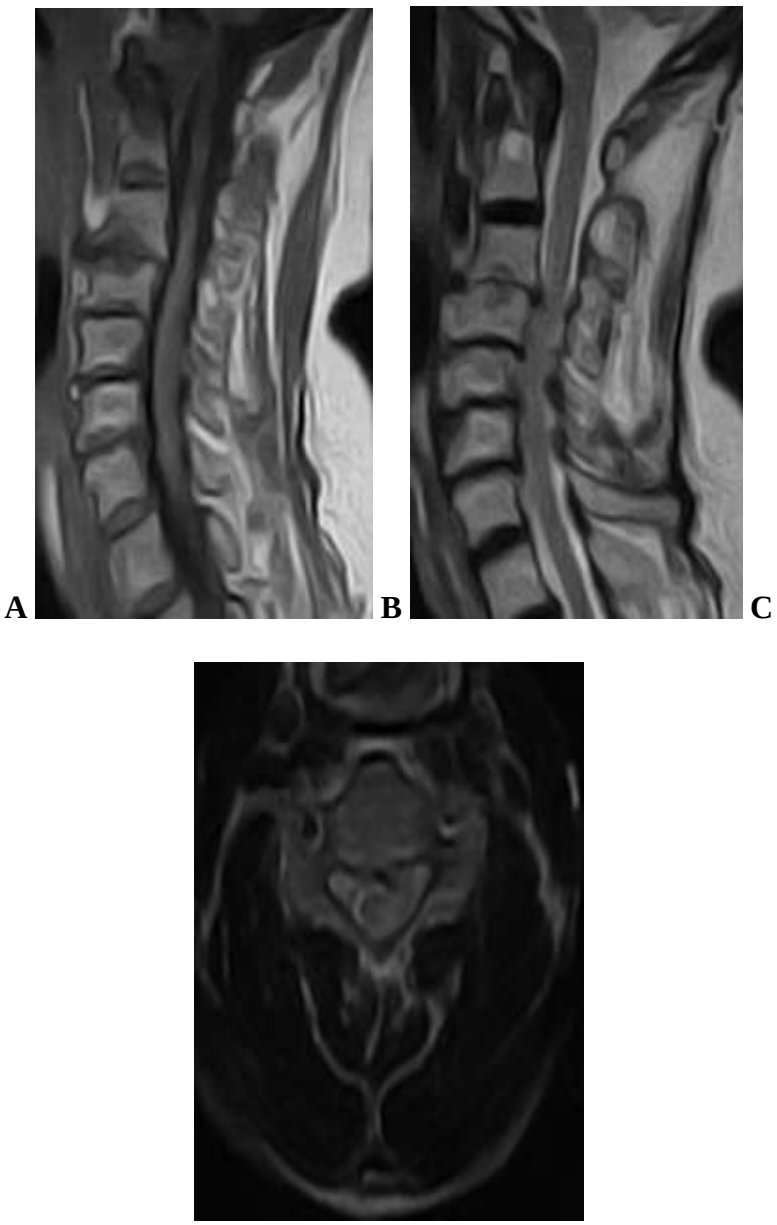


Figure 4.13: Cervical spine MRI of a 74-year-old man with a history of pain, upper limbs weakness, and numbness of both hands for 2 years. A. On T1WI sagittal plane multilevel osteophytes, C2 posterolisthesis relative to C3 and Modic III changes at C3 inferior and C4 superior endplates. B. T2WI sagittal image revealed multilevel intervertebral disc desiccation, reduced C3/4 disc height, LFH at C5, C6 and C7 level and spondylosis compressing the spinal cord at C3/4, C4/5, C5/7 and C6/7. C. Axial T2W1 at C7 inferior endplate revealed an osteophyte causing deformity of the cord associated with spinal cord hyperintensity.

CHAPTER FIVE: DISCUSSION

5.1 CLINICAL CHARACTERISTICS

5.1.1 Age

The participants in this study had an average of 51.7 years (range 30-87 years) and this was comparable to findings of an international multicenter study on DCM which recorded an average age of 56.4 (+/-11.8 years) globally while those from Asia Pacific (53.95 +/-12.20 years), Latin America (54.23 +/-10.65 years), Europe (57.44 +/-11.85 years) and North America (57.33 +/-11.77 years) (Fehlings et al., 2018). Similarly, Yue et al in their control study found that the patients with DCM had a mean age of 56.7 years which was significantly higher than that of subjects in the control group whose mean age was 43.3 years (Yue et al., 2001). This is in agreement with Takamiya et al, who found that advanced age was a significant risk factor for degenerative cervical spine disease since it an end product of progressive structural changes that result from wear and tear of body tissues over a long period of time (Takamiya et al., 2006).

Northover et al study reported a slightly higher mean age of patients with cervical myelopathy of 63.8 years (range 37–88) compared to our study probably because they only recruited preoperative patients who had already developed spinal canal stenosis of less than 13mm secondary to degenerative pathology (Northover et al., 2012). Our study involved all symptomatic patients with radiological features of DCM without any regard on the caliber of their vertebral foramen.

It was also noted that the average age of the female patients with DCM was 10 years less than that of their male counterparts (47.8 versus 57 years) in our study. This was comparable to findings from Northover et al study which upon analysis of 42 respondents with DCM found the average age of the female participants (57 years) to be less than that of the male (66.5 years) (Northover et al., 2012). Our study and the

Northover study had a common limitation which was a small sample size. On the contrary larger multicenter studies found that there was no difference between the mean age of female and male cases (Fehlings et al., 2018; Nouri, Tetreault, Côté, et al., 2015).

5.1.2 Gender

Slightly more than half of the participants in this study (58%) were female and the male to female ratio was 1:1.4. On the contrary, Nouri et al and Northover et al observed that men were more susceptible to developing DCM than their female counterparts with a male to female ratio of 3:2 and 2.7:1 respectively. Therefore, poor prognostic MRI features of DCM such as malalignment, multilevel cord compression and multilevel cord T2WI hyperintense foci were observed more in men than women (Nouri, Martin, Tetreault, et al., 2016) (Northover et al., 2012).

None of this studies involved Africa, hence differences in environmental and occupational predisposing factors of DCM. This was explained by fact that certain African cultural practices such as carrying domestic loads on the head is usually regarded as a female activity therefore development of cervical spine degenerative disease fall disproportionately on African women due to frequent increase in axial load on the cervical spine (Porter et al., 2013). In addition, osteoarthritis rates in body parts such as the knee, spine and hip have been found to be higher in women than men. Therefore female patients were more likely to develop osteoarthritis of cervical column which may subsequently lead to DCM (Cooper, Javaid, & Arden, 2014).

5.1.3 Clinical presentation

The average duration of the main neurological symptoms in our study was 10.5 months. An international multicenter study reported the average duration of DCM symptoms of patients from Latin America Asia-Pacific, Europe and North America was (37.96±30.92 months), (22.04±35.68 months), (24.89±32.48 months) and (26.55±42.92 months) respectively (Fehlings et al., 2018). Unlike our study, this retrospective study involved patients who had already undergone surgical intervention hence might have had significant neurological dysfunction and longer duration of symptoms. Since degenerative changes are usually progressive and cumulative over time (Mohanty et al., 2015).

5.2 Cervical Spine Magnetic Resonance Imaging in DCM

5.2.1 Spectrum of degenerative cervical spine pathology

Degenerative changes in the spine involve a host of specific pathology including hypertrophy or ossification of the posterior longitudinal ligament, disc herniation, bone spurs, ligamentum flavum hypertrophy, vertebral bone thickening, degenerative kyphosis and subluxation (Epstein, 2002). Cervical spine spondylosis is characterized by multilevel disc and vertebral bone degenerative changes (Martin et al., 2018).

The most commonly observed degenerative pathology in this study was cervical spondylosis 91.2% (n=52) followed by hypertrophy of the ligamentum flavum at 26.32% (n=15). Nouri et al reported similar findings, the prevalence of spondylosis from four continents involved in their multicenter study was (89.7%) while that of LFH was (56.8%). Spondylosis was the most common DCM pathology with a mean of 86.2% in Latin America, 93.5% in North America, 86.9% in Asia Pacific and 87.1% in Europe (Nouri, Martin, Tetreault, et al., 2016).

According to Yamaguchi et al study, spondylosis contributes to more than 90% of DCM pathology and is commonly seen in over 90% of individuals after the age of 40 years (Yamaguchi et al., 2017). Cervical spine spondylosis has been found to be the most common causes of DCM in all these studies probably because the degenerative process typically begin at the level of the intervertebral discs and vertebral body endplates hence they are almost always involved in degenerative process (Martin et al., 2018).

Majority of our study participants (43.9%) had three cervical spinal segments with concurrent degenerative pathology. Similarly, a multicenter study on MRI analysis of DCM found that three segments were commonly affected concurrently by degenerative changes (Nouri, Martin, Tetreault, et al., 2016). Another study on myelography and post-myelography computed tomography evaluation of cervical spine of elderly also reported that multi-segmental lesions with an average of three lesions contributed to the myelopathy (Belachew et al., 2007). Degenerative cervical myelopathy often presents with multiple degenerative changes causing varying degree of cord compression at different levels probably because the degenerative process affects different levels simultaneously (Eduwem, 2014) (Martin et al., 2018) (Nouri, Martin, Tetreault, et al., 2016).

5.2.2 Congenital cervical spinal canal stenosis

Majority of the participants had normal cervical spinal canal parameters. 14% of the respondents in this study had congenital cervical vertebral canal stenosis (SCOR ≥70).Nouri et al reported a global prevalence of 8.4%, Asia Pacific (11.6%), Latin America (9.8%), North America8.6%, and Europe 2.3%.(Nouri, Martin, Tetreault, et al., 2016). Another skeletal specimen based study carried in Cleveland in United States of America, indicated that cervical stenosis was present in 4.9% of the adult population

(M. J. Lee et al., 2007). Jenkins and colleagues studied 1000 cervical MRIs of patients with and without DCM reported overall prevalence of CCSS with 6.8% (Jenkins et al., 2016). The prevalence in our study was higher compared to this other studies carried out in other continents which did not include Africa. Therefore racial differences might explain variation of the prevalence of CCSS. Taitz study on South African cadavers found that the black race vertebral canal were generally narrower than those from the white cadavers (Taitz, 1999)

All participants in this study with CCSS also had spondylosis and T2WI cord hyperintensity. This is comparable to two other studies that revealed that narrow canal had significantly greater osteoarthritic changes (Yamaguchi et al., 2017) (L. Tetreault et al., 2015). Congenitally narrow cervical canal have increased segmental mobility which may in turn result in localized increased strain and shear forces to the spinal cord leading to axonal injury which may indicated by signal intensity changes (Morishita et al., 2009). Furthermore, an inborn narrow spinal canal has limited space available to accommodate the spinal cord hence it is more vulnerable to compression by less substantial degenerative pathology (Martin et al., 2018).

5.2.3 Cervical spinal cord compression

In this study, C5-C6 cervical spine level was also the most frequent site of maximum spinal cord compression (43.7%). Research studies done Northover et al and Nouri et al also reported similar findings with 39.7% and 48.8% of their participants having maximum cord compression at C5-C6 level respectively (Northover et al., 2012), (Nouri, Martin, Tetreault, et al., 2017)**.** This is was likely due to fact that C5/C6 level most flexion and extension movements hence it is more vulnerable than other levels to degenerative disease (Martin et al., 2018). Furthermore, the spinal canal is narrowest at C5/6 yet spinal cord anteroposterior diameter is widest at this level occupying three

quarter of the canal in the normal cervical spine. Therefore, the spinal cord at C5/6 is more prone to compression by age-related structural changes compared to other levels (Gore D.R et al., Robinson R.A et al.).

5.2.4 Increased cervical spinal cord signal intensity on T2WI

Intramedullary cervical spinal cord hyperintense foci observed on T2WI sagittal spin echo sequences provide clear evidence of the location of the spinal cord injury in patient with severe disease (Nouri, Martin, Tetreault, et al., 2017). This phenomenon tend to be observed more often in older patients and those with extensive spondylotic burden (Mohanty et al., 2015). In this study, 45.6% of the respondents had T2WI hyperintense spinal cord lesions. Multicenter studies carried out on preoperative patients with significant degenerative disease recorded higher prevalence of between 76.5% respectively (Fehlings et al., 2016; Nouri, Martin, Mikulis, et al., 2016). This was probably because unlike our study, they evaluated preoperative patients had with severe disease hence the higher propensity to more significant spinal cord injury indicated by foci of increased signal intensity on T2WI. Our study included all symptomatic patients regardless of the therapeutic modality therefore the lower prevalence T2WI hyperintensity could have been attributed to majority of the patients with mild disease. Moreover, the neurological dysfunction caused by neurogenic claudication or altered cord tension may not be associated with altered cord signal intensity (Nouri, Martin, Tetreault, et al., 2017).

The foci of increased signal on T2WI within the cervical spinal cord was most frequently (36.8%) observed at C5-C6. This was coincidentally also the level where maximum spinal cord compression was most frequent observed, hence the cord at this level was more vulnerable to injury compared to other levels (Martin et al., 2018).

Nouri et al and Smorgick et al recorded similar findings in their studies on degenerative cervical spine disease (Nouri, Martin, Tetreault, et al., 2017; Smorgick et al., 2015).

Assessment of the sagittal extension of the T2WI hyperintense spinal cord lesion is crucial in evaluation of DCM severity and prediction of post-therapeutic functional outcome (Nouri, Tetreault, Zamorano, et al., 2015). Our study showed that majority of the study participants (23%) with spinal cord T2WI hyperintensity involved a single level. This was attributed to increase in signal intensity on T2WI at the cervical spinal level of maximum cord compression due injury leading to edema, necrosis, myelomalacia, cavitation or spongiform changes (L. Tetreault et al., 2015).

Other studies that reported similar findings was a multicenter study on the spectrum of DCM pathologies found that (63.3%)of the participants had a single level affected (Nouri, Martin, Mikulis, et al., 2016). Another study on evaluation of MRI signal intensity and surgical outcome of patients with DCM also reported that 73% of all the participants had intramedullary T2WI hyperintensity at a single level (Nouri, Martin, Kato, et al., 2017)**.**

5.3 Relationship between cervical spine MRI findings in DCM and clinical variables.

5.3.1 Relationship between cervical spine MRI findings in DCM and age

Multilevel cervical spinal cord compression was observed in all patients with 60 years and above. This is probably due to the fact that degenerative structural changes are usually progressive and cumulative over time, hence involvement of multiple levels are likely to be observed more in older individuals (Martin et al., 2018).

Similar findings were reported by Mohanty et al where patients above sixty years presented with more extensive spondylotic burden than younger patients (Mohanty et

al., 2015). Furthermore, Yue et al in their control study also reported that patients with cervical spinal cord compression (mean age, 56.7 years) were significantly older than those in the control group (mean age, 43.3 years) (Yue et al., 2001). The number of levels with cord compression has also been found to be directly proportional to age (Northover et al., 2012).

In our study, there was no statistically significant difference in age with respect to presence of congenital cervical vertebral canal stenosis (p=0.672) among the fifty seven participants recruited. On the contrary, a multicenter study carried out in four continents by Nouri et al found that more DCM patients with inherent narrow spinal canal were found to be on average, 5.5 years younger than those with normal vertebral foramen (50.8 years vs 56.3 years, p=0.03) (Nouri et.al 2016). The difference in findings of this multicenter research study from ours may probably be attributed to our limited study population size.

According to Martin et al, degenerative cervical myelopathy tend develop early in life among patients with congenital spinal canal stenosis due to limited space available to accommodate the spinal cord hence it is more likely to be compressed by less substantial degenerative pathology (Martin et al., 2018). Furthermore, increased segmental mobility has been observed in patients with inherent narrow vertebral foramen hence tend to develop degenerative changes earlier in life (Morishita et al., 2009).

There was no statistically significant association between presence of T2WI hyperintensity and age (p=0.382) among in this study. Northover et al also reported similar findings in their retrospective study at Leicester General Hospital, United Kingdom which involved forty one patients with cervical myelopathy (Northover et al., 2012). On the contrary, presence of spinal cord on T2WI hyperintensity was found to

be directly proportional to increase in age. It was observed in 85% of DCM patients with 60 years and above in a multicentre study by Nouri et al (Nouri et.al 2016). The larger study population size in this multicenter research study, unlike the Northover et al and our study, would probably explain the differences in the variation in the findings with regard to the association between increased T2WI signal intensity changes and age. Furthermore, Kato et al also reported that chronic insult to the cord over a prolong period of time may result either in reversible damage such as edema or ischemia or irreversible changes including necrosis, myelomalacia, and cavitation leading T2WI spinal cord hyperintensity (Kato et al., 2012).

5.3.2 Relationship between cervical spine MRI findings in DCM and gender

There was no significant differences between gender with respect to multilevel cervical spinal cord compression (p=0.151). This contrasts with a multicenter study findings in which multi-level pathology were observed in men more than women (92.3% males versus 85.6% females, p=0.017) (Nouri, Martin, Tetreault, et al., 2016). The women were also found to have fewer levels with degenerative pathology compared to men (two versus three levels) (Northover et al., 2012). This differences in results might be attributed to the fact that the proportion of male participants in this multicenter study (M: F=3:2) was higher than our study (M: F=1:1.4)

In this study, there was also no significant differences between gender with respect to presence of congenital cervical vertebral canal stenosis (p=0.224) and presence of increased spinal cord T2WI signal intensity. (p=0.788). Comparable findings were recorded by Nouri et al where the prevalence of CCSS was not different between both gender (9.5% males versus 6.6% females, p=0.37) (Nouri, Martin, Tetreault, et al.,

2016). Lack of gender predilection of this developmental anomaly may explain the similarity in results both studies.

The findings of this study were in agreement with those of Northover et al study which evaluated 42 respondents, in that, there was no significant relationship established between presence of increased T2WI signal intensity changes and gender (Northover et al., 2012). Similarity to our study to the Northover et al study in the United Kingdom, was a small sample size. On the contrary, a multicenter research study involving a large study population drawn from four continents reported a lower frequency of T2WI hyperintensity of the cervical spinal cord among the female participants compared to their male counterparts (66.7% females versus 82.7% male participants, p= <0.001) in (Nouri, Martin, Tetreault, et al., 2016).

5.3.3 Relationship between cervical spine MRI findings in DCM and duration of symptoms

In this study, all patients with symptoms for more than one year had multilevel cervical spinal cord compression. This is may be due to the insidious and progressive natural course of DCM and the neurological deficits being cumulative over time (Mohanty et al., 2015). Bednarik et al and Tetreault et al reported contrasting results which revealed that there was no relationship established between duration of symptoms and number of levels with cervical cord compression (Bednarik et al., 2008) (L. Tetreault et al., 2015).

Duration of symptoms in this study did not have any significant association with presence of congenital cervical canal stenosis (p = 0.751). This was comparable to another study that found that the duration of symptoms was not significant different in between DCM patients with CCSS and those normal cervical vertebral canal (28.65 ± 34.12 months versus 29.68 ± 37.61months, p=0.85) (Nouri, Tetreault, et al., 2017).

DCM often presents with subtle, intermittent and subjective symptoms that varies from one individual to another (Lebl et al., 2011).

Finally, a statistically significant association was recorded in this study between presence of T2WI cord hyperintensity and neurological symptoms of one year and above (81%, p= 0.0007). This is probably because T2WI spinal cord hyperintensity is attributed to chronic insult to the cord which typically occur over a prolong period of time (Kato, et al., 2012).This findings were in agreement with those reported by Nouri et al where they found that patients with spinal cord T2 hyperintensity had relatively longer duration of myelopathy symptoms (24.7months) compared to those without (17 months). (Nouri, Tetreault, Singh, et al., 2015). Similarly, Bednarik et al. also reported that prolonged neurological symptoms were associated with presence of cervical cord T2WI hyperintensity (p=0.347) (Bednarik et al., 2008). According to Tetreault et al however, there was no relationship between duration of the symptoms and the presence of T2 hyperintensity. Moreover, MRI features associated with severe disease were observed in asymptomatic individuals (Tetreault et al., 2015).

5.4 Study Limitations

- Selection bias could be due to the fact this was a hospital based study hence only symptomatic patients referred for MRI of the cervical spine at MTRH were recruited. Therefore, the prevalence reported in this study would not be representative of the general population.
- Recall bias could have occurred when patients were asked to state the duration of their symptoms. DCM often has a subtle onset and may have prolong intermittent course hence the exact time when the symptoms commenced may not well established.

CHAPTER SIX: CONCLUSION AND RECOMMENDATION

6.1 Conclusion

There several conclusions deduced from this study. The results on clinical characteristics of patients with DCM who underwent MRI at MTRH revealed that the female participants with DCM pathology were slightly more and were on average ten years younger than their male counterparts.

The cervical spine MRI findings of these patients showed that spondylosis was the most common DCM pathology and C5-C6 was the most frequently level where maximum cord compression and T2WI cord hyperintensity was observed. In addition, all respondents with congenital cervical spinal canal stenosis had a foci of increased signal intensity within their cervical spinal cord on T2WI.

Finally, on determination of relationships between the cervical spine MRI findings and the clinical characteristics of patients with DCM, a statistically significant association was established between presence of T2WI cord hyperintensity and neurological symptoms lasting for one year and above.

6.2 Recommendation

1. Multi-center study to further elucidate the gender differences with regard to the prevalence and presentation of DCM pathology in Africa.
2. High index of suspicion of spondylosis and C5-C6 cervical spine level involvement in patients suspected to have degenerative cervical myelopathy.
3. Assessment of the caliber of the cervical vertebral canal in patients with degenerative pathology particularly those with T2WI hyperintense foci within their cervical spinal cord.
4. Early diagnosis and treatment of symptomatic patients with degenerative cervical myelopathy.

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APPENDICES

Appendix I: Consent Form

A. ENGLISH:

My name is Dr. Cheruiyot Dorothy. I am a qualified medical doctor, registered by the Kenya

Medical Practitioners and Dentists Board. I am currently pursuing a Master degree in Radiology and Imaging at Moi University. I would like to recruit you into my research whose aim is to establish MRI findings of patients diagnosed with degenerative cervical myelopathy.

The information you give will be kept confidential and in line with that your name or any other of personal identification will not be entered anywhere. You have a right not to participate in the study if you so wish and you will still receive health care services that you are seeking without prejudice or discrimination. Your participation in this study is on voluntary basis and it will not predispose you to any added risk. We will keep a copy of your results confidential and give you the original copies of the results along with their explanations.

This study has been approved by the Institutional Research and Ethics Committee (IREC) of Moi University/ Moi Teaching and Referral Hospital. In case you need further clarifications please contact IREC using the address below.

The Chairman IREC,
Moi Teaching and Referral Hospital,
PO Box 3,
Eldoret.
Tel: 33471/2/3

Should you choose to participate in this study, kindly sign below

Sign: …….

Name: …….

Date: …….

B. KISWAHILI:

Jina langu ni Daktari Cheruiyot Dorothy. Mimi ni daktari aliyefuzu nakusajiliwa na bodi ya madaktari ya Kenya (Kenya Medical Practitioners and Dentists Board). Mimi ni msomi wa shahada ya juu (Masters) ya udaktari ya Radiology and Imaging katika chuo kikuu cha Moi. Ningependa kukusajili kwa huu utafiti wa kuangalia aina za shida zinazohusu uti wa mgongo kwenye shingo zinazoonyeashwa kwa picha ya MRI.

Tutayaweka matokeo yako kwa njia ya kuheshimu haki yako ya kutojulisha mtu yeyote.

Tutakujulisha kuhusu matokeo yako kinaga ubaga. Iwapo utachagua ama usichague kushiriki katika uchunguzi huu bado utaendele kupokea matibabu yanayokufaa. Maelezo yote yatakayotolewa yatakuwa ni siri na jina yako haitaandikwa mahali popote. Una haki ya kutoshiriki katika utafiti kama hivyo ndivyo unavyotaka.Una uhuru wa kuuliza maswali yoyote. Uchunguzi huu umehidhinishwa na kamati ya kusimamia machunguzi ya wasomi na haki ya wanaochunguzwa (Institutional Research and Ethics Committee-IREC) katika chuo kikuu cha Moi na hospitali kuu ya Moi Teaching and Referral. Iwapo unahitaji maelezo zaidi tafadhali wasiliana na IREC kwa kutumia anwani ifuatayo.

Mwenyekiti IREC,

Moi Teaching and Referral Hospital,

S. L. P. 3,

Eldoret.

Simu: 33471/2/3

Kama unakubali kushiriki katika utafiti huu, tafadhali weka sahihi yako hapa.

Sahihi: …….…….

Jina: ….…….…….……

Tarehe: ……..…….

Appendix II: Questionnaire

DATE OF DATA COLLECTION ……**REF NO**…….

Please answer all questions in the spaces provided. Tick the most appropriate answer in the box provided. It is crucial that all questions have a response. Do not write your name or any other of personal identification in this form

SECTION A:

1. DEMOGRAPHIC DATA

1.1 Gender Female ☐ Male ☐

1.2 Date of Birth. ……

2. CLINICAL PROFILE

1.1. Which of the following symptoms do you experience?

☐ Upper limb numbness ☐ Upper limb weakness

☐ Lower limb weakness ☐ Weakness of all limbs

☐ Difficult with micturition Others……

1.2. When did you first experience the symptom(s) stated above?

……....

SECTION B: MRI FINDINGS (For official use only)

1. State the level of cervical spinal cord compression on T2WI caused by the following degenerative pathology.

    1.1 Spondylosis

C2-C3 ☐ C3-C4 ☐ C4-C5 ☐ C5-C6 ☐ C6-C7 ☐ C7-TI ☐

    1.2 Ligamentum flavum hypertrophy

C2-C3 ☐ C3-C4 ☐ C4-C5 ☐ C5-C6 ☐ C6-C7 ☐ C7-TI ☐

    1.3 Posterior longitudinal ligament hypertrophy

C2-C3 ☐ C3-C4 ☐ C4-C5 ☐ C5-C6 ☐ C6-C7 ☐ C7-TI ☐

    1.4 Spondylolisthesis

C2-C3 ☐ C3-C4 ☐ C4-C5 ☐ C5-C6 ☐ C6-C7 ☐ C7-TI ☐

2. State the level of the cervical spine with maximum spinal cord compression on mid-sagittal T2WI.

C2-C3 ☐ C3-C4 ☐ C4-C5 ☐ C5-C6 ☐ C6-C7 ☐ C7-TI ☐

3. State the levels of the cervical spinal cord with T2WI hyperintensity.

C2-C3 ☐ C3-C4 ☐ C4-C5 ☐ C5-C6 ☐ C6-C7 ☐ C7-TI ☐

4. State the cervical spine Spinal Cord Occupation Ratio (SCOR) which is the midsagittal mean spinal cord diameter as a proportion of the midsagittal mean vertebral canal diameter on T2WI sagittal plane, above and below the sites with degenerative pathology, at the midpoint of C3 and C7 vertebral bodies ……%

Appendix III: Moi Teaching and Referral Hospital Cervical Spine Magnetic Resonance Imaging Protocol

Magnetic resonance imaging of the cervical spine was performed using 0.36 tesla Magsence 360 machine (Mindray, China) at the MTRH MRI department. The patient lied supine on the MRI couch and cushions were used to immobilize the head within the head and neck coil. Other cushions was placed under the legs for extra comfort. Laser beam localizer was centered over the mid-neck, 2.5cm below the chin in chin-down position. Using the cervical spine phased array coil, sagittal and axial T1-weighted turbo spin echo (repetition time/echo time of 400-600/15-25ms) and T2-weighted turbo spin echo (repetition time/echo time of 3,000-4000/100-120ms) images were acquired. A slice thickness of 4.5mm, a field of view between 260-280mm and a matrix of 256 by 256 were used.

A 3-plane T1weighted low resolution scan localizer was used for planning. Sagittal slices was planned on coronal plane using the position block placed parallel to the spinal cord and the field of view capturing the whole cervical spine from the level of the pons to 4^{th} thoracic vertebra and both lateral borders of the transverse processes. Axial images were planned on sagittal plane with position block perpendicular to the spinal cord and parallel to the intervertebral discs on coronal plane with a field of view that covered the whole spine from C2 to T1. Saturation band was placed in front of the spine prevent motion artifacts from the neck. The soft copy images were printed onto laser film hard copies and stored directly as DICOM (Digital Imaging and Communications in Medicine) files in the workstation and in CD-ROMs.

Appendix IV: Time Frame

TIME PERIOD	ACTIVITY	DURATION
October 2015- December 2015	Development of Research Topic and submission to the department graduate studies committee	2months
January2016 – May 2016	Writing of the proposal	4 months
May 2016 – June 2016	Supervisors correction of the proposal	2 months
July 2016	Submission of proposal to IREC	1 month
July 2016 – December 2016	Testing and correction of data collecting tools Recruiting and training of research assistant	6 months
January 2017 – December 2017	Data collection and data cleaning	12 months
January 2018	Data entry and data analysis	1 month
February -July 2018	Writing of draft report and submission of draft to Supervisors & Correction	6 months
August 2018	Writing Final Report and submission	1 month

Appendix V: Budget

ITEM	**QUANTITY**	**UNIT PRICE(KSHS)**	**TOTAL (KSHS)**
Laptop	1	50,000	50,000
Printing, Photocopying and Binding	-	35,000	35,000
Stationery	-	15,000	15,000
Storage devices e.g. flash disc and CD-ROM	200 CD- ROMS 4 flash disks	30 3000	6000 12000
Internet services	32 months	3000 per month	96000
Publication	-	60000	60000
Biostatistician Consultation	-	25000	25000
Research assistant training and stipend	2 assistants for 12months	4000 per month	96000
Contingencies (10%)			39500
TOTAL			**434, 500**

Appendix VI: IREC Approval

INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOITEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471//2/3

MOIUNIVERSITY
SCHOOL OF MEDICINE
P.O. BOX 4606
ELDORET
Tel: 33471/2/3

27th September, 2018

Reference IREC/2016/120
Approval Number: 0001691

Dr. Dorothy Cheruiyot,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
27 SEP 2018
APPROVED
P. O. Box 4606-30100 ELDORET

Dear Dr. Cheruiyot,

RE: APPROVAL OF AMENDMENT

The Institutional Research and Ethics Committee has reviewed the amendment made to your proposal titled:-

"Magnetic Resonance Imaging Findings in Relation to Clinical Characteristics among Patients with Degenerative Cervical Myelopathy at Moi Teaching and Referral Hospital".

We note that you are seeking to make amendments as follows:-

1. To change the title to above from "***Magnetic Resonance Imaging Findings in Patients with Degenerative Cervical Myelopathy at Moi Teaching and Referral Hospital in Eldoret, Kenya***".
2. To change of study broad objective to "Determine the cervical spine MRI findings of patients with DCM in relation to their clinical characteristics at Moi Teaching and Referral Hospital, Eldoret, Kenya.

The amendments have been approved on 27th September, 2018 according to SOP's of IREC. You are therefore permitted to continue with your research.

You are required to submit progress(s) regularly as dictated by your proposal. Furthermore, you must notify the Committee of any proposal change(s) or amendment(s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. The Committee expects to receive a final report at the end of the study.

Sincerely,

DR. S. NYABERA
DEPUTY-CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc: CEO - MTRH Dean - SPH Dean - SOM
Principal - CHS Dean - SOD Dean - SON

INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471/2/3

MOI UNIVERSITY
SCHOOL OF MEDICINE
P.O. BOX 4606
ELDORET
Tel: 33471/2/3

Reference: IREC/2016/120

16th October, 2017

Approval Number: 0001691

Dr. Dorothy Cherulyot,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
16 OCT 2017
APPROVED
P. O. Box 4606 - 30100 ELDORET

Dear Dr. Cherulyot,

RE: APPROVAL OF AMENDMENT

The Institutional Research and Ethics Committee has reviewed the amendment made to your proposal titled:-

"Degenerative Cervical Myelopathy: Magnetic Resonance Imaging Findings and Its Clinical Correlations at Moi Teaching and Referral Hospital, Eldoret, Kenya".

We note that you are seeking to make an amendment to your title as follows:-

1. ***Magnetic Resonance Imaging Findings in Symptomatic Patients with Degenerative Cervical Myelopathy at Moi Teaching and Referral Hospital in Eldoret.***

The amendment has been approved on 16th October, 2017 according to SOP's of IREC. You are therefore permitted to continue with your research.

You are required to submit progress(s) regularly as dictated by your proposal. Furthermore, you must notify the Committee of any proposal change(s) or amendment(s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. The Committee expects to receive a final report at the end of the study.

Sincerely,

DR. S. NYABERA
DEPUTY-CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc: CEO - MTRH Dean - SPH Dean - SOM
Principal - CHS Dean - SOD Dean - SON

INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471/2/3

MOI UNIVERSITY
SCHOOL OF MEDICINE
P.O. BOX 4606
ELDORET
Tel: 33471/2/3

Reference IREC/2016/120
Approval Number: 0001691

3rd October, 2017

Dr. Dorothy Cheruiyot,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
03 OCT 2017
APPROVED
P. O. Box 4606 - 30100 ELDORET

Dear Dr. Cheruiyot,

RE: APPROVAL OF AMENDMENT

The Institutional Research and Ethics Committee has reviewed the amendment made to your proposal titled:-

"Magnetic Resonance Imaging Findings in Patients with Degenerative Cervical Myelopathy at Moi Teaching and Referral Hospital in Eldoret, Kenya".

We note that you are seeking to make amendments as follows:-

1. To change the title to above from "***Cervical Spondylotic Myelopathy: Magnetic Resonance Imaging Findings and Its Clinical Correlations at Moi Teaching and Referral Hospital, Eldoret".***
2. To change study period from September 2016 – September 2017 to January 2017 – January 2018.

The amendments have been approved on 3rd October, 2017 according to SOP's of IREC. You are therefore permitted to continue with your research.

You are required to submit progress(s) regularly as dictated by your proposal. Furthermore, you must notify the Committee of any proposal change(s) or amendment(s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. The Committee expects to receive a final report at the end of the study.

Sincerely,

DR. S. NYABERA
DEPUTY-CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc: CEO - MTRH Dean - SPH Dean - SOM
Principal - CHS Dean - SOD Dean - SON

INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471/2/3

MOI UNIVERSITY
SCHOOL OF MEDICINE
P.O. BOX 4606
ELDORET

Reference: IREC/2016/120
Approval Number: 0001691

28th July, 2016

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
28 JUL 2016
APPROVED
P. O. Box 4606-30100 ELDORET

Dr. Dorothy Cheruiyot,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

Dear Dr. Cheruiyot,

RE: FORMAL APPROVAL

The Institutional Research and Ethics Committee has reviewed your research proposal titled:-

"Degenerative Cervical Myelopathy: Magnetic Resonance Imaging Findings and Its Clinical Correlations at Moi Teaching and Referral Hospital, Eldoret, Kenya".

Your proposal has been granted a Formal Approval Number: ***FAN: IREC 1691*** on 28th July, 2016. You are therefore permitted to begin your investigations.

Note that this approval is for 1 year; it will thus expire on 27th July, 2017. If it is necessary to continue with this research beyond the expiry date, a request for continuation should be made in writing to IREC Secretariat two months prior to the expiry date.

You are required to submit progress report(s) regularly as dictated by your proposal. Furthermore, you must notify the Committee of any proposal change (s) or amendment (s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. The Committee expects to receive a final report at the end of the study.

Sincerely,

PROF. E. WERE
CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc CEO - MTRH Dean - SOP Dean - SOM
Principal - CHS Dean - SON Dean - SOD