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Evidence-Based Tropical phytotherapeutic Treatment Protocol For Lumbar slipped Disc: An Approach With Biochemical, Anatomical, Functional Disability and Radiological parameters

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Abstract
Introduction: *Lumber slipped disc (LSD) attributes to a problem with an intervertebral disc of the lumber spine, whereby a gel-like material (nucleus-pulposus) inside the disc that protrudes through a crack in the outer-wall (annulus-fibrosus) of the disc and compressed a nearby nerve root causes inflammation, pain, numbness or weakness in the leg that lead to abnormal quality of life. The aim of the study is to normalize the LSD with the aberrant levels of Interleukin-10 (IL-10), Tumor necrosis factor-alpha (TNF-α), Creatine kinase-muscle (CK-MM) and AldolaseA (AldoA)along with anomalous anatomical and international acclaimed functional disability parameters and radiological images by topical phytotherapeutic treatment protocol within six-week.*
Methods*: Baseline data were collected and evaluated from 108 patients, aged 58.60±9.94 years, suffering with LSD for 4.68±2.22years. Serum IL-10, TNF-α, CK-MM and AldoA levels were measured for all the patients at the baseline and post-treatment using appropriate kits. All patients underwent standardized physical, radiographic examinations, and completed a questionnaire.*
Results: *The abnormal levels of above-mentioned biomarkers during LSD were recorded as their mean±SD values, 16.06±1.98pg/ml, 12.54±0.95pg/ml,106.89±30.06U/L, and 5.28±1.13U/L respectively at post-treatment and all were highly significant($p<0.0001$). The improvements on deranged anatomical features, international-approved functional disability parameters and reduction of over-weight under VAS, KPS, LEFS, ODI, and BMI were all highly significant($p<0.0001$) and radiological images under KL scale at post-treatment when compared to the baseline.*
Conclusions: *It is firmly concluded that LSD resulted in the anomalous levels of above-mentioned biomarkers along with the aforesaid aberrant parameters can be successfully normalized by topical phytotherapeutic treatment protocol within six-week.*
Key word: *Lumber slipped disc; Lumber herniated disc; Phytotherapy for prolapsed disc; Alternative treatment for lumber slipped disc; Lumber slipped disc without surgery*

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I. Introduction

Lumber slipped disc (LSD) or lumber herniated disc (LHD) is painful and debilitating lumbar disc disorder caused by wear and tear of the disc known as disc degeneration [1-4]. It can occur at any age, but most common for men between the ages 20 to 50 years[5]. The formation of LSD can be well explained as under: there are spaces between the bones or vertebrae of the spine maintained by a round spongy cartilage called intervertebral disc (IVD). Each IVD is made up of two components such as annulus fibrosus and nucleus pulposus. The annulus fibrosus is the tough outer portion of the disc and nucleus pulposus is the inner jell material so rounded by the annulus fibrosus. These discs act much like shock-absorbers towards the spinal columns to cushion the bones as the body moves. During aging, the vertebral discs loose some of the fluid that helps them maintain flexibility. LSD is characterized as a condition whereby jelly-like soft material, the nucleus pulposus, slips out through a crack in the tough outer wall, the annulus fibrosus, and put pressure on the nerves and irritate nerves by the chemical so released from the soft jelly causes pain, numbness, weakness in the leg and leads to aberrant quality of life [3-4,6].

The common symptoms of LSD are numbness and tingling, weakness in the muscles and pain in the spine radiating to the arms and legs. When the pain causes in the regions of buttocks, thighs, calves, and feet due to the LSD, it is referred to as sciatica because the pain travels along the path of the sciatic nerve which is the longest nerve in the body that runs from the back of the pelvis, through buttocks, down both legs to the feet. In acute case, LSD can cause permanent weakness around the inner thighs, the backs of the legs, and rectum, paralysis, loss of bowel and bladder control and sexual dysfunction [7].

The researchers have studied the various risk factors influenced the LSD which include: inherited a predisposition; overweight; occupational hazards such as involvement of repetitive lifting, pushing, pulling, bending or twisting; unsafe lifting technique of heavy items like apply force from the legs not the back; sedentary lifestyle with wrong posture; smoking and drinking habits which lead to reduce the oxygen supply to the discs that grinding-down of the tissues; heavy exercises; long continuous driving or riding on bumpy roads in a vehicle damages both the discs and spinal structure[8-9].

The primary diagnosis of LSD by physical examination with the observation of symptoms such as reflexes, identification of tender regions in the back, muscle strength, range of motion, walking ability, and sensitivity to touch. After the physical examination in order to confirm the LSD various diagnostic methods are adopted such as X-ray to rule out the compression between the vertebrae, formation of osteophytes, etc; Magnetic Resonance Imaging (MRI) or Computer Tomography (CT) images that can pinpoint the location of the disk and the affected nerves; a Discogram that can be pinpoint the cracks in the individual disc; and finally Myelogram to check the herniated disc exerting any pressure on the spinal cord and nerves[10-14].

The present study attempted for the first time, to identify that biochemical markers viz. IL-10, TNF-α, CK-MM and Aldo A are the risk factors for LSD. The elevated level of TNF-α have been considered as a pro-inflammatory marker to identify quantum of inflammation around the vertebral regions [15-16] while the level of serum IL-10 is an anti- inflammatory marker to detect inflammation during the prevention of disks or muscles damage [17-18]. The level of serum CK-MM is a biochemical marker to detect connective tissue damage [19] and elevated level of serum AldoA have been considered a biomarker to identify the skeletal muscle damage and inflammatory muscle diseases [20]. Moreover, all the tests can be done easily with minimum cost. However, a combined approach using all these biomarkers to detect risk factors for LSD has not so far been attempted.

At present the treatment of LSD include medication, physical therapies and finally surgery. Various types of medications are used to treat LSDs such as some kinds of non-steroidal anti-inflammatory drugs (NSAIDs) like gabapentin, pregabalin and amitriptyline for relieving nerve pain; a drug with a combination of oxycodone and acetaminophen called narcotics which has side effects include, nausea, sedation, confusion, and constipation; cortisone injections for reducing inflammation and pain; to minimize pain and swelling in and around the spinal nerve roots, epidural injections are commonly used; and muscle relaxants to reduce muscle spasms but has side effects such as dizziness and sedation [21].A number of physical therapies are used to minimize herniated disc pain such as hot and cold fomentation treatment; ultrasound to stimulate the affected area for improving blood flow; traction in order to alleviate pressure on the affected nerve; use of lumbar support; electric impulses to improve blood circulation thus to reduce pain. Finally, if numbness persists or if bladder control for urination and bowel movement is restricted or mobility becomes worsen even after medications and physical therapies, the surgical intervention is necessary because of persistent symptoms such as laminotomy/laminectomy, discectomy/microdiscectomy, artificial disc surgery or spinal fusion surgery to release the compression. But the success of conventional surgeries has some limitations such as presence of neuropathy; muscle and fascial fibrosis; diral fibrosis; archnoidal adhesions; and mechanical instability resulting from the partial removal of boney and ligamentous structures required for surgical exposure and decompression. Therefore, it was observed that oxygen-ozone therapy, lumbosacral epidural steroid injection, surgical techniques, acupuncture, yoga and exercise therapy, non-surgical treatment, etc. are commonly recommended for the treatment of LSD, in the past and recent research [22-28].

The researchers are investigated that the overall strength of the spine mainly depends on the muscle's strength of thighs, glutinous and calves regions [29]. Therefore, muscle impairment causes pain, inflammation and functional disabilities in the patients of LSD. But the combination of analyses of biochemical markers and anatomical measurements along with different parameters for identifying pain and physical functional disabilities to diagnosis LSD and thereafter treatment are lacking.

It has been attempted earlier that decreased IL-10 level and elevated TNF-α, CK-MM and Aldo A levels in blood attend on their normal levels after completion of topical application of natural compounds (phytochemicals) extracted from seven Indian medicinal plants such as *Calotropis gygantea* (root and leaves), *capsicum (*fruit), *Zingiber officinalis* (rhizome), *Rosmarinus officinalis* (leaves and flowers), *Boswellia serratia* (resin), *Curcuma longa* (rhizome) and *Withaniasomnifera* (root) [30-32]. According to Ganguly et al. [30], Ganguly, [31], Belcaro et al. [32], this is a novel technique and observed first time with the help of aqueous phytoextraction as remedial measures

In traditional knowledge, researchers investigated the plant-based therapies only for pain relief in the patients of different parts of the globe as North Jeolla Province of Korea, Central Himalaya of India, etc. [33-34]. Some of medicinal plants like ginger is used for antiinflammation [35]. It has been reported that both inflammation and pain treatment achieved by phytomedicines of medicinal plants at Africa [36]. According to Dragos et al. [37], phytomedicines from medicinal plants are suitable to remediate musculoskeletal disorders, inflammation, pain, oxidative stress, etc.

The objective of present study is to normalize the problem of LSD by analyzing the anomalous serum levels of biochemical parameters such as IL-10, TNF-α, CK-MM and AldoA, deranged anatomical features, abnormal international acclaimed functional disabilities and overweight like VAS,KPS, LEFS, ODI and BMI together with improved radiological images as assessed by KL grading scale in the patients with the help of specialized topical phytocostituents extracted from above-mentioned seven plants mixed with sesame oil and beehive-wax for six-week.

II. Materials and methods

2.1 Recruitment of participants

Four hundred forty-one patients aged 35 to 65 years old, from ten centres of OPTM Health Care (P) Ltd, Kolkata, Delhi, Mumbai and Pune, India from July 2016 to February 2017 were enrolled into this study. Initially, 252 patients (91 females and 161 males) out of 441were selected, based on the sign, symptoms and radiological changes consisted with degenerative changes in lumbar spine along with pain on other limbs. The total of 108 patients suffering for more than four years (normally they report to the clinic) with degenerative changes in the lumbar spine (specially LSD) were selected using exclusion criteria as stated below.

The study protocol was evaluated and approved by the OPTM Research Institute Ethics Committee. The institute is registered with the government. An Institutional Review Board-approved consent form for the physical examinations, blood sample collections and radiological images (CT-scan or X-ray or MRI) required for the study was signed by all patients in the first phase of the screening procedure.

2.2 Exclusion criteria

a) Eighty three patients (41females and 42 males) out of 252 patients were excluded for having another pathological condition that could explain the existing symptoms, such as rheumatic diseases, osteochondritis diseases, inter-articular fractures, congenital dysplasia, radicular syndrome, joint symptoms caused by malignant tumors, Baker's cyst, Perthes disease, Plico syndrome, dermatomyositis and polymyositis diseases, iliopectineal or trochanteric bursitis, bone and joint infectious diseases and ischemic bone necrosis.

b) The following additional exclusion criteria of 61 patients (14 females and 47 males) out of balanced 169 patients were considered: patients with multiple drug dependence; a history of cancer, including caranomatosis and granulocytic leukemia; patients with cuts, wounds, or any type of chronic skin disease; a history of severe neurological diseases; a history of chronic liver, kidney and heart diseases; and patients who did not agree to a physical evaluation and/or attend weekly follow-up visits.

2.3 Study design

After evaluating the exclusion criteria, 144 of the remaining 108 patients (36 females and 72 males) with significant pain syndromes, discomfort, imbalanced quality of life, impaired joint and lower limb functions due to muscle wasting, weakness and degeneration in the lower lumber regions of the body, as evidenced by elevated levels of serum IL-10, TNF-α, CK-MM and AldoA, abnormal anatomical features, and radiological images (CT-scan or X-ray or MRI) were considered in the final study group. Separate evaluations were performed for subjects regarding various complaints and supplements taken to diminish pain or improve fitness. The present studied protocol has been designed to control pain, to maintain joint flexibility, to optimize joint and limb functions and to improve quality of life without any kinds of drug therapy such as acetaminophen, NSAIDs, including COX-2 inhibitors, corticosteroids and hyaluronic injections, glucosamine sulphate, chondroitin, calcium and other alternative treatments such as homeopathic, ayurvedic and hence patients were advised to stop using any kind of above-mentioned drug therapy one day prior to inclusion in the study. Each patient completed a questionnaire, providing details regarding demographics, medical history, nutritional status, ethnic barriers and work status at the baseline and summarized in Table 1. Co-morbidities were also assessed using the Charlson co-morbidity index and methods described by Katz et al. [38] and Singh et al. [39].

2.4 Evaluation of specific biochemical parameters in blood

A 4-ml of blood was collected in tubes coated with heparin (25 IU/ml) by venom puncture from each patient with LSD before and after the treatment. Blood samples were then centrifuged at 1000×g for 10 min at 4º C to obtain serum. According to Vilcek and Lee [40] and Gesser et al., [41], the biochemical parameters as TNF-α and IL-10 in blood of patients were measured by ELISA (enzyme-linked immunosorbent assay) method using the kits from R&D System, Germany (Cat.# DY210 and DY217B). All other chemicals were used in analytical grade supplied by Sigma (St. Lousis, MO, USA). The antibody of TNF-α and IL-10 were collected from Santa Cruze, Biotechnology, Inc (CA, USA). The lower limits of detection for the both assays were 0.195ng/ml.

A 5-ml blood sample was collected in a plain vial from each patient. Blood samples were then centrifuged at 1000×g for 10 min at 4º C to obtain serum. Finally, the serum was used to analyse CK-MM, and

AldoA levels for each patient at the baseline and at the end of six weeks of treatment. The biomarkers were rigorously analysed. CK-MM (U/L) levels were quantitatively assessed using a Creatine Kinase-MM kit (CK-MM/CPK-MM/CK-3) and an immunoassay (Aalto Scientific, Limited, USA). The kit was developed based on the methods reported by Cabaniss [42]. AldoA levels (U/L) were quantified using an ALDOLASE (ALS) RX MONZA AD 189 kit (Randox Laboratories Ltd, Antrim, UK) based on a photometric assay at a wavelength of 340 nm. The kit was developed according to the method reported by Feissli [43]. The subjects suffering from SD with muscle degeneration and skeletal muscle damage were studied to identify a specific biochemical parameter, such as CK-MM, and AldoA levels, in the affected population. Each test for each patient has been rechecked by the BS-240 Mindray fully automated biochemistry analyser before reporting the final test results at the baseline and after the treatment.

All blood tests were conducted under the supervision of the Chief biochemist and the Chief pathologist in the Galaxy Medical Centre, an ISO 9001: 2015 certified lab with Registration No. L/004-(05)-15/0129 under the W.B Clinical Establishment Act, 1950.

The mean, standard deviation (SD) and their mean differences (MDs), 95% confidence intervals (CIs), and p-values of the biomarkers such as IL-10, TNF-α, CK-MM and AldoA respectively were evaluated at the baseline and at the end of six weeks of treatment. Their percentages of improvements after the treatment were graphically evaluated.

The ratio of two biomarkers such as IL-10 and TNF-α, and CK-MM and Aldo A at the baseline and at the end of the treatment respectively were evaluated and their mean standard deviation, mean difference and 95% CI were also evaluated.

2.5 Evaluation of anatomical parameters

Physical examinations were evaluated at the baseline and at the end of 6 weeks of post-treatment including anatomical measurements such as bilateral gap at the knees between the point of short head of the biceps femoris at the lateral knee and the surface of the bed while supine (KGB), bilateral diameter of muscles at the thighs (DTM), the calves (DCM), bilateral diameter of muscles connected with the knee joints 4 cm above the patella (DAP) and 4 cm below the patella (DBP), bilateral straight legs raising in supine (SLRS), in prone (SLRP) and in sitting (SLRSit), bilateral angles of flexion in supine (KFS), in prone (KFP), in standing (KFSt) and bilateral angles of extension in supine position (KES), in prone(KEP) and in standing (KESt).

A meter scale was used to measure KGB. The parameters viz. DTM, DCM, DAP and DBP measurements were performed using a meter tape and a goniometer was used for straight leg raising, flexion and extension measurements in accordance with the American Academy of Orthopaedic Surgeons (AAOS) [44].

The mean, standard deviation (SD) and their mean differences (MDs), 95% confidence intervals (CIs), and p-values of the above-mentioned anatomical parameters were evaluated at the baseline and at the end of six weeks of treatment. Their percentages of improvements after the treatment were graphically evaluated

2.6 Evaluation of pain under Visual analogue scale (VAS)

Visual analogue scale (VAS) for pain is a one-dimensional measure of pain intensity [45]. Observation of patient's perceived symptoms of pain intensity in the last 24 hours was point out on the line of 100 mm. The pain intensity marked as no pain (0-4 mm), mild pain (5-44 mm), moderate pain (45-74 mm) and severe pain (75-100 mm) separately for right leg, left leg and lower back pain under the scale was evaluated for each patient at the baseline and at the end of treatment. The percentage of improvement was evaluated at the end of treatment for all the patents separately compared with the baseline. Their mean, SD and p-values for overall and separately by gender were also graphically evaluated.

2.7 Evaluation of Karnofsky Performance Status (KPS) score

Karnofsky performance status (KPS) score is used to determine a patient's prognosis to carry out daily activities. This is used to compare effectiveness of different therapies and to assess the prognosis in individual patient. A higher score indicates the patient is better able to carry out daily activities and its range from 0 to 100 [46]. The percentage rating criteria of the scale has been broadly classified as under: Normal no complaints; no evidence of disease (100%); Able to carry on normal activity; minor signs or symptoms of disease (90%); Normal activity with effort; some signs or symptoms of disease (80%); Cares for self; unable to carry on normal activity or to do active work (70%); Requires occasional assistance, but is able to care for most of his personal needs (60%); Requires considerable assistance and frequent medical care (50%); Disabled, requires special care and assistance (40%); Severely disabled; hospital admission is indicated although death not imminent (30%); Very sick; hospital admission necessary; active supportive treatment necessary (20%); Moribund; fatal processes progressing rapidly (10%); Dead (0%). The KPS is evaluated for each patient at the baseline and at the end of treatment. The percentage of improvement was evaluated at the end of the treatment

for all the patents separately compared with the baseline. Their mean, SD and p-values for overall and separately by gender were graphically evaluated.

2.8 Evaluation of the Lower Extremity Functional Scale (LEFS)

According to Binkley et al. [48], the Lower Extremity Functional Scale (LEFS) is a 20-item questionnaire pertaining to the patient's ability to perform everyday activities. Each of 20 items in the scale are awarded several points varying 0 to 4, depending on the degree of the impairment when performing the specific activity such as: Extreme difficulty or unable to perform activity (0); Quite a bit of difficulty (1); Moderate difficulty (2); A little bit of difficulty (3); and No difficulty (4). The LEFS is evaluated for each patient at pre- and post-treatment. The percentage of improvement was evaluated at the end of the treatment for all the patents separately compared with the baseline. Their mean, SD and p-values for overall and separately by gender were graphically evaluated.

2.9Evaluation of Oswestry Disability Index (ODI)

The Oswestry Disability Index (ODI) or the Oswestry Low Back Pain Disability Questionnaire is an important test of low back functional outcome tool to evaluate a patient's permanent functional disability [47]. In this questionnaire, there are six questions in each ten sections such as *Pain intensity; Personal care (washing, dressing etc); Lifting; Walking; Sitting; Standing; Sleeping; Sex life (if applicable); Social life; and Travelling* to identify the back or leg pain affecting patient's ability to manage in everyday life. The interpretation of scores have been divided into five categories such as minimal disability (0% to 20%); moderate disability (21% to 40%); severe disability (41% to 60%); crippled (61% to 80%) and patients are either bedridden or exaggerating their symptoms (81% to 100%). The ODI is evaluated for each patient at the baseline and at the end of treatment. The percentage of improvement was evaluated at the end of the treatment for all the patents separately compared with the baseline. Their mean, SD and p-values for overall and separately by gender were graphically evaluated.

2.10 Evaluation of Body mass index (BMI)

Body weight (in kilograms) was measured without shoes or heavy clothing using an electronic scale. Height (in meters) was measured without shoes using a wall-mounted stadiometer [49]. Body mass index (BMI) was calculated for all the patients based on measured weights and heights at the baseline and at the post treatment as weight/ hight^2. The percentage of improvements was evaluated at the end of treatment for all the patents separately. Their mean, SD and p-values for overall and separately by gender were also graphically evaluated.

2.11 Evaluation of Lumbar spine radiographic assessment under KL grading scale

Lateral radiographs of the lumbar spine were obtained with 108 subjects lying on their side with knees bent, Radiographs were scored for lumbar degenerative disc using Kellgren-Lawrance (KL) grade developed by Kellgren and Lawrence[50] as follows: Grade 0, normal; Grade 1,slight anterior wear and osteophyte formation; Grade 2, definite anterior wear and osteophyte formation; Grade 3, osteophyte formation and narrowing of disc; Grade 4, large osteophytes, marked disc narrowing, sclerosis of vertebral plates and posterior subluxation. The present study defined a lumbar spine with disc space narrowing with osteophytes or without osteophytes or with bone sclerosis, disc spec narrowing and large osteophytes. KL grades were evaluated at the intervertebral levels from L_1-L_2 to L_5-S_1 at the baseline and at the end of six weeks of specialized treatment protocol. The lateral view of X-ray images of lumbar vertebrae of two such patients among 108 patients, (before and after the treatment), were separately reviewed and depicted.

2.12 Evaluation of Pearson's correlation coefficients between two biomarkers

The Pearson's correlation coefficients between two biochemical markers such as IL-10 at the baseline ($IL\text{-}10^b$) and IL-10 after the treatment ($IL\text{-}10^t$), TNF-α at the baseline ($TNF\text{-}\alpha^b$) and TNF-α after treatment ($TNF\text{-}\alpha^t$), CK-MM at the baseline ($CK\text{-}MM^b$) and CK-MM after the treatment ($CK\text{-}MM^t$), Aldo A at the baseline ($Aldo\ A^b$) and Aldo A after the treatment($Aldo\ A^t$), the ratio of the IL-10 at the baseline and TNF-α at the baseline ($IL\text{-}10^b : TNF\text{-}\alpha^b$), IL-10 after the treatment and TNF-α after the treatment ($IL\text{-}10^t : TNF\text{-}\alpha^t$), CK-MM at the baseline and Aldo A at the baseline ($CK\text{-}MM^b : AldoA^b$) and CK-MM after the treatment and Aldo A after the treatment ($CK\text{-}MM^t : Aldo\ A^t$) along with their respective p-values were evaluated.

2.13 Evaluation of Indian medicinal plants, their phytoconstituants from aqueous extracts and their established mechanisms of action

The treatment involves topical application of phytoconstituents from the extracts of seven Indian medicinal plants namely *Capsicum* (fruit), *Calotropis gigantea* (root and leaves), *Zingiber officinalis* (rhizome),

Rosemarinus officinalis (leaves and flowers), *Boswellia serrata* (resin), *Curcuma longa* (rhizome) and *Withaniasomnifera* (root) mixed with virgin sesame oil (extracted from seeds at room temperature) and beehives wax to make viscous phyto-based oil without using any preservatives or chemicals in order to preserve the phytochemical properties of plants intact [30-32, 37, 51]. The virgin sesame oil is acted as bio-preservative and beehive-wax helps to reduce joint pain, to relieve stiffness, to stimulate circulation and to moisturize skin [30-32]. Several researchers had already reported the medical effects (specially on pain, muscle weakness, inflammation and stiffness of muscles) on human body of the phytochemicals contained in above-mentioned seven medicinal plants and *Sesamum indicum* and their mechanism of actions [30-32].

2.14 Phytotherapeutic treatment protocol

The main objectives of the treatment are: to increase the muscular strength without using supporting belt on the waist or such other means; to reduce pain, inflammation and stiffness of muscles without dependence upon any types of pain killers or corticosteroid injection or arthrocentesis; to rectify calcifications/degeneration of bones; and abnormal levels of biochemical parameters such as IL-10, TNF-α, CK-MM and AldoA occurred during LSD[30-32, 52]. The treatment protocol is based on well-defined certain principles and theories and based on the applications of well-known chemical, mechanical, thermal and electrical stimuli which improve the fundamental properties of all muscles such as excitability, conductivity, contractibility, elasticity and viscosity [30-32, 53-54]. Each 30-ml of said viscous phyto-based oil prepared from the extracts of seven Indian medicinal plants mixed with virgin sesame oil and beehive-wax is to be applied with the tip of three fingers in particular technique over the skin three times a day with minimum interval of two hours for six weeks ; lying in six different postural positions such as supine, prone, right and left contra-lateral and right and left cross contra-lateral in different programmed sequences in order to nourished the effected group of badly damaged muscles and nerves in the legs and lumber regions during the disease [30-32, 53-54, 55-57].

To achieve the ultimate objectives of the treatment, the period of treatment has been fixed for six weeks, three sessions a day. One session in the clinic and two sessions a day with a minimum interval of two hours in the house or thirteen weeks at home (three sessions a day with a minimum interval of two hours). In the clinic, after the application of phytochemicals contained paste with the help of wooden device (WD) and tip of three fingers, number of medicated fomentation devices (MFDs) with control temperature at 106 °F were rapped from the origins to the insertions over the muscles affecting the movement of knee joints and lower spine in different postural positions such as supine, prone, right and left contra-lateral and right and left cross contra-lateral in the first phase of treatment [30-32, 53-54, 55-57]. In the second phase of treatment, a computerized muscle stimulator operated with battery of 9-volt DC was applied over the various connective tissues through the skin for a maximum period of 5 to 10 minutes. These helped to disperse the coagulated blood or effusions might be present in the affected areas of patients. In the house treatment of thirteen weeks, only phytochemicals contained paste with the help of wooden device and tip of three fingers is to be applied, three sessions a day with programmed sequences of different postural positions supplied in advanced according to the conditions of the patients [30-32, 53-54, 55-57].

Strong massaging technique of application of the phyto-pest is strictly prohibited as this will affect the sarcolemma badly. Each patient has been requested to visit the clinic for review in every week. Sometimes depending upon the severity of the pain as well as condition of the deformities, the sequence of the programmed postural positions was altered restricted to two positions in a session. Based on observations for optimum results had tried on more than thousand patients, the maximum period of treatment had been fixed for six weeks (one session in the clinic and two sessions in the house with two-hourly interval) or thirteen weeks at home (three sessions a day with a minimum interval of two hours) [30-32, 53-54, 55-57].

2.15 External study reviewers

All results and data before and after the treatment were evaluated by an external reviewing panel, not in contract with the registry patients.

2.16 Data collection and Statistical analysis

Data were summarized using descriptive statistics for continuous variables (e.g., mean, standard deviation, number of patients, minimum, maximum), frequency tables, or ratios for discrete variables, and 95% confidence intervals. 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. The comparison was done between baseline and after six weeks of phytotherapeutic treatment. An alpha level of 5% was established i.e., a p-value less than 0.05 was considered statistically significant.

III. Results

3.1 Enrolment and baseline characteristics of patients

A total of 108 patients aged 58.60± 9.94 years (66.67% men) were included in the study. All the patients were suffering with LSDs for 4.68± 2.22 years having inflammation, pain, weakness in the muscle specially in the buttock, thigh and calf regions confirmed by the serum tests ofIL-10, TNF-α, CK-MM and Aldo A, and anatomical parameters. The patients were suffering with severe pain, weakness in muscles and physical functional disabilities as well as increased body weight confirmed by VAS, KPS LEFS, ODI and BMI and radiological images. The baseline demographic characteristics of all patients are shown in Table 1. The patients were not being treated by oral medications; injections and any type of alternative interventions or treatments for diminishing pain or inflammation, for muscle relaxation or for improvement of skeletal muscles one day prior to inclusion in the study and had not undergone discectomy or other kind of surgical intervention to release the compression between the vertebrae within four months prior to the blood tests such as Il-10, TNF-α, CK-MM and Aldo A evaluated at the baseline and at the end of the topical phytotherapeutic treatment for 6 weeks.

3.2 Biochemical parameters

The biochemical parameters such as IL-10, TNF-α, CK-MM and Aldo A were measured and rechecked by the S-240 Mindray fully automated biochemistry analyzer before reporting the final test results at the baseline and after the end of treatment for six weeks.

Table 1: Demographic data and baseline characteristics of patients

	Total	**Male**	**Female**
No of Patients (%)	**108**	**72 (66.67)**	**36 (33.33)**
Mean age in years (SD)	58.60 (9.94)	58.92 (9.22)	57.97 (11.36)
Mean weight (SD) in kg	69.71 (5.05)	69.12 (5.11)	71.13 (6.12)
Mean height (SD) in meter	1.69 (0.92)	1.71 (0.88)	1.67 (0.93)
Mean BMI in kg/m² (SD)	31.71 (3.62)	31.72 (3.22)	31.68 (4.32)
Mean symptom duration in years (SD)	4.68 (2.22)	4.65 (2.37)	4.75 (1.89)
Indian ethnic group (%)			
Bengali	32 (29.63)	18 (25.00)	14 (38.88)
Gujarati	11 (10.18)	6 (8.33)	5 (13.89)
Marwari	10 (9.26)	7 (9.72)	3 (8.33)
Marathi	13 (12.05)	10 (13.89)	3 (8.33)
Tamil	12 (11.11)	10 (13.89)	2 (5.56)
Punjabi	11(10.18)	6 (8.33)	5 (13.89)
Shindhi	9 (8.33)	7 (9.72)	2 (5.56)
North East India	10 (9.26)	8 (11.12)	2 (5.56)
Dietary habit (%)			
Vegetarian	65 (60.18)	38 (54.78)	27 (61.11)
Non - Vegetarian	43 (39.82)	34 (45.22)	9 (38.89)
Other habits			
Smoking	45 (29.41)	22 (20.37)	23 (51.11)
Drinking alcohol	14 (9.15)	6 (5.55)	8 (17.78)
Drinking tea and coffee	69 (45.10)	57 (52.78)	12 (26.67)
Chewing tobacco	25 (16.34)	23 (21.30)	2 (4.44)
Kellgren- Lawrence System for classification (%)			
≥ Grade 2	1 (0.92)	1 (1.39)	0 (0.00)
≥ Grade 3	9 (8.33)	5 (6.94)	4 (11.11)
≥ Grade 4	98 (90.75)	66 (91.67)	32 (88.89)
Multiple complaints or Comorbidities (%)			
Constipation	97 (89.81)	68 (94.44)	29 (80.55)
Acidity & Reflux	94 (87.04)	66 (91.67)	28 (77.78)
Insomnia	87 (80.55)	56 (77.78)	31 (86.11)
Varicose Vein	67 (62.04)	46 (63.89)	21 (58.33)
Urinary Incontinence	56 (51.85)	28 (38.89)	28 (77.78)
Crepitus during knee flexion	63 (58.33)	46 (63.89)	17 (47.22)
Morning stiffness (<30 min)	71 (65.74)	43 (59.72)	28 (77.78)
Measures taken to diminish pain and inflammation (%)			

Lumber belt use	56 (51.85)	30 (41.67)	26 (81.25)
Paracetamol and NSAID use	105 (97.22)	70 (97.22)	35 (97.22)
Exercise and physiotherapy done	45 (41.67)	12 (16.67)	33 (91.67)
Use of corticosteroid injection	62 (57.41)	33 (45.83)	29 (80.55)
Massage with herbal or other gels	98 (90.74)	65(90.28)	33 (91.67)
Homeopathic treatment	105 (97.22)	71(98.61)	34 (94.44)
Ayurvedic treatment	106 (98.15)	71 (98.61)	35 (97.22)
Stick/ a walker use	32 (29.63)	13 (18.05)	19 (52.78)
Supplements taken to reduce pain or improve fitness (%)			
Calcium	106 (98.15)	71(98.61)	35 (97.22)
Vitamin D	97 (89.81)	69 (95.83)	28 (77.78)
Glucosamine	68 (62.96)	49 (68.05)	19 (52.78)
Glucosamine and chondroitin	35 (32.41)	18 (25.00)	17 (47.22)
Work Status (%)			
Employed fulltime	33 (30.55)	23 (31.94)	10 (27.78)
Employed part time	3 (2.78)	2 (2.78)	1 (2.78)
Housewife / Home- maker	21 (19.44)	21 (29.17)	-
Retired	31 (28.70)	17 (23.61)	14 (38.89)
Self employed	20 (18.53)	9 (12.50)	11 (30.55)
Marital status (%)			
Single	13 (12.04)	7 (9.72)	6 (16.67)
Married	70 (64.81)	47 (65.28)	23 (63.90)
Separated	7 (6.48)	4 (5.55)	3 (8.33)
Divorced	5 (4.63)	3 (4.17)	2 (5.55)
Widowed	13 (12.04)	11 (15.28)	2 (5.55)
Stages of Herniation (%)			
Sequestration	11(10.18)	7 (9.72)	4 (11.11)
Extrusion	17 (15.74)	11 (15.28)	6 (16.67)
Prolapse	37 (34.26)	28 (38.89)	9 (25.00)
Disc degeneration	43 (39.82)	26 (36.11)	17 (47.22)

Table 2 shows that the mean±SD levels of IL-10 and TNF-α for 108 combined-sex patients, 36 female-only patients and 72 male-only patients with LSDs were recorded to their normal limits (IL-10 >12pg/ml and TNF-α<15pg/ml) and their differences were highly significant ($p<0.0001$) when compared to the baseline. Moreover, the ratios of Il-10 and TNF-α at the baseline ($IL\text{-}10^b$: $TNF\text{-}\alpha^b$) and at the end of six weeks of treatment ($IL\text{-}10^t$:$TNF\text{-}\alpha^t$) were highly significant ($p<0.0001$) when compared to the baseline for both overall and separately by gender.

Table 2: Statistical analysis of Pre- and Post-treatment of IL-10 & TNF-α and ratio of IL-10 and TNF-α of 108 patients

Biochemical parameter	Gender	Pre-treatment	Post-treatment	Improvement on the level of biomarkers at the end of 6-week			
				MD	95% CI of difference		p-value
		Mean (SD)	Mean (SD)		Lower limit	Upper limit	
IL-10 (pg/ml)	Combined (n=108)	6.86 (2.53)	16..06 (1.98)	-9.20	-10.10	-8.30	<0.0001
	Female (n=36)	6.61 (2.05)	15.62 (1.98)	-9.01	-9.81	-8.21	<0.0001
	Male (n=72)	7.51 (3.48)	17.05 (1.66)	-9.54	-10.62	-8.46	<0.0001
TNF-α (pg/ml)	Combined (n=108)	25.33 (6.08)	12.54 (0.95)	12.79	11.06	14.52	<0.0001
	Female (n=36)	26.69 (6.13)	12.69 (0.94)	14.00	12.26	15.74	<0.0001
	Male (n=72)	21.83 (4.44)	12.15 (0.89)	9.68	8.41	10.95	<0.0001
Ratio of IL-10 & TNF-α	Combined (n=108)	0.30 (0.17)	1.29 (0.19)	-0.99	-1.06	-0.92	<0.0001
	Female (n=36)	0.27 (0.13)	1.24 (0.18)	-0.97	-1.03	-0.91	<0.0001
	Male (n=72)	0.38 (0.25)	1.41 (0.18)	-1.03	-1.12	-0.94	<0.0001

Table 3 shows that the mean±SD levels of CK-MM and Aldo A for combined-sex, male-only and female-only patients with LSDs were reduced to their normal limits (CK-MM: for male <171 and female <145 U/L and Aldo A: <7.6U/L and their differences were highly significant ($p<0.0001$) when compared to the baseline. Moreover, the ratios of CK-MM and AldoA at the baseline ($CK\text{-}MM^b$:$AldoA^b$) and at the end of six weeks of treatment ($CK\text{-}MM^t$: Aldo A^t) were also highly significant ($p<0.0001$) when compared to the baseline for both overall and separately by gender.

Table 3: **Statistical analysis of Pre- and Post-treatment of CK-MM, Aldo A and ratio of CK-MM and Aldo A of 108 patients**

Biochemical parameter	Gender	Pre-treatment	Post-treatment	Improvement on elevated level of biomarkers at the end of 6-week			
				MD	95% CI of difference		p-value
		Mean (SD)	Mean (SD)		Lower limit	Upper limit	
CK-MM (U/L)	Combined (n=108)	248.94 (98.84)	106.89 (30.06)	142.05	122.45	161.64	<0.0001
	Female (n=36)	249.30 (95.35)	102.29 (34.30)	147.01	113.33	180.69	<0.0001
	Male (n=72)	248.80 (101.19)	109.19 (27.68)	139.61	115.17	164.05	<0.0001
Aldo A U/L)	Combined (n=108)	8.81 (3.00)	5.28 (1.13)	3.53	2.92	4.14	<0.0001
	Female (n=36)	9.10 (3.42)	5.27 (1.03)	3.83	2.64	5.02	<0.0001
	Male (n=72)	8.70 (2.78)	5.28 (1.19)	3.42	2.71	4.12	<0.0001
Ratio of CK-MM & AldoA	Combined (n=108)	30.17 (12.47)	21.35 (8.15)	8.82	5.99	11.64	<0.0001
	Female (n=36)	29.40 (11.80)	20.19 (8.50)	9.21	4.37	14.04	<0.0001
	Male (n=72)	30.55 (12.78)	21.93 (7.98)	8.62	5.11	12.13	<0.0001

Table 4 shows the levels of correlation coefficients between CK-MM at the baseline ($CK\text{-}MM^b$) and at the end of treatment ($CK\text{-}MM^t$), and between Aldo A at the baseline ($AldoA^b$) and at the end of treatment (Aldo A^t) were all highly significant ($p<0.05$) for combined-sex patients. But the correlation coefficients: between CK-MM at the baseline ($CK\text{-}MM^b$) and AldoA at the baseline ($AldoA^b$), between CK-MM at post-treatment ($CK\text{-}MM^t$) and AldoA at the end of treatment (Aldo A^t), and between the ratio of CK-MM and Aldo A at the baseline ($CK\text{-}MM^b$: $AldoA^b$) and at the end of 6-week of treatment ($CK\text{-}MM^t$: Aldo A^t) for combined-sex were not significant ($p=0.073$, $p=0.957$ and $p=0.092$) respectively.

Table 4: Analysis of correlation coefficients between the Pre- and Post-treatment of CK-MM and AldoA of 108 patients

Gender	$CK\text{-}MM^b$ vs. $CK\text{-}MM^t$		$AldoA^b$ vs. Aldo A^t		$CK\text{-}MM^b$ vs. Aldo A^b		$CK\text{-}MM^t$ vs. Aldo A^t		$CK\text{-}MM^b$: Aldo A^b vs. $CK\text{-}MM^t$: Aldo A^t	
	R-value	p-value	R-value	p-value	R-value	p-value	R-value	p-value	R-value	p-value
Combined (n=108)	0.202	0.036	0.198	0.040	0.173	0.073	-0.005	0.957	0.163	0.092
Female (n=36)	0.193	0.260	0.335	0.046	0.246	0.147	-0.036	0.834	0.077	0.653
Male (n=72)	0.207	0.080	0.175	0.124	0.128	0.282	-0.043	0.722	0.171	0.150

$CK\text{-}MM^b$: baseline data of CK-MM, $CK\text{-}MM^t$: data after treatment of CK-MM,Aldo A^b: baseline data of Aldo A, Aldo A^t: data after treatment of AldoA

Table 5 shows none of the correlation coefficients between the pre- and post-treatment of IL-10 and TNF-α were not significant for both overall and separately by gender. The percentage of improvements of the biomarkers such as IL-10, TNF-α, CK-MM and Aldo A after the end of treatment were highly significant ($p<0.0001$) both overall and separately by gender and shown in Figures 1 and 2.

Table 5: Analysis of correlation coefficients between the pre- and Post-treatment of IL-10 and TNF-α of 108 patients

Gender	IL-10^b vs. IL-10^t		TNF-α^b vs. TNF-α^t		IL-10^b vs. TNF-α^b		IL-10^t vs. TNF-α^t		IL-10^b: TNF-α^b vs. IL-10^t: TNF-α^t	
	R-value	p-value	R-value	p-value	R-value	p-value	R-value	p-value	R-value	p-value
Combined (n=108)	-0.126	0.385	-0.327	0.020	-0.477	0.0001	-0.095	0.511	-0.245	0.086
Female (n=36)	-0.120	0.684	-0.538	0.047	-0.692	0.006	0.023	0.937	0.515	0.059
Male (n=72)	-0.130	0.450	-0.009	0.959	-0.399	0.016	-0.063	0.716	-0.221	0.194

IL-10^b: baseline data of IL-10, IL-10^t: data after treatment of IL-10, TNF-α^b: baseline data of TNF-α, TNF-α^t: data after treatment of TNF-α

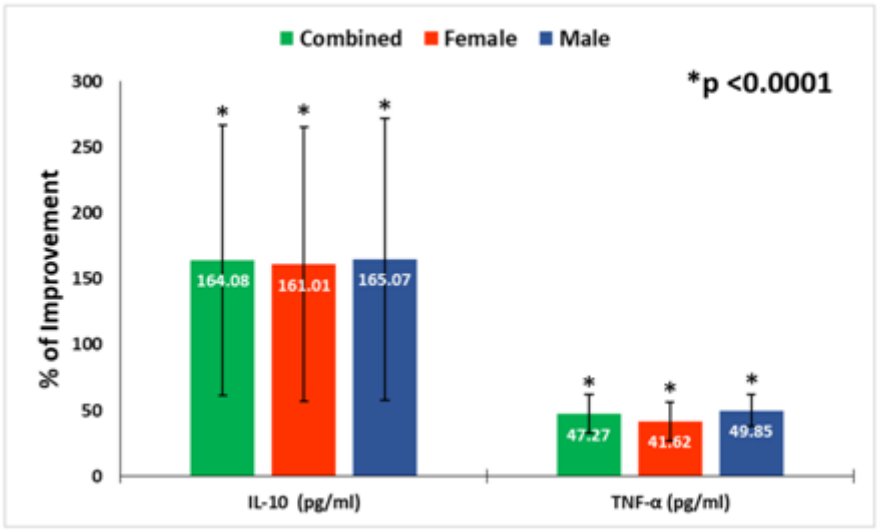

Figure 1: Analysis of % of improvements of IL-10 and TNF-α and their ratio at post-treatment of 108 patients

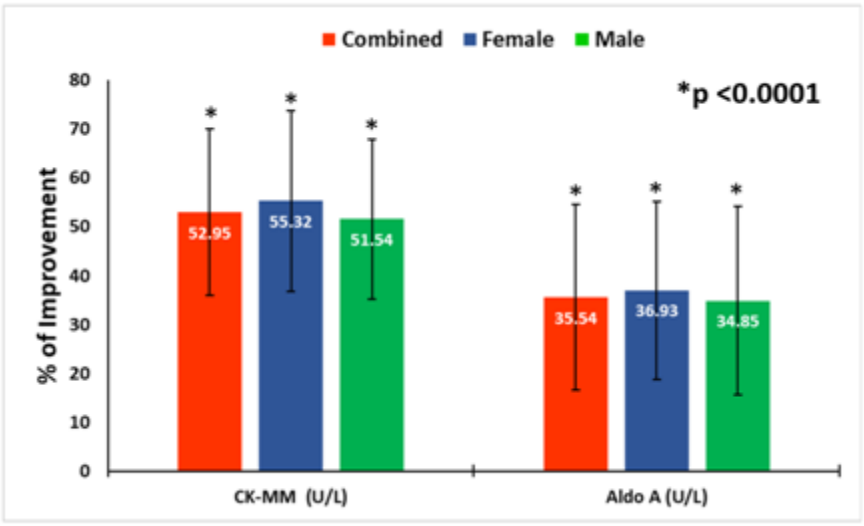

Figure 2: Analysis of % of improvements over CK-MM and AldoA and their ratio at post-treatment of 108 patients

3.3 Anatomical parameters

Table 6 shows that the mean ±SD values of SLR while supine, prone and sitting positions and KFS in supine, prone and standing positions at post-treatment were all increased and that were decreased for KES while supine, prone and standing and observed to be all symmetrical for both the legs. All the differences were highly

significant ($p<0.0001$) when compared to pre-treatment for both overall and separately by gender. [The data for SLRP, SLRSit, KFP, KFSt., KEP and KESt are not shown]

Table 6: Statistical representation for repairing the damage of skeletal muscles through the measurements of SLR, KFS and KES of 108 patients

Anatomical parameter	Gender	Pre-treatment (Analysis of muscle damage)		Post-treatment (Analysis of damaged muscle repairing)		Improvement due to repairing the damage of skeletal muscles in right and left legs at post-treatment of 6-week			
		Mean (SD)		Mean (SD)		Right Leg		Left Leg	
		Right leg	Left leg	Right leg	Left leg	MD (95%CI)	p-value	MD (95%CI)	p-value
SLR (degree)	**Combined (n=108)**	33.25 (2.60)	27.84 (2.30)	72.82 (4.03)	72.82 (4.03)	-39.57 (-40.48, -38.68)	<0.0001	-44.98 (-45.86, -44.10)	<0.0001
	Female (n=36)	33.78 (3.17)	28.56 (2.19)	74.08 (3.78)	74.08 (3.78)	-40.30 (-41.94, -38.66)	<0.0001	-45.52 (-46.97, -44.07)	<0.0001
	Male (n=72)	32.98 (2.21)	27.48 (2.27)	72.19 (4.01)	72.19 (4.01)	-32.21 (-33.28, -31.14)	<0.0001	-44.71 (-45.78, -43.64)	<0.0001
KFS (degree)	**Combined (n=108)**	83.87 (6.36)	79.04 (6.90)	143.47 (2.10)	143.47 (2.10)	-59.60 (-60.87, -58.33)	<0.0001	-64.43 (-65.80, -63.06)	<0.0001
	Female (n=36)	81.11 (5.78)	76.89 (6.12)	144.12 (2.17)	144.12 (2.17)	-63.01 (-65.06, -60.96)	<0.0001	-67.23 (-69.39, -65.07)	<0.0001
	Male (n=72)	85.25 (6.18)	80.12 (7.01)	143.14 (1.98)	143.14 (1.98	-57.89 (-59.40, -56.38)	<0.0001	-63.02 (-64.72, -61.32)	<0.0001
KES (degree)	**Combined (n=108)**	22.91 (2.10)	23.86 (2.02)	8.22 (0.48)	8.44 (0.48)	14.65 (14.28, 15.10)	<0.0001	15.64 (15.25, 16.03)	<0.0001
	Female (n=36)	23.17 (2.13)	24.19 (2.05)	8.15 (0.65)	8.15 (0.65)	15.02 (14.28, 15.76)	<0.0001	16.04 (15.32, 16.75)	<0.0001
	Male (n=72)	22.78 (2.07)	23.69 (1.98)	8.26 (0.37)	8.26 (0.37)	14.52 (14.03, 15.01)	<0.0001	15.43 (14.96, 15.89)	<0.0001

The overall measurements of DAP and DBP were all reduced to symmetrical for both the legs at the end of 6-week of treatment and were also highly significant ($p<0.0001$) when compared to the baseline [data not shown].

Table 7 shows that the overall measurements of KGB, DCM and DTM were all reduced/increased and observed to be symmetrical for both the legs at post-treatment. The difference of mean± SD values of KGB for both the legs were extremely statistically significant ($p<0.0001$) whereas the values of DCM and DTM were not significant for both right and left legs ($p=0.499$ and $p=0.585$; $p=0.104$ and $p=0.641$) respectively for combined-sex when compared to the baseline.

Table 7: Statistical representation for repairing the damage of connective tissue muscles through the measurements of KGB, DTM and DCM

PARAMETER	GENDER	Pre-treatment (Analysis of muscle damage) Mean (SD)		Post-treatment (Analysis of damaged muscle repairing) Mean (SD)		IMPROVEMENT DUE TO REPAIRING THE DAMAGE OF SKELETAL MUSCLES IN RIGHT AND LEFT LEGS			
						Right Leg		Left Leg	
		Right leg	Left leg	Right leg	Left leg	SMD (95% CI)	p-value	SMD (95% CI)	p-value
		Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)				

KGB in cm.	Combined (n=108)	7.37 (1.38)	7.41 (1.46)	3.05 (0.04)	3.05 (0.04)	4.32 (4.04, 4.54)	<0.0001	4.36 (4.08, 4.66)	<0.0001
	Female (n=36)	7.32 (1.33)	7.32 (1.57)	3.08 (0.38)	3.08 (0.38)	4.24 (3.91, 4.56)	<0.0001	4.24 (3.86,4.61)	<0.0001
	Male (n=72)	7.47 (1.48)	7.59 (1.20)	2.99 (0.43)	2.99 (0.43)	4.48 (3.96, 5.00)	<0.0001	4.60 (4.17,5.02)	<0.0001
DTM in cm.	Combined (n=108)	48.42 (5.48)	48.43 (5.45)	48.92 (5.47)	48.92 (5.47)	-0.50 (-1.97,0.96)	0.4991	-0.49 (-1.96,0.97)	0.5855
	Female (n=36)	48.62 (5.77)	48.76 (5.81)	49.31 (5.81)	49.31 (5.81)	-0.69 (-2.60,1.21)	0.4731	-0.55 (-2.46,1.37)	0.5721
	Male (n=72)	48.01 (4.91)	47.75 (4.62)	48.14 (4.69)	48.14 (4.69)	-0.12 (-2.38,2.13)	0.9123	-0.39 (-2.58,1.8)	0.7242
DCM in cm.	Combined (n=108)	34.46 (3.92)	34.59 (3.99)	33.59 (3.91)	33.59 (3.91)	0.87 (-0.18,1.92)	0.1036	1.00 (-0.06,2.06)	0.0641
	Female (n=36)	34.81 (4.32)	35.02 (4.42)	34.02 (4.31)	34.02 (4.31)	0.78 (-0.64,2.21)	0.2772	1.00 (-0.44,2.44)	0.1714
	Male (n=72)	33.78 (2.87)	33.74 (2.80)	32.74 (2.81)	32.74 (2.81)	1.04 (-0.29,2.38)	0.1241	1.00 (-0.32,2.32)	0.1350

3.4 Dermatomes of the lower extremities

Other reasons for measuring the above-mentioned anatomical parameters were to identify the damages occur during LSD as these can be distinctly marked in the dermatomal picture shown in Figure 3 and details of the location of pain and motor deficit in association with the nerve root involvement of each lumbar disc level shown in Table 8.

Table 8: Dermatomes of the Lower extremities showing the location of pain and motor deficit in association with nerve root involvement of each lumber disc level

Disc Level	Location of Pain	Motor Deficit
$T_{12} – L_1$	Pain in inguinal and medial thigh	None
$L_1 – L_2$	Pain in anterior and medical aspect of upper thigh	Slight weakness in quadriceps; slightly diminished supra patellar reflex
$L_2 – L_3$	Pain in antero-lateral thigh	Weakness quadriceps diminished patellar or supra patellar reflex
$L_3 – L_4$	Pain in postero-lateral thigh and anterior tipial area	Weakness quadriceps diminished patellar reflex
$L_4 – L_5$	Pain in dorsum of foot	Extensor of big toe and foot
$L_5 – S_1$	Pain in lateral aspect of foot	Diminished or absent Achilles reflex

Source: Scott Bodel (1999)

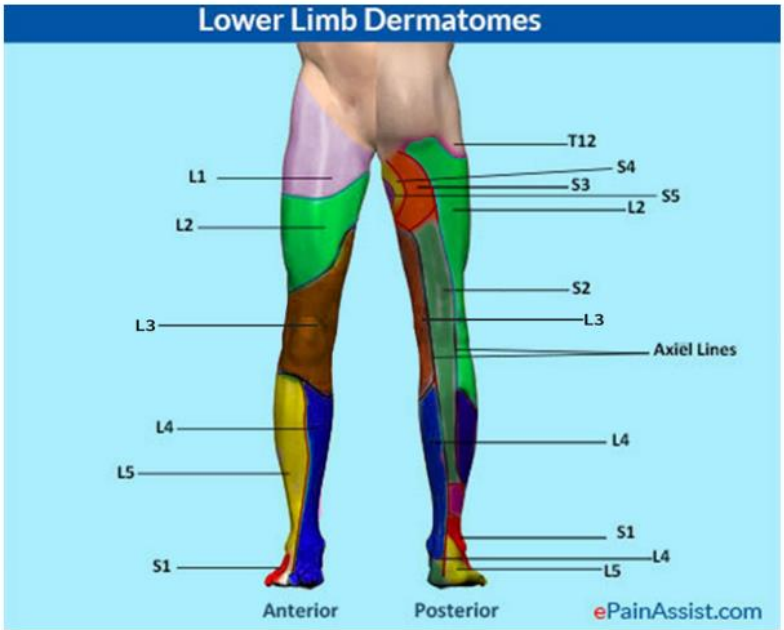

Figure 3: Dermatomes of Lower Limb effecting the lumbar vertebrae L1 – L5
(Source: ePainAssist.com)

3.5 Performance status, Back pain related parameters and BMI

The percentage of improvements on pain after the treatment for combined-sex, female-only and male-only patients under VAS was highly significant ($p<0.05$) both overall and separately by gender and depicted in Figure 4.

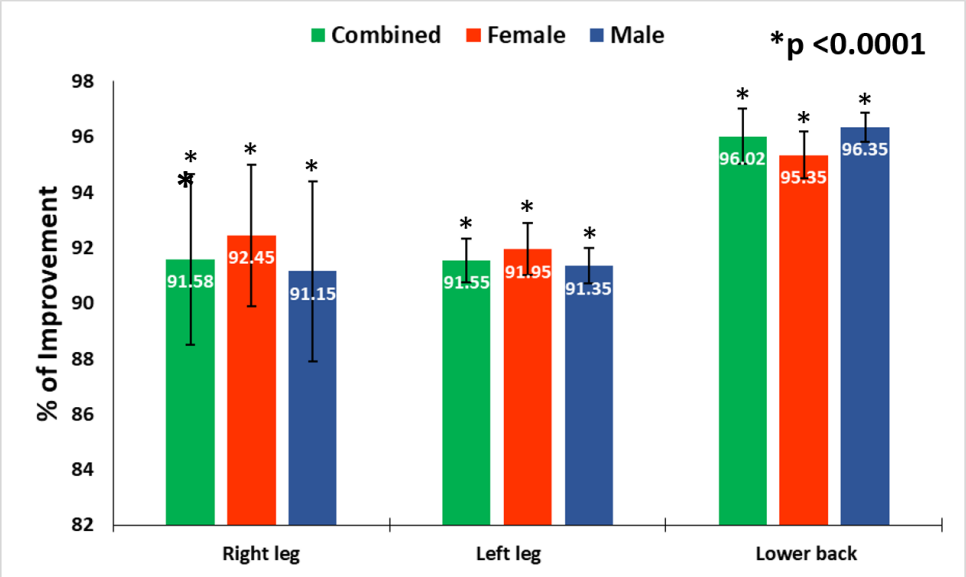

Figure 4: Analysis of percentage of improvement of pain under visual analogue scale (VAS) (*p <0.0001)

The percentage of improvements on the performance on daily activities under KPS, status of the patient specific functional and disability separately assessed under the scales LEFS and ODI and reduction of body weight confirmed by BMI were all highly significant ($p<0.0001$) at post treatment of 6-week when compared with the baseline and shown in Figures 5 to 8.

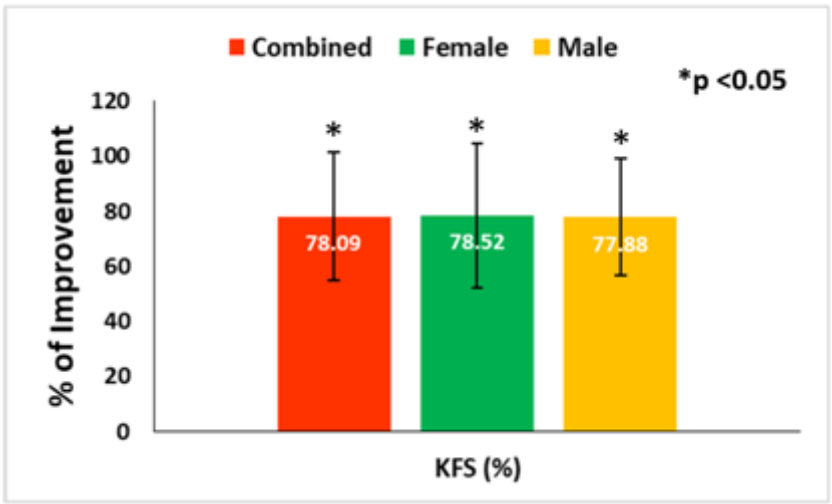

Figure 5: Analysis of percentage of improvement of performance under KFS scale (*p <0.05)

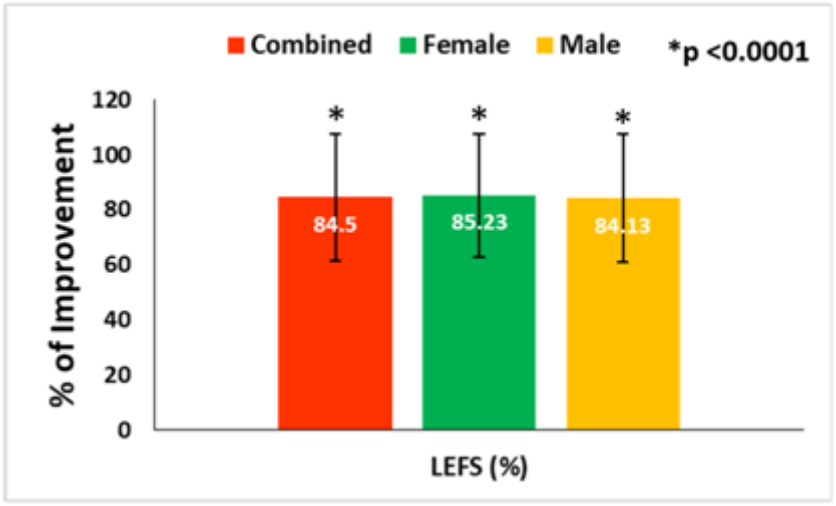

Figure6: Analysis of percentage of improvement of performance under Lower Extremity Functional Scale (LEFS) (*p <0.0001)

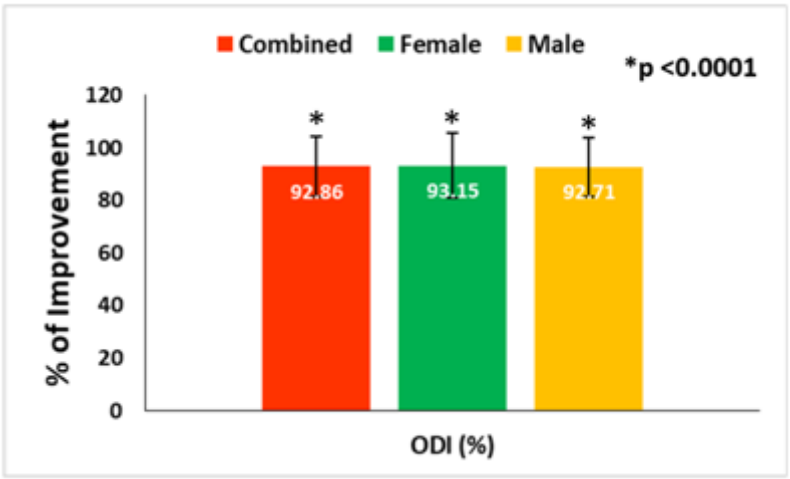

Figure7: Analysis of percentage of improvement of performance under Oswestry Disability Index (ODI) (*p <0.0001)

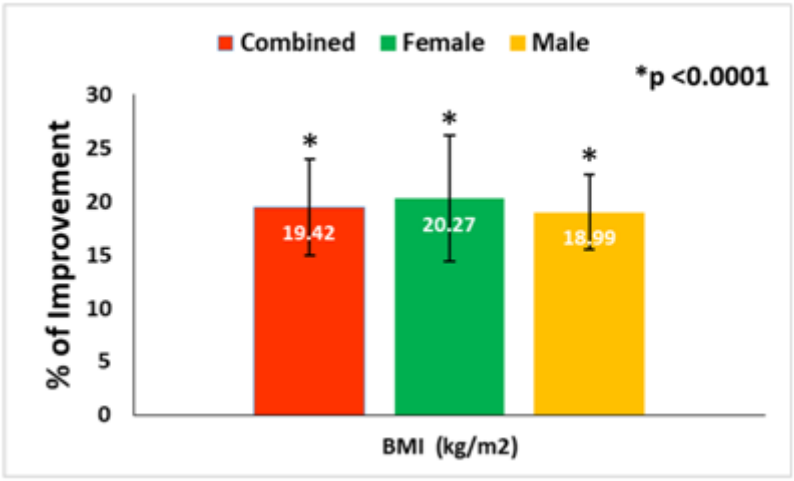

Figure8: Analysis of percentage of improvement of weight under Body mass index (BMI) (*p <0.0001)

3.6 Improvement on LSD as per radiological images as assessed by K-L grading scale

All the lateral views of the X-rayed of 108 patients with LSD at the baseline exhibited degenerative changes, particularly at the region of one or more of the intervertebral levels of L_1-L_2 to L_5-S_1 with marked disk narrowing and osteophyte formation. Some cases exhibited bone sclerosis, disc space narrowing and large osteophytes. The lateral views of X-rayed of the lumbar vertebrae of the patients were observed no such narrowing of dice and osteophyte formation after six weeks of specialized treatment protocol and their assessment under K-L grading scale shown in Table-9. X-ray images of two such patients suffering with LSD in the lumbar region before and after the treatment are depicted in Figure 9.

Table 9: KL grading scale for disc degenerative

	Pre-Treatment		**Post-Treatment**	
	No of Patient	**Percentage**	**No of Patient**	**Percentage**
Grade 1:	None	None	46	42.59
Grade 2:	None	None	42	38.89
Grade 3:	73	67.59	12	11.11
Grade 4:	35	32.41	8	7.41

Grade 0: Normal; Grade 1: Slight anterior wear and osteophyte formations; Grade 2: Definite anterior wear and osteophyte formations; Grade 3: Osteophyte formation and narrowing of disc; Garde 4: Large osteophytes, marked disc narrowing, sclerosis of vertebral plates and posterior subluxation

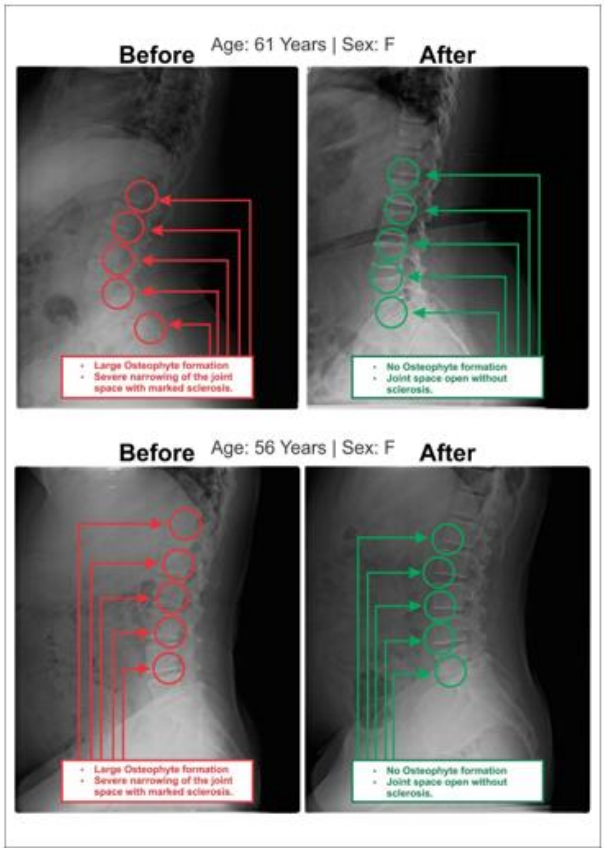

Figure9: Lateral view X-rays showing before and after the treatment of lumbar slip disc with phytotherapy

IV. Discussion

From the present study findings, we describe and suggest the novel topical phytotherapeutic treatment protocol to restore LSD evidenced by normalization of the anomalous levels of biomarkers such as IL-10,TNF-α, CK-MM and AldoA, deranged anatomical features, and abnormal international acclaimed outcome measurements for pain, stiffness, numbness, or weakness in lower limbs that leads to aberrant quality of life along with normal radiological images as assessed by KL grading scale without using any costly medications including injections and surgery more easily and at minimum cost within 6-week.

LSD is a chronic inflammatory IVD degenerative disease at and just below the waist. The IVD is an important mechanical structure which comprises a tough outer circumferential annulus fibrosus and soft-jelly-type inner cell-sparse, matrix-rich nucleus pulposus, bordered superiorly and inferiorly by two cartilaginous

endplates and it allows the range of motion of the spinal column. Therefore, LSD is resulted in degeneration of IVD, incited by aging, overweight, bad habits such as drinking, smoking, wrong sitting posture, occupational hazards, traumatic insult, genetic predisposition or other factors.

The balance between tumor necrosis factor-alpha (TNF-α) (standard value <15pg/ml) and interleukin-10 (IL-10) (standard value >12pg/ml) is important for immune homeostasis maintenance. Exuberant production of TNF-α contributes to overwhelming inflammatory response and tissue damage. At the same time, IL-10 is known as human cytokine synthesis inhibitory factor (CSIF) and it is an anti-inflammatory cytokine. Therefore, it is capable of inhibiting synthesis of pro-inflammatory cytokine (TNF-α) expression and release from alveolar macrophages and peripheral blood monocytes. Increase in TNF-α is counter balanced by simultaneous synthesis of an anti-inflammatory cytokine IL-10, which suppresses production of many activating and regulatory mediators. Due to a decrease in IL-10 levels, TNF-α levels are not regulated effectively as IL-10 regulates the TNF-α converting enzyme. Inflammatory processes exacerbated by cytokines TNF-α and IL-10 are believed to be key mediators of IVD degenerative disease like LSD.

The level of serum CK-MM is found to be elevated from the standard value (for male <171 and female <145 U/L) in response to muscular dystrophy, connective tissue damage, etc.[58-59, 60-62], and AldoA level increases from the standard value <7.6 U/L due to skeletal muscle damages, polymyositis, muscular dystrophy and inflammatory muscle disease and bone erosion [62], suggesting that these markers may also be risk factors for LSD. Previous studies have utilized an individual research approach for different diseases [58-59] but have not studied in combined affect in the serum levels of IL-10, TNF-α, CK-MM and AldoA in the treatment of LSD.

The author had already established previously that the elevated levels of C-reactive protein (CRP), CK-MM and AldoA which represent the predictive risk factors for inflammation, muscle degeneration and skeletal muscle damage during osteoarthritic disorders (OADs) and normalized their elevated levels by the treatment of specialized topical phytotherapeutic technique within 6-week. Therefore, the diagnostic and treatment protocol have already been established so far as only OADs are concerned but not in LSD.

LSD is a chronic, progressive condition, and current therapies including physical are limited and often focused on symptomatic pain relief rather than curtailing the progression of the disease. It is often defined by functional and structural changes in the tissue including excessive breakdown of the extracellular matrix and increased disc cell senescence and death and compromised biomechanical function of tissue thus to develop numbness, weakness, loss of strength of muscles of the lower limbs.

Simultaneously, the normalization of the levels of these biomarkers along with improved deranged anatomical features, pain parameter under VAS, improvements of physical functional abilities and quality of life under KPS scale, LEFS, ODI and lowering obesity under BMI by topical phytotherapeutic treatment protocol for a period of 6 weeks, which was an endeavour in the present study. Generally, phytomedicines from medicinal plants derived compounds are well-established for the prevention of arthritis, obesity, oxidative stress, inflammation, neuro-degenerative diseases, muscle weakness etc. [30-31, 55-57]. It was observed in the present study that all the biomarkers were normalized after topical application of aqueous extract of medicinal plants as per research protocol developed by Ganguly et al. [53] and Ganguly and Ganguly [63], followed by Belcaro et al. [32]. Both the levels of the biomarkers and their ratios were substantial within normal limits at the end of six weeks of treatment in case of percentage improvement study separately done for combined-sex, female-only and male-only patients.

The percentage improvements for the study of pain and related parameters were substantially achieved under the well-known guidelines for the standard clinical outcomes such as VAS, KPS, LEFS and ODI and there is a reduction of body weight as assessed by BMI at the end of six weeks of phytotherapy treatment for all studied subjects.

The result from the deranged anatomical parameters shows that there are substantial increasing and decreasing phenomenon of the group of muscles connected with various joints and both the legs were symmetrical in respect of the measurements of KGB, DAP, DBP, DCM, DTM, SLR, KFS and KES at six weeks of post-treatment which indicate the improvements of muscular wasting, muscle weakness and degeneration that were occurred during LSD at the baseline. Moreover, the result shows that the Pearson's correlation coefficients (r-values) were almost highly predictive between the two biomarkers in patients with LSD when they are separately compared with the pre-treatment data.

Several researchers have emphasized for the normalization of above-mentioned parameters along with prevention of osteoarthritis in animal and human [30-31, 37, 55-57, 64] but the present study indicates aqueous extracts of medicinal plants and their phytoconstituents may participate individually and/or combinations repair LSD in relation to normalization of biochemical markers. The correlation coefficient interactions were almost highly improved after the treatment when compared to baseline data.

It is well known that the abnormal relationship and increased levels of CRP, CK-MM and Aldo A in the blood of human indicate inflammation, muscular wasting and skeletal muscle damage occurred in the tissue

[61-63, 65] in which abnormal muscles anatomy, pain and degenerative changes in bones were found. The present study revealed that the normalization of LSD of patients is possible with the help of specialized phytotherapeutic treatment protocol by the evidences of normalization of relationship between IL-10 and TNF-α (for IL-10 >12pg/ml , TNF-α< 15pg/ml) declining levels of CK-MM and AldoA (for female <145 U/L and for male <171) and Aldo A (<7.6 U/L) followed by normalization of anatomical parameters along with recovery of pain, muscle stiffness, and normal physical day to day functional activities and reduction of body weight as assessed by the standard international clinical outcomes such as VAS, KPS, LEPS, ODI and BMI together with the confirmed improvement in radiological images as assessed by KL grading scale.

The author has further established the deranged anatomical features are the risk factors for OADs Ganguly [53] and also established the normalization of the deranged anatomical features for OADs with the help of established phytotherapy [30-31, 37, 55-57].

It is indicated from the present results that the various anatomical parameters are deranged due to muscle wasting, weakness and degeneration, connective tissue damage, evidenced from the figure of dermatoses because of which both the legs become asymmetrical, when patient suffers with LSD. When we further analyses the limb-wise deformities, we find that the KGBs are increased and not touching the back of knee joints (popliteal region) on the bed while supine and become asymmetrical due to the cumulative effects of muscle wasting, weakness, inflammation and stiffness of the connective muscles during the diseases condition.as well as these further increased due to prolong use of knee supports, hyaluronic acid injections or corticosteroidal injections or arthrocentesis used for quick diminishing of pain, stiffness, inflammation and for increasing the strength of muscles temporally. There is increased in asymmetrical of DTM between the legs because of the cumulative effects of muscular wasting/ muscular bulging in the posterior region of the thighs and may be commonly compressed the sciatic nerve which is originating from the tubersity of the ischium and inserting to the tibia resulting which patient is complaint the acute pain in the lumbar region along with knee pain. The reason for decreased asymmetrical DCM of both legs is due to cumulative muscular wasting / stiffness of gastrocnemius muscles for which further compressed the tibial nerve which is a branch of sciatic nerve, may be affected of prolong use of knee supports, tenderness of Achilles tendon, soleus, calcaneus spurs, rigidity of ankle joints and such other reasons. Therefore, the slight difference of the diameter of the calf muscle of two legs trigger up the compression in the lumbar vertebrae as they misaligned. The asymmetry of DAP is the reason of cumulative effects of muscular wasting, inflammation, effusion or blood clotting due to engorgement of saphenous vein may be the extra reason of using knee braces, hyaluronic acid injections or corticosteroidal injections or arthrocentesis used for quick diminishing of pain, stiffness and inflammation and at the same time the condition of asymmetry for both the DBPs arise due to the cumulative effects of muscular wasting, inflammation, effusion or blood clotting on the anterior, posterior, lateral and medial parts of lower legs especially tibialis and anterior extensor hallucis longus and digitorial longus, gastrocnomius, and Achilles tendon.

Moreover, it is known that the knee flexion and extension are two main activities of the knee joint. All the muscles that move these joints are in the anterior, posterior and lateral thigh region and for the flexion activity the muscles nerve root is sciatic nerve and for extension is femoral nerve. From the results, it reveals that SLR, KFS, KFP and KFSt are all reduced and at the same time the KES, KEP and KESt are all increased during LSD because of massive muscular wasting, stiffness and muscle degeneration especially the quadriceps muscles and tendons, and healthy muscle fibers replaced by fibrosis and fat making muscle tissues in the thigh region and the legs become asymmetry. These asymmetrical phenomena of lower limbs can be easily identified from the figure of dermatomes of the lower extremities wherein the location of pain and motor deficit in association with nerve root involvement of each lumber disc level without going through any sophisticated tests.

Therefore, the measurements of the above-mentioned areas firmly indicate the condition of muscular wasting, weakness, degenerative status along with the condition of bone joints of the legs immediately without using MRI or CT-can or X-ray without any cost. Moreover, to identify the status of muscular wasting, weakness and degeneration especially skeletal muscles during LSD various muscles ought to be examined, but it is not at all possible to capture images or tests of multiple places with the help CT-can or MRI or X-ray etc. which are not only time taking but also expensive. Hence, to diagnose along with treatment for LSD, the measurements of anatomical parameters have been taken care in addition to four biochemical tests.

Moreover, during LSD, patients suffer with severe pain, stiffness of muscles, deteriorate the functional activities of daily living and the quality of life which can be easily identified with the help of international acclaimed scales such as VAS, KPS, LEFS, and ODI as well as obesity is another important criteria for LSD which can be measured by BMI. Major research works have been emphasized individual parameter especially pain relief therapy by using synthetic drugs and/or herbal treatment by traditional knowledge and/or yoga therapy [22-28]. Hence, when framing the novel treatment protocol through topical phytotherayfor LSD, the above-mentioned parameters are well taken care along with biochemical and anatomical features which are not at all possible with the help of radiological images or other established costly sophisticated tests.

The present study has an endeavor and first-time approach for the treatment of LSD with the help of anatomical abnormalities, biochemical markers and international-acclaimed pain and disability parameters such as VAS, KPS, LEFS, ODI, and BMI indices along with radiological images as assessed by KL grading scale, which are lacking in earlier studies.

V. Conclusions

It is firmly concluded from the results that the patients suffering with LSD would be normalized with a unique topical phytotherapeutic treatment technique within six weeks as confirmed by achieving the normal levels of biomarkers such as IL-10, TNF-α, CK-MM and AldoA along with normalized deranged anatomical features, and improved levels of international-acclaimed pain and disability parameters and decreased obesity as assessed by VAS, KPS, LEFS, ODI and BMI together with improved radiological images as assessed by KL grading scale.

Future research should be undertaken on: phytochemicals characterization by using Mass Spectroscopy; receptor and legend binding activities through molecular docking to know which compounds responsible in normalization of SD and prevention thereon.

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Conflicts of interest

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

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