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Evaluation of Cost-Effective Diagnostic Method for Cervical Radiculopathy Based On Aberrant Outcome Measures, Biomarkers, and Upper Extremities: A Randomized Sample Study

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Abstract
Objective: *To develop a cost-effective diagnostic method for cervical radiculopathy (CR) by evaluating the impact of functional instabilities in theoutcome measures, biomarkers, and upper-extremities.*
Methods*: Separate analyses for each participant suffering with CR for 4.74±1.82yrs (experimental group; n=117; 51.84±7.15yrs) and without CR (control group; n=117; 52.86±7.52yrs) were performed in relation with theaberrant outcome measures (Upper extremity functional index,Numeric pain rating scale, Patient-specific functional scale, Neck disability index, and Body mass index); biomarkers (C-reactive protein, Creatine kinase-muscle, and Aldolase-A); and upper-extremities (angles of cervical flexion, extension, and rotation; bilateral angles of shoulder flexion, extension,abduction; and diameters of forearm 8cm below the acromion-clavicular).*
Results*: The mean± standard deviations of the studiedoutcome measures:10.70±6.13pts, 1.00±0.86mm, 80.80±8.04%, 1.74±0.47pts, and32.51±1.46kg/m^{2}respectively; biomarkers:7.05±3.59mg/L, 238.57±86.43U/L, and 8.75±3.17U/L respectively; and upper-anatomical features:65.12±5.94^0, 58.02±4.27^0, (67.02±8.09^0 right, 67.80±7.47^0 left), (127.78±7.70^0 right, 128.84±6.20^0 left), (29.92±8.48^0 right, 30.64±7.01^0 left), (124.70±8.08^0 right, 125.54±7.69^0 left), and (29.35±2.88cm right, 29.13±2.01cm left) respectively for the experimental subjects were significantly worse than those in the controls (p<0.0001).*
Conclusion*: Resultssuggestedmonitoring the aberrant parameters of outcome measures, biomarkers, and upper-extremities may be an economical diagnostic method for CR.Further research recommends for the alternative treatment for CR with this diagnostic protocol.*
Key words: *Cervical Radiculopathy; Diagnosis protocol; Cost-effective; Biomarkers; Outcome measures.*

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I. Introduction

Parkinson was first used the term cervical radiculopathy (CR) or radiculitis in1817 [1].

Thereafter, it was acknowledged by several researchers in early twentieth century [1-2].CR is a chronic pathologic feature characterised by intervertebral disc protrusion or chronic spondylosis resulting in spinal cord compression, nerve roots irritation or inflammation associated with acute pain, numbness and/or weakness, loss of sensation, or tingling and loss of coordination in the upper extremity and leads to impaired quality of life [1-5].The commonly effected nerve root is C_7at C_6- C_7 level followed by C_6 and /or C_8 roots at C_5-C_6 and C_7-T_1 levels respectively [2-5].The normal risk factors associated with CR include old age, poor posture, obesity, abnormal inflammation, damage of muscles and tendons, postmenopausal women, vigorous unplanned body building practice, traumatic injury, smoking habits, certain occupational hazards, and inactive older [1,6-7].It is slightly predominant in men than women with the age groups of 20-70 years [1,8].

The primary diagnostic protocol for CR are physical tests [4, 8-11],in the clinic based on information received from the patients through history taking and physical examination which is then confirmed by way of diagnostic imaging or supported by surgical findings [8,11];provocation tests [12-16]; X-rays; Magnetic Resonance Imaging (MRI); Computerized Tomography (CT) scan; Electromyography (EMG); and Nerve Conduction Velocity (NCV) [17-20]. Researchers have emphasized, beside the ambiguous concept of CR [6-7],the diagnostic precision evaluated by using physical test, provocation tests and diagnostic imaging is equivocal, and the incidence, pervasiveness, and epidemiologic data are also inadequate for CR [1, 7,21-24].Regardless of little advantages of scanning the damaged conditions of bony pathology, the exorbitant costly

radiologic and electro-physiologic studies such as X-rays, or MRI, or CT scan, having some unavoidable limitations [25-27], may be unaffordable by common people. However, the North American spine surgeons' clinical guidelines for the diagnosis and treatment of CR has recommended the diagnostic imaging is required only for the patients who need interventional or surgical treatment [4,7].

Therefore, in the present study an alternative diagnostic protocol for CR is proposed with affordable minimum cost and significant duration, even at the early stage of CR, based on variabilities in: (1) clinical outcome measures including impaired quality of life, (2) biochemically assessed the status of inflammation, muscle degeneration, and skeletal muscle damage, and (3) upper anatomical features include muscle stiffness, wasting, atrophy, and restricted movements of joints in contradiction to the mysterious costly conventional diagnostic technique through the studies of physical tests , provocation tests, and diagnostic images [7, 11-12].

The main common phenomena in CR [28] is the pain parameters as well as psychometric quality of life. These are suggested to be well-thought-out as per international approved clinical pain-related outcome measures such as Upper Extremity Functional Index (UEFI) [29], Numeric Pain Rating Scale (NPRS) [30]based on visual analogue scale, Patient-Specific Functional Scale (PSFS) [31], and Neck Disability Index (NDI) [32-34] along with obesity which is the another major causing factor of pain and disability as assessed by Body Mass Index (BMI) [35]. In pursuance of identify the second most common features in CR namely, inflammation, connective tissue damage, skeletal muscle damage, and nerve functions have proposed to be appraised the biochemical parameters such as serum C-reactive protein (CRP) [36], Creatine kinase-muscle (CK-MM) [37], and Aldolase-A (AldoA) [38-39].Finally, the measurements of deranged upper-anatomical parameters have also recommended in connection with muscle stiffness, wasting and atrophy (bulging) and range of motion of various joints such as angles of cervical flexion (ACF), extension (ACE), and rotation (ACR); bilateral angles of shoulder flexion (ASF), extension (ASE), and abduction (ASA), and bilateral diameters of muscles of forearm 8cm below the acromion-clavicular (DBA) that usually damaged during CR. Remarkably all the parameters may be identified with reasonable cost and minimum time even at the early stage of CR when no malformations in the bones or muscles are identified in the previous diagnostic images.

The objective of the study was to elucidate the diagnostic protocol for CR by evaluating the abnormal levels of outcome measures including obesity, biomarkers, and upper-anatomical features, even at early progressive stage for developing, to our knowledge, an alternative best cost-effective diagnostic tool for detecting CR than previous studies. Up till now nobody has yet attempted by evaluating these parameters to diagnose for CR with most affordable minimum cost and time.

The present study has portent the novelty concepts for the diagnosis with CR, into the categories of the international approved outcome measures, the specific biochemical markers, and relevant neuro-muscular-upper-anatomical features.

II. Materials And Methods

Study design and subjects:

From eight centres of OPTM Health Care (P) Ltd, India, 354 cohorts, aged 20-70 years old, were recruited in the study between January 2018 to November 2018; based on the sign and symptoms of pain evaluated under outcome measures and aberrations in the upper anatomical features.

The study protocol was evaluated and approved by the OPTM Research Institute Ethics Committee. An Institutional Review Board-approved consent form for the physical examinations, blood sample collections and radiological images required for the study was signed by all participants.

After evaluating the exclusion criteria of 120 cohorts as mentioned in the previous studies [25-26], 117 (72 females and 45 males) of the remaining 234 subjects with significant pain syndromes, discomfort, imbalanced quality of life, impaired neck and upper-limb functions due to inflammation, muscle wasting, weakness and degeneration in the cervical and shoulders regions as evidenced by the elevated levels of biomarkers (CRP, CK-MM and AldoA), and radiological images (CT-scan or X-ray or MRI) were considered as experimental cohorts and termed as 'subjects with CR'. The remaining 117 (61.54% females) subjects with no complaints of pain or visual inflammation or no signs of CR as evidenced by the analyses of studied biochemical markers and radiological images were considered as healthy control subjects and termed as 'subjects without CR'. Each cohort completed a questionnaire, providing details regarding demographics, medical history, nutritional status, ethnic barriers and work status at the baseline and summarized in Table 1.

Evaluation of pain and paresthetic symptoms:

The characteristics of symptomatic pain and paresthetic on neck, arm, scapular, shoulder, chest, headache, angina, and across the dermatomal pattern were evaluated for experimental subjects.

Evaluation of international-approved outcome measures including Body mass index (BMI):

Observation of the patient's perceived symptoms of pain intensity and functional activities with psychometric properties namely personal care, lifting, reading, headache, concentration, work, driving, sleeping and recreation in the last 24 hours were evaluated separately for each cohort of experimental and control groups under the following approved protocols as per international acclaimed outcome measures such as UEFI [29], NPRS [30], PSFS [31], and NDI [32-34]. Seven activities such as lifting, writing, dressing up/ washing up, concentrating, sleeping and recreation are considered while measuring the outcome under PSFS [31].The assessment of Body Mass Index (BMI) [35] has been calculated individually for both the groups as per previous study [26].

Evaluation of specific biochemical parameters in blood:

A 5-ml blood sample was collected from each subject of experimental and control groups. Blood samples were then centrifuged at 1000×g for 10 min at 4^{o} C to obtain serum. The serums were used to analyse the biomarkers such as C-reactive protein (CRP), Creatine kinase-muscle (CK-MM), and Aldolase-A (AldoA) for each subject of both the groups separately. All the biomarkers are measured and tested according to the methods and protocols elaborated in detail in the previous studies [39].

Evaluation of Pearson's correlation of all the biomarkers between experimental and control cohorts:

To determine the predictive values for each biochemical marker (CRP, CK-MM and AldoA) in patients with CR, the Pearson's correlation coefficients of were evaluated between experimental and control subjects along with their respective p-values.

Evaluation of anatomical parameters:

Physical examinations were evaluated for each subject of both the groups including upper anatomical measurements such as ACF, ACE, ACR, ASF, ASE, ASA, and DBA.

Cervical Range of Motion (CROM) device40was used to measure ACF, ACE and ACR. ASF, ASE and ASA were measured using goniometer in accordance with the American Academy of Orthopedic Surgeons (AAOS) [41].The measurements of DBA were performed using special meter tape.

Evaluation of cervical joints radiographic assessment under KL grading scales:

Lateral radiographs of the cervical spine were obtained for all the cohorts of both the groups. Radiographs were classified and scored for cervical degenerative intervertebral levels from C_4-C_7 and osteoarthritic changes in cervical region using Kellgren-Lawrance (KL) grading scales developed by Kellgren and Lawrence [42].

External study reviewers:

All results and data of experimental and control groups separately were evaluated by an external reviewing panel, not in contract with the registry subjects.

Data collection and Statistical analysis:

Data were summarized using descriptive statistics for continuous variables (e.g., mean, standard deviation, number of patients), frequency tables, for discrete variables, and 95% confidence intervals (CIs).The mean values, standard deviations (SDs), their 95% confidence intervals (CIs), and their p-values for all the outcome measures, biochemical, and upper anatomical parameters, were evaluated for overall and separately by gender for both the groups. Statistical analyses were done by using software (Graph Pad Prism, Version,5.0) with repeated measures for student-t test to determine significant values at $p<0.05$ level along with r (Pearson's correlation coefficient) values to determine strong and weak correlation among two variables for measuring different improvement parameters of combined-sex, female and male patients separately. An alpha level of 5% was established i.e., a p-value less than 0.05 was considered statistically significant.

III. Results

Enrolment and baseline characteristics of patients:

Two-hundred and thirty-four subjects were included in the analysis divided into equal numbers of cohorts with and without CR, fully described in Tables 1. The characteristics features of upper extremity pain symptoms with CR elaborated in Table 2.

International-approved pain related outcome measures and BMI:

Figure 1 showed the location of pain, sensory and weakness in association with compression of nerve roots during CR. The mean ± SD values of all pain related outcome measures under UEFI, NPRS, PSFS, and NDI and the increased obesity confirmed by BMI for combined-sex of experimental group were all significantly increased ($p<0.0001$), when compared with the subjects of control group (Table 3).

Table 1: Demographic data and baseline characteristics of subjects

Characteristics	Experimental group	Control group
No of subjects	117	117
Females	72 (61.54 %)	72 (61.54 %)
Age (yrs), [mean (SD)]	51.84 (7.15)	52.86 (7.52)
Height (in m), [mean (SD)]	1.53 (0.71)	1.49 (0.78)
Weight (in kg.), [mean (SD)]	74.23 (4.17)	60.42 (4.78)
BMI (kg/m²) [mean (SD)]	31.72 (3.31)	27.22 (3.38)
Period of suffering (yrs), [mean (SD)]	4.74 (1.82)	-
Indian ethnic group (%)		
Bengali	36 (30.76)	33 (28.20)
Gujrati	11 (9.40)	13 (11.11)
Marwaree	10 (8.55)	12(10.26)
Marathi	12 (10.26)	11 (9.40)
Tamil	12 (10.26)	13 (11.11)
Punjabi	13 (11.11)	12 (10.26)
Shindhi	12 (10.26)	13 (11.11)
North East India	11 (9.40)	10 (8.55)
Food habit (%)		
Vegetarian	85(72.65)	72 (61.54)
Non - vegetarian	32 (27.35)	45 (38.46)
Other habits (%)		
Drinking excessive tea and coffee	44 (37.61)	42 (35.90)
Smoking	30 (25.64)	31 (26.50)
Drinking Alcohol	28 (23.93)	27 (23.08)
Chewing tobacco	10 (8.55)	9(7.69)
Work status (%)		
Employed fulltime	51(43.59)	48 (41.03)
Employed part time	11 (9.40)	10 (8.55)
Housewife / Homemaker	12 (10.26)	17(14.52)
Retired	19 (16.24)	21 (17.95)
Self employed	24 (20.51)	21(17.95)
Multiple complaints (%)		
Constipation	68 (58.12)	21 (17.95)
Acidity & reflux	72 (61.54)	17 (14.53)
Insomnia	78 (66.67)	12 (10.26)
Varicose vein	39 (33.33)	15 (12.82)
Urinary incontinence	58 (49.57)	17 (14.53)
Morning stiffness (<30 minute)	27 (23.08)	-
Measures taken to diminish pain (%)		
Using a collar belt	54 (46.15)	-
Using a sick	12 (10.26)	-
Using wheel chair	14 (11.97)	-

Table 2: Baseline characteristics of pain symptoms of experimental patients

Characteristics of pain	No. of patient	Percentage
Neck pain:	114	97.43
Arm pain:	91	77.78
Scapular pain:	72	61.54
Pain or paraesthesia in a dermatomal pattern:	65	55.56
Pain or paraesthesia in a diffuse or non-dermatomal pattern	50	42.73
Anterior chest pain:	21	17.95
Headache:	12	10.26
Cervical angina	2	1.71
No pain or paraesthesia	1	0.85

Table 3: Mean and standard deviation of outcome measures of experimental and control subjects

Outcome Measures	Control Group	Experimental Group	Elevated levels of biomarkers			
	Mean (SD)	Mean (SD)	MD	95% CI of difference		p-value
				Lower	Upper	
UEFI (pts)	79.60 (4.32)	10.70 (6.13)	-68.9	-71.01	-66.79	<0.0001
NPRS (pts)	8.85 (1.04)	1.00 (0.86)	-7.85	-8.23	-7.47	<0.0001
NDI (%)	12.45 (3.31)	80.80 (8.04)	68.35	65.91	70.79	<0.0001
PSFS (pts)	9.64 (0.24)	1.74 (0.47)	-7.90	-8.05	-7.75	<0.0001
BMI (kg/m^2)	27.51 (1.67)	32.51 (1.46)	5.00	4.38	5.62	<0.0001

SD= Standard deviation, MD= Mean Difference

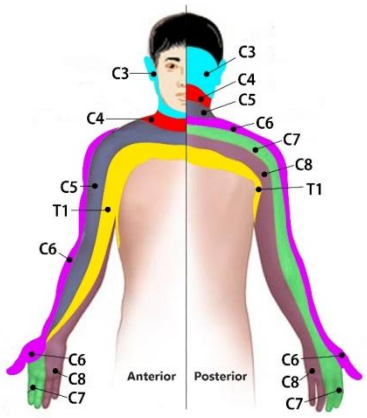


Figure 1: Cervical dermatomes with the directions of sensory symptoms of neurogenic pain

Biochemicals parameters:

All the biochemical parameters such as CRP, CK-MM and AldoA of experimental subjects were increased significantly ($p<0.0001$) compared to the control subjects (Figures 2A-2C). Moreover, the predictive values of correlation coefficients between the elevated levels of CRP and AldoA representing to inflammation and skeletal muscles damage in patients with CR were highly significant ($p<0.0001$), but the values of correlation coefficients between the elevated levels of CRP and CK-MM and between CK-MM and AldoA were not significant when compared with the subjects without CR (Table 4).

Anatomical parameters:

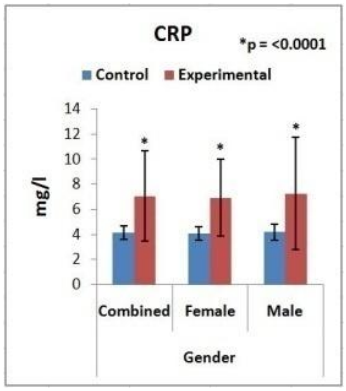
The mean ± SDs of all the abnormal upper-anatomical features were highly significant ($p<0.0001$), whereas, the measurements of bilateral diameter of arms were not highly significant ($p<0.05$), when compared to the control cohorts. The angular movements of neck and shoulders, and diameter of arms were observed to be all asymmetrical for both the sides of the neck with CR, when compared to the symmetrical control cohorts without CR (Table 5).

Analysis of radiological images of cervical spine as assessed by K-L grading scale:

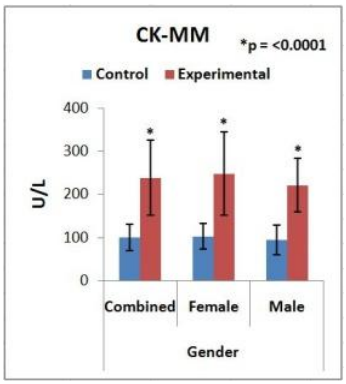
All the lateral views of cervical spine X-ray reports of 117 patients with CR exhibited definite anterior osteophyte formation, narrowing of disc space (> 25- 75%) and sclerosis of the endplates with irregularities. The percentages of deterioration of grades under the KL grading scale for cervical intervertebral disc degeneration were more in grade 4 (Table 6). X-ray image of such a patient suffering with CR depicted in Figure 3.

Table 4: Statistical analysis of correlation coefficient and their p- values in relation to biochemical parameters between control group and experimental group

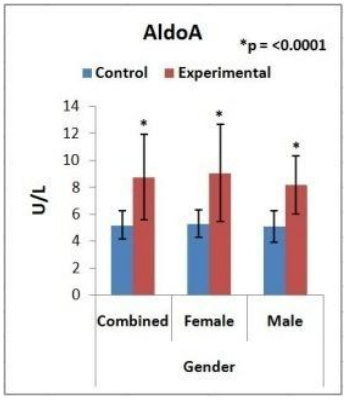
Control group	Correlation Coefficient and their p-values	Experimental group		
		CRP	CK-MM	Aldo A
CRP	Correlation Coefficient (r)	0.365	0.065	-0.399
	p-value	0.001	0.655	0.001
CK-MM	Correlation Coefficient (r)	0.017	0.182	-0.006
	p-value	0.908	0.207	0.965
AldoA	Correlation Coefficient (r)	-0.206	0.231	0.447
	p-value	0.857	0.107	0.001



2A: Comparative Mean & SD values of CRP Levels of Experimental & Control subjects



2B: Comparative Mean & SD values of CK-MM Levels of Experimental & Control subjects



2C: Comparative Mean & SD values of AldoA Levels of Experimental & Control subjects

The risk factors for CR:

The parameters of the risk factors in CR were shown in the algorithm (Figures 4A-4C).

IV. Discussion

In the present study, it was suggested a cost-effective diagnostic protocol for CR can be developed by assessing the abnormal international acclaimed clinical outcome measures, elevated levels of biomarkers such as CRP, CK-MM and AldoA, and aberrant upper-anatomical features along with radiological images assessed by KL grading in comparison with the controversial costly conventional diagnostic method for CR with physical tests, provocation tests, X-ray or MRI or CT scan, or EGM especially in developing countries like India [4, 11-24]. From the past, the main diagnostic tool for detecting CR is based on patient's history with physical tests, provocation tests, costly diagnostic imaging such as MRI or X-ray or CT scan or EGM [4, 11-24].

The interpretation of the diagnosis for cervical radiculopathy during physical examination depend upon the several factors such as the setting the primary or secondary care of examination, the characteristic features of the study population and the comparative standard test references namely neuro-physiological testing, radiological imaging or surgical outcomes. According to review reports of the several researchers, despite the various diagnoses are performed for cervical radiculopathy based on information from the patient's history, physical examination including kyphosis, scoliosis, loss of lordosis, and neurological tests such as key muscle strength, tendon reflexes, and sensory impairments, and diagnostic imaging, but the assessment of their diagnostic accuracy for CR is obscure [8,12,17-24].

According to Rubinstein et al.[12], provocative tests including: Spurling test; Shoulder abduction test; Traction/neck distraction (axial manual distraction test);Valsalva maneuver; and Upper limb tension showed high specificity and low to moderate sensitivity. But several researchers have negatively reported the reliability and accuracy of these provocative tests [10,12-14].

Although, MRI is the gold standard for evaluating the relationship of disc material to soft tissue and neural structures. But the main issue in the management of patients with cervical disc disease and nerve root compression is correlation of imaging findings with clinical presentation and symptomatology to guide treatment and intervention. Moreover, the researchers have already highlighted that the various nerve roots compression during CR cannot be diagnosed with the help of MRI [25-27]. Therefore, the causing factors of compressed nerve roots such as inflammation, pain, numbness or weakness identified in the upper extremities along with deranged anatomical features which are developed simultaneously during CR cannot be diagnosed with the help of MRI. In addition to that MRI has certain critical limitations such as metal objects implanted in the body viz. pacemakers, prosthetic joints, rods and certain tattoos and restricted to overweight, very tall and claustrophobic patients and at the same time diagnosis of CR through Discogram or Myelogram cannot emphasize either muscle weakness and numbness nor inflammatory status [25-27].

Again, in case of X-ray, CR can be identified only in advance stage for assessing the condition of bones at musculoskeletal joints of cervical vertebrae by using lateral radiographs of the cervical spine by four graded scale developed by Kellgren and Lawrence [42], but definite status of inflammation, muscle degeneration and skeletal muscle damage affecting damage of intervertebral disc along with pain symptoms cannot be identified from X-ray images

Rubinstein et al.[12] has clearly suggested that there is need for an economical, accurate and non-invasive diagnostic protocol for patients with CR instead of confirmed expensive advanced diagnostic imaging such as MRI, or EMG, or CT-myelograph and intrusive or painful nerve conduction test. At the same time, Tong HC et al. [43] has strongly emphasized on the inherent restrictions of clinical and radiological diagnoses,

and electrophysiological testing for CR. Moreover, no published clear guidelines are available from professional bodies for the appraisal and management of CR [6,7].

Table 5: Mean and standard deviation of upper-anatomical parameters of experimental and control subjects

Anatomical parameter		Control Group	Experimental Group	Elevated levels of Anatomical Parameters			
		Mean (SD)	Mean (SD)	MD	95% CI of difference		p-value
					Lower	Upper	
ACF (degree)		87.02 (2.20)	65.12 (5.94)	21.90	20.12	23.68	<0.0001
ACE (degree)		66.80 (2.29)	58.02 (4.27)	8.78	7.42	10.14	<0.0001
ACR (degree)	Right	87.34 (2.12)	67.02 (8.09)	20.32	17.97	22.67	<0.0001
	Left	87.34 (2.12)	67.80 (7.47)	19.54	17.36	21.72	<0.0001
ASF (degree)	Right	175.28 (3.35)	127.78 (7.70)	47.50	45.14	49.86	<0.0001
	Left	175.28 (3.35)	128.84 (6.20)	46.44	44.46	48.42	<0.0001
ASE (degree)	Right	57.38 (7.15)	29.92 (8.48)	27.46	24.35	30.57	<0.0001
	Left	57.38 (7.15)	30.64 (7.01)	26.74	23.93	29.55	<0.0001
ASA (degree)	Right	146.62 (2.18)	124.70 (8.08)	21.92	19.57	24.27	<0.0001
	Left	146.62 (2.18)	125.54 (7.69)	21.08	18.84	23.32	<0.0001
DBA (cm)	Right	27.84 (2.84)	29.35 (2.88)	-1.51	-2.64	-0.37	0.0097
	Left	27.84 (2.84)	29.13 (2.01)	-1.29	-2.27	-0.31	0.010

Table 6: KL grading scale for disc degenerative

	Experimental Group		Control Group	
	No of Patient	Percentage	No of Patient	Percentage
Grade 1:	None	None	109	93.16
Grade 2:	None	None	8	6.84
Grade 3:	50	42.74	-	-
Grade 4:	67	57.26	-	-

Furthermore, Onks and Billy [44] described that neck pain, shoulder pain, arm pain or chest pain or paraesthesia are the common features in CR. Table 2 shows number of patients suffering with neck pain is most predominate than the other areas of upper extremity and cervical angina is the least during CR. However, Pain and psychometric disabilities along with obesity are the major factors for any musculoskeletal diseases. Therefore, different indices of pain, functional disabilities, psychometric factors and obesity are also suitable diagnostic tools, which found increasing phenomenon in the present study for the experimental group compared to controls. According to several researchers, different indices such as UEFI [29], NPRS [30], PSFS [31], and NDI [34], as well as obesity (BMI) [35] have been well-established in joint disorders along with psychometric disorders. Moreover, Young IA et al. [34] has indicated, for the pain and psychometric disorders the evaluations of NDI and NPRS are more reliable than PSFS in patients with CR. But in the present study, contradict the statement as UEFS (93.70%) and NPRS (87.99%) are more reliable than PSFS (82.00%) and NDI (77.90%) along with BMI (18.44%). Therefore, these outcome measures can be considered as one of the suitable parameters to diagnose for CR (Table 3).

Again, radicular pain, a part of the cervical radiculopathy, occurs due to inflammation without evident of compressions[3]. But there is no protocol followed in the present conservative diagnostic system to identify the biochemical status for inflammation in case of CR. The serum CRP levels have documented as a potential marker for inflammation [36]. Although, there is another non-specific inflammation marker is Erythrocyte Sedimentation Rate (ESR), the rate at which red blood cells sediment is measured in a period of an hour for some specific diseases [39]. The author had already discussed the causing factors of high ESR in the previous study [39]. Figure 2Ashows CRP increases 71.95% in case of experimental cohorts compared to control subjects. Therefore, the level of CRP can be considered as an inflammatory marker to diagnose CR. Again, all the bones and their joints are connected with muscles through tendons. Thus, the primary cause of joints pain is the damage of connective muscles along with inflammation resulting which there is restricted movement of the joints with stiffness and decreased range of motion. The author had already been discussed elaborately that the levels of CRP, CK-MM and AldoA are suitable biomarkers for detecting risk factors for lumber herniated disc, muscular dystrophy during osteoarthritic disorders, and osteoarthritic disorders [25-27,39].The common phenomena of CR are skeletal muscles damage, connective tissue damage or polymyositis. Figures 2B & 2Cindicate 175.87% of CK-MM and 67.95% AldoA increased in the experimental subjects over controls during CR. For these reasons, serum levels of CK-MM and AldoA have also considered as biomarkers to diagnose CR.

Previous studies have utilized an individual research approaches for different diseases[36-38]but no one have studied in combined effects of the serum levels of these markers in CR. Figures 2A- 2C clearly indicate the elevated levels of these biomarkers during the progression of CR. Table 3 shows the predictive risk factors through the analysis of correlation coefficients of CRP, CK-MM and AldoA between control and experimental cohorts, wherein the relation between the status of inflammation and damage of skeletal muscles is firmly established during CR.

Furthermore, the researchers have emphasised that there is no consensus on the specific protocol followed for measuring the range of motion during CR [7,40].But noticeable abnormalities are observed in the muscle strength, movement of joints, muscle morphology during physical examination for CR. Moreover, the functionality of the cervical spine is based on the complex interplay of different motion segments and muscular activities. The ability of shoulders and neck to move in a normal range depends on the health of muscles, ligaments, bones and individual joints. The results from the deranged upper-anatomical parameters indicate that there are substantial increasing or decreasing phenomena of the group of muscles connected with various joints and both the parameters for right and left sides of the neck were asymmetrical in respect of the measurements of ACF, ACE, ACA, ASF, ASE, ASA, and DBA of the experimental cohorts with CR whereas all the parameters are symmetrical so far as the subjects without CR are concerned, which indicate the muscular wasting, muscle weakness, joint effusions and degeneration that were occurred during CR (Table5). Moreover, in the present study women are more predominate than men which contradict the earlier study [9]. It may be the reason for small sample size, more research is required to confirm the same.

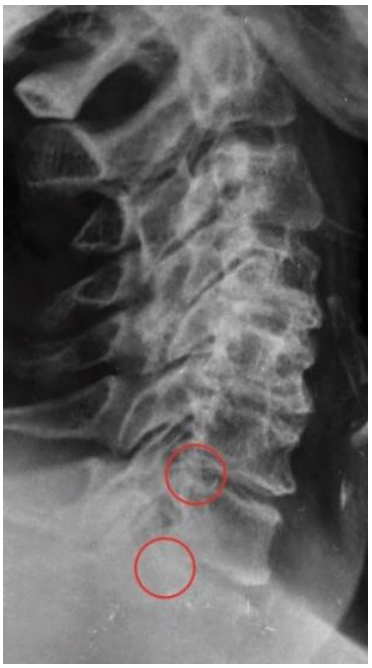


Figure 3: Lateral radiological feature of a patient having Cervical Radiculopathy

In the present study, the algorithm of diagnosis for CR (Figures 4A-4C) indicates the clear view of risk factors in detecting CR in most affordable low cost in early stage of CR where there is no pain syndrome or discomfort, or deformities observed in the upper extremities much before focusing in the radiological images

Therefore, the present study has found triangular approach such as anomalous pain, functional disabilities and obesity indices with dermatomes in a combined form, elevated levels of biochemical parameters, and upper- anatomy of musculoskeletal features with radiography (KL grading scale) can be confirmed as an affordable low-cost diagnostic tool for CR, not yet been identified till date.

However, there are some limitations in our study protocol that have to be considered. The patients suffering from rheumatic diseases; osteochondritis diseases; congenital dysplasia; joint symptoms caused by malignant tumours; dermatomyositis and polymyositis diseases; Ischemic bone necrosis; bone and joint infectious diseases; chronic skin and infectious diseases; parallel multiple drug dependence for concomitant diseases or risk conditions requiring drug treatment including psychiatric diseases etc.; a history of cancer, including carcinomatosis and granulocytic leukaemia; a history of severe neurological diseases including Parkinson; a history of chronic liver, kidney and heart diseases are restricted to participate in the present study.

V. Conclusion

From the results and discussion, it is firmly concluded that careful analyses of the risk factors of the international acclaimed functional disability outcome measures (UEFI, NPRS, PSFS, NDI and BMI), biomarkers namely CRP, CK-MM and AldoA, and upper limbs anatomical parameters such as ACF,ACE,ACR,ASF,ASE, ASA, and DBA along with confirming with cervical spine radiographic images as assessed by the KL grading scale may be the effective diagnostic protocol for detecting CR at minimum cost and time. Further researches recommend for cost-effective alternative treatment with the help of these diagnostic protocol.

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Conflicts of interest

The author declares that there are no conflicts of interest regarding the present study.

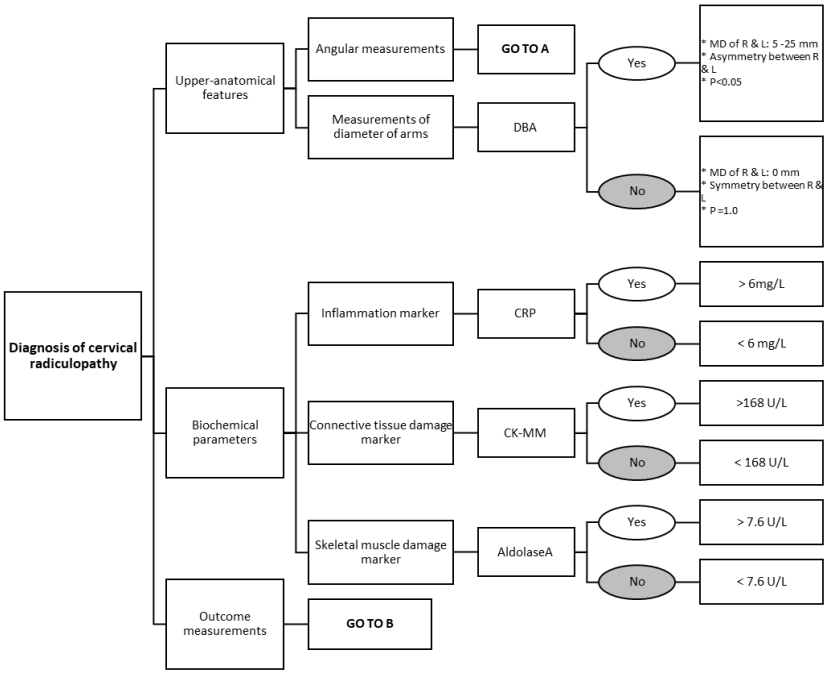
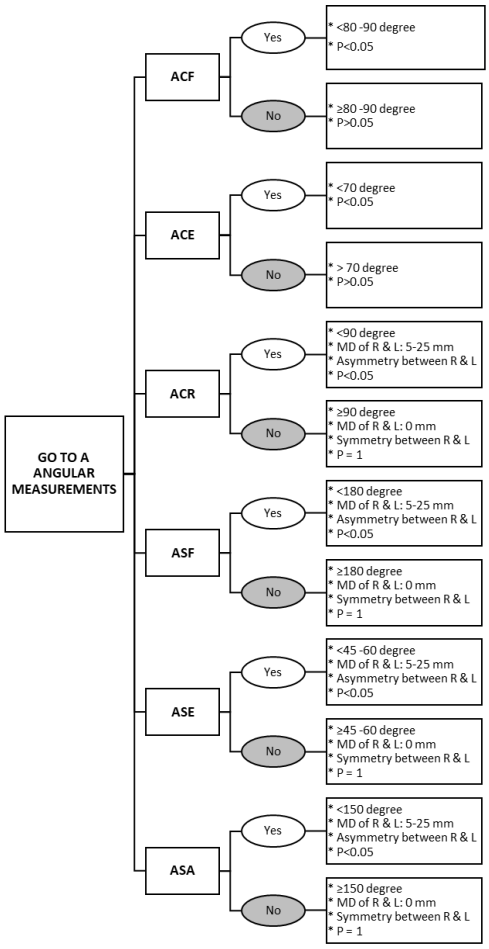
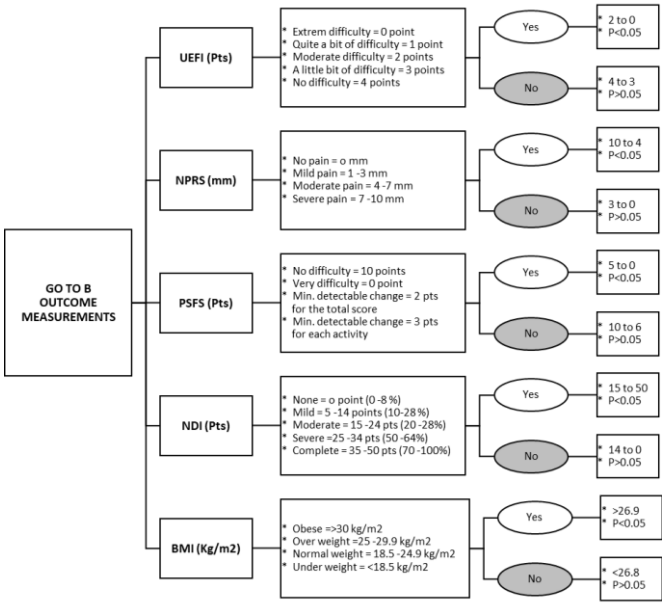


Figure 4A: Algorithm for diagnosis of cervical radiculopathy



***p = significant value, MD = minimum difference, R & L = right and left sides**

Figure 4B: Algorithm of upper angular measurements, a part of diagnosis of cervical



***p = significant value**

Figure 4C: Algorithm of outcome measures, a part of diagnosis of cervical

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