International Research Journal of Ayurveda & Yoga Vol. 8(5), pp. 73-78, May, 2025
Available online at http://irjay.com
ISSN: 2581-785X
DOI: 10.48165/IRJAY.2025.80513

REVIEW ARTICLE

A Review Article on *Katishoola* with Special Reference to Lumbar Spondylosis

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ARTICLE INFO

Article history:
Received on: 14-04-2025
Accepted on: 12-05-2025
Published on: 31-05-2025

Key words:
Katishoola,
Lumbar Spondylosis,
Vataja Nanatmaja Vyadhi

ABSTRACT

In the new millennium, the progressive and fast lifestyle, unhealthy eating habits, work which includes long sitting hours, improper sitting and sleeping postures, frequent traveling, jerks while traveling, sports activities, and lack of physical and mental exercises have been known to cause one of the most common complain to visit a doctor which is the low backache. Spondylosis refers to the degenerative changes in the spine, such as bone spurs and degenerative changes in the intervertebral disc. Lumbar spondylosis is a musculoskeletal disorder in which there is degeneration of the lumbar spine which causes low backache. The degenerative change is followed by the narrowing of the intervertebral disc space, which leads to compression of the spinal nerves that exit the spinal cord. This compression of the spinal nerves leads to pain, numbness, stiffness, and tingling sensation in the legs. In Ayurveda, low backache can be correlated with *Katishoola,* which is a "*Vataja Nanatmaja Vyadhi*" and produces symptoms such as pain and stiffness in the *Katipradesha*.

1. INTRODUCTION

Lumbar Spondylosis is a degenerative condition of the lumbar spine that presents with narrowing of the disc space and compression of the spinal nerves, which further leads to pain in the lower back radiating to the legs and also cause numbness, stiffness, and tingling sensation in it. Unhealthy eating, a modern lifestyle, repetitive trauma to the spine, lifting heavy weights on the back, and long sitting hours with improper posture are known to act as the aggravating factors of low backache.

In Ayurveda, this condition can be correlated with *Katishoola*. According to *Acharya Sharangdhara, Katishoola* is a "*Vataja Nanatmaja Vyadhi*." Among the *Tridoshas* mentioned in the classical texts, *Vata dosha* plays a major role in the occurrence of diseases as the other *doshas, dhatus*, and *malas* are said to be "*Pangu*" without *Vata dosha* as mentioned by *Acharya Sharagdhara. Katishoola* has not been described as a separate disease in the classical texts, but references of *Katishoola* as a symptom of various diseases, such as *Asthimajjagata Vata, Ajeerna, Pakwashayagata Vata, Gudashrita Vata, Bhagandara, Amavata*, can be found scattered in the Ayurvedic literature.

Katishoola may be considered a disease or a symptom of a disease in which the vitiated *Vata dosha* gets localized in the *Katipradesha*. Therefore, the pathogenesis occurs due to the obstruction of "*Rasa and Rakta Dhatu*" circulation by *Kaphavrutta Vyanavayu*. This leads to structural changes in the *Katipradesha,* which produces pain, stiffness, numbness, restricted movements, etc.

The increasing incidence of low backache has raised concern about finding a better treatment approach to provide relief to patients suffering from backache and the ability to cope with work and live a healthy life.

1.1. Description of *Katishoola*

The word "*Kati*" is constituted by two words, "*Kati*" and "*Shoola*." The word "*Kati*" is derived from the dhatu "*Kati+in*" *Streelinga Pratyaya,* which is considered a "*Sharira Avyava Vishesha*." It may also be termed as *Shroniphalaka, Shroni,* or *Shronidesha*. According to *Shabdakalpadruma*, the word *Shoola* is formed by the moola "*Gany*" which means "*Shoolana*." According to Monier Williams, the meaning of *Shoola* is the pain, catch, or catch hold.[1]

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Katishoola can be defined as a seizing or catching type of pain that restricts the movement of the lumbar spine. This pain occurs due to the vitiation of the *Vata dosha* which may either be *sama or nirama*. According to *Acharya Sushruta*, pain cannot be produced without the vitiation of *Vata dosha*. Although *Katishoola* has not been explained as a separate disease in the Ayurvedic literature, in *Gadanigraha,* a separate disease named "*Katigraha*" has been described in *Vatavyadhi Rogadhikara*. According to *Gadanigraha*, there is a movement of the vitiated *sama vayu* in *Katipradesha,* which causes stiffness, and further produces pain. It suggests the presence of *Dhatu Kshayatmaka* (degenerative) and *Margavrodhaka* (obstructive) types of *samprapti*. *Katigraha* is *Shosha* (degeneration), *Stambha* (stiffness), and *Shoola* (pain) predominant disease.

Ruksha, Laghu, Sheeta, Shukshma, Chala, Vishada, and *Khara* are the *gunas* of *Vata*. *Katu, Tikta, Kashaya rasa, Anshana, Vishmasana, Vegadharana, Atirakta sravana, Dhatukshaya, Ativyavaya, Ativyamama,* and *Ratrijagrana*, etc. have been said to cause an increase in *Vata dosha*. According to the principle of "*Sarvada Sarvbhawanama Samanyama Vruddhikarnama,*" similar properties between two things lead to an increase. Hence, anything that possesses the *gunas* similar to those of *vayu* leads to its increase, for e.g., *Ratri Jagrana* causes an increase in the *Ruksha* guna in the body, which increases the *Vata dosha.* Similarly, *Ativyavaya, Ativyamama, Dhatukshaya,* etc., also cause an increase in *Vata dosha*.

Mandagni is another factor contributing to the pathogenesis of the disease. *Mandagani* leads to the formation of *amarasa* in the body. This *amarasa* leads to *srotavrodha* which hampers the process of *dhatu* formation further affecting the process of *dhatu poshana*. Since *rasa dhatu* is not formed properly, the formation of other *dhatus* is also affected and results in *dhatukshaya*. *Meda dhatu* is responsible for the *snighdhata* of the body. Due to *dhatukshaya*, the formation of *medadhatu* is also hampered which increases the *ruksha* guna in the body which further increases the *Vata dosha*. *Dhatukshaya* also leads to *asthi-majja dhatu kshaya* and according to the principle of "*Ashraya Ashrayi Bhava*," *asthikshaya* leads to an increase in *Vata dosha*. This explains the *dhatukshaya* type of pathology.

Vyana vayu is said to be *sarvadehchari* and powerful. *Vyana vayu* plays a pivotal role in orchestrating various bodily functions and "*rasa samvahana*." It controls all the movement-related functions of the body, such as flexion, extension, bending, upward movement, and lateral movement. It also controls the circulation of *rasa* and other *drava dhatus* such as *rakta*. Hence, it can be considered that there is a vitiation of *Vyana vayu* in *Katishoola.*

1.2. Backache[2]

The importance of back and neck pain in our society is underscored by the following: (1) the cost of chronic back pain in the United States is estimated at more than $200 billion annually; approximately one-third of this cost is due to direct health-care expenses and two-thirds are indirect costs resulting from loss of wages and productivity; (2) back symptoms are the most common cause of disability in individuals <45 years of age; (3) low back pain (LBP) is the second most common reason for visiting a physician in the United States; and (4) more than four out of five people will experience significant back pain at some point in their lives.

1.3. Causes of Backache[3]

1.3.1. Lumbar disk disease

Lumbar disk disease is a common cause of acute, chronic, or recurrent low back and leg pain. Disk disease is most likely to occur at the L4-L5 or L5-S1 levels, but upper lumbar levels can also be involved. The cause is often unknown, but the risk is increased in overweight individuals. Disk herniation is unusual before age 20 years and is rare in the fibrotic disks of the elderly. The pain may be located in the low back only or referred to a leg, buttock, or hip. A sneeze, cough, or trivial movement may cause the nucleus pulposus to prolapse, pushing the frayed and weakened annulus posteriorly. With severe disk disease, the nucleus can protrude through the annulus (herniation) or become extruded to lie as a free fragment in the spinal canal.

The inner annulus fibrosus and nucleus pulposus are normally devoid of innervation. Inflammation and production of proinflammatory cytokines within a ruptured nucleus pulposus may trigger or perpetuate back pain. Ingrowth of nociceptive (pain) nerves for some cases of chronic "discogenic pain." Nerve root injury (radiculopathy) from disk herniation is usually due to inflammation, but lateral herniation may produce compression in the lateral recess or intervertebral foramen.

Contrast-enhancing fears in the annulus fibrosus or disk protrusions are widely accepted as common sources of back pain.

1.4. Degenerative Conditions

Lumbar spinal stenosis (LSS) describes a narrowed lumbar spinal canal. Neurogenic claudication consists of pain, typically in the back and buttocks or legs, that is brought on by walking or standing and relieved by sitting. Unlike vascular claudication, symptoms are often provoked by standing without walking. Unlike lumbar disk disease, symptoms are usually relieved by sitting. The patient feels relief in a flexed position because flexed positions increase the anteroposterior spinal canal diameter and reduce intraspinal venous hypertension, producing pain relief. Focal weakness, sensory loss, or reflex changes may occur when spinal stenosis is associated with neural foraminal narrowing and radiculopathy.

1.5. Spondylosis and Spondylolisthesis

Spondylosis, or osteoarthritic spine disease, typically occurs in later life and primarily involves the cervical and lumbosacral spine. Patients often complain of back pain that increases with movement, is associated with stiffness, and is better with inactivity. Osteophytes, combined disk osteophytes, or a thickened ligamentum flavum may cause or contribute to central spinal canal stenosis, lateral recess stenosis, or neural foraminal narrowing.

Spondylolisthesis is the anterior slippage of the vertebral body, pedicles, and superior articular facets, leaving the posterior elements behind. Spondylolisthesis can be associated with spondylolysis, congenital anomalies, degenerative spine disease, or other causes of mechanical weakness of the pars interarticularis (e.g., infection, osteoporosis, tumor, trauma, and earlier surgery). The slippage may be asymptomatic or may cause LBP, nerve root injury (the L5 root most frequently), symptomatic spinal stenosis, or CES in rare, severe cases. A "step-off" on palpation or tenderness may be elicited near the segment that has slipped (most on L5 or occasionally L5 on S1).

1.6. Neoplasms

Back pain is the most common neurologic symptom in patients with systemic cancer and is the presenting symptom in 20%. The cause is usually vertebral body metastasis (85-90%) but can also result from the spread of cancer through the intervertebral foramen (especially with lymphoma), carcinomatous meningitis, or metastasis to the spinal cord. The thoracic spine is most often affected. Cancer-related back pain tends to be constant, dull, unrelieved by rest, and worse at night. By contrast, mechanical causes of LBP usually improve with rest.

1.7. Infections/Inflammation

- Vertebral osteomyelitis is most often caused by hematogenous seeding of staphylococci, but other bacteria or tuberculosis (Pott's disease) may be responsible. The primary source of infection is usually the skin or urinary tract. Other common sources of bacteremia are IV drug use, poor dentition, endocarditis, lung abscess, IV catheters, or post-operative wound sites. Back pain at rest, tenderness over the involved vertebra, and an elevated erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) are the most common findings in vertebral osteomyelitis.
- Spinal epidural abscess presents with back pain (aggravated by movement or palpation of the spinous process), fever, radiculopathy, or signs of spinal cord compression.
- Lumbar adhesive arachnoiditis with radiculopathy is due to fibrosis following inflammation within the subarachnoid space. The fibrosis results in nerve root adhesions and presents as back and leg pain associated with multifocal motor, sensory, or reflex changes. Causes of arachnoiditis include multiple lumbar operations (most common in the United States), chronic spinal infections (especially tuberculosis in the developing world), spinal cord injury, intrathecal hemorrhage, myelography (rare), intrathecal injections (glucocorticoids, anesthetics, or other agents), and foreign bodies.

1.8. Trauma

A patient complaining of back pain and an inability to move the legs may have a spine fracture or dislocation; fractures above L1 place the spinal cord at risk for compression. Vertebral fractures frequently occur in the absence of trauma in association with osteoporosis, glucocorticoid use, osteomyelitis, or neoplastic infiltration.

- Sprains and strains: The terms low back sprain, strain, and mechanically induced muscle spasm refer to minor, self-limited injuries associated with lifting a heavy object, a fall, or a sudden deceleration, such as in an automobile accident. The pain is usually confined to the lower back. Patients with paraspinal muscle spasms often assume unusual postures.
- Traumatic vertebral fractures: Most traumatic fractures of the lumbar vertebral bodies result from injuries producing anterior wedging or compression. Traumatic vertebral fractures are caused by falls from a height, sudden deceleration in an automobile accident, or direct injury.

1.9. Metabolic Causes

- Osteoporosis: Immobilization, osteomalacia, the post-menopausal state, renal disease, multiple myeloma, hyperparathyroidism, hyperthyroidism, metastatic carcinoma, or glucocorticoid use may accelerate osteoporosis and weaken the vertebral body, leading to compression fractures and pain. The most common non-traumatic vertebral body fractures are due to a post-menopausal cause or to osteoporosis in adults >75 years old. The sole manifestations of a compression fracture may be localized back or radicular pain exacerbated by movement and often reproduced by palpation over the spinous process of the affected vertebra.
- Osteosclerosis: Osteosclerosis, an abnormally increased bone density often due to Paget's disease, can sometimes be a source of back pain. It may be associated with an isolated increase in alkaline phosphatase in an otherwise healthy older person. Spinal cord or nerve root compression can result from bony encroachment.

1.10. Autoimmune Inflammatory Arthritis

Autoimmune inflammatory disease of the spine can present with the insidious onset of low back, buttock, or neck pain. Examples include rheumatoid arthritis (RA), ankylosing spondylitis, reactive arthritis, psoriatic arthritis, or inflammatory bowel disease.

1.11. Congenital Anomalies of the Lumbar Spine

- Spondylolysis is a bony defect in the vertebral pars interarticularis (a segment near the junction of the pedicle with the lamina), a finding present in up to 6% of adolescents. The cause is usually a stress microfracture in a congenitally abnormal segment. Spondylolysis is the most common cause of persistent LBP in adolescents and is often associated with sports-related activities.
- Scoliosis refers to an abnormal curvature in the coronal (lateral) plane of the spine. With kyphoscoliosis, there is, in addition, a forward curvature of the spine. The abnormal curvature may be congenital, due to abnormal spine development, acquired in adulthood due to degenerative spine disease, or progressive due to paraspinal neuromuscular disease.
- Spina bifida occulta (closed spinal dysraphism) is a failure of closure of one or several vertebral arches posteriorly; the meninges and spinal cord are normal.
- Tethered cord syndrome usually presents as a progressive cauda equina disorder, although myelopathy may also be the initial manifestation. The patient is often a child or young adult who complains of perineal or perianal pain, sometimes following minor trauma.

1.12. Referred Pain from Visceral Disease

Diseases of the thorax, abdomen, or pelvis may refer to pain in the spinal segment that innervates the diseased organ. Occasionally, back pain may be the first and only manifestation. Upper abdominal diseases generally refer to pain in the lower thoracic or upper lumbar region (eighth thoracic to the first and second lumbar vertebrae), lower abdominal diseases to the mid-lumbar region (second to fourth lumbar vertebrae), and pelvic diseases to the sacral region. Local signs (pain with spine palpation and paraspinal muscle spasm) are absent, and little or no pain accompanies routine movements.

2. LITERATURE REVIEW

The references to *Katishoola* are found scattered in the Ayurvedic literature. Although *Katishoola* is a commonly encountered problem in clinical practice, it has not been described in the *Bhrihatrayi* as a separate disease. However, various *Acharyas* have mentioned *Katishoola* as a symptom of various diseases such as *Ajeerna, Amavata, Pakwashayagata Vata, Asthimajjagata Vata, Sandhigata Vata, Snayugata Vata*. In some diseases, pain may also be referred to as *Katipradesha,* such as *Amashaya-Pakwashaya Vrana, Pitta Ashmari, Mutrashayakala Shotha*, and a few gynecological disorders.

A brief description of *Katishoola* can be found in *Bhavaprakasha Amavata Rogadhikara* and *Gada Nigraha Vatavyadhi Rogadhikara*.

2.1. *Charaka Samhita*

In *Charaka Samhita,* references related to *Katishoola* can be found scattered under different diseases. *Acharya Charaka* has not described *Katishoola* as a disease, but he has mentioned the symptoms of spinal diseases such as *Prushthagraha, Trikagraha* as *Vataja Nanatmaja Vyadhi in Cha.Su.20*. Excess consumption of *Katu rasa* has been mentioned to cause the *Vata vikara* of *Prushtha*.

Charaka has described *Katishoola* as a symptom of *Gridhrasi*.[4] *Trikavedana* has been described as a symptom of *Pakwashayagata Vata. Trika* and *Prushtha Vedana* have been mentioned as a symptom of *Gudashrita Vata*. In *Vataja Jwara*, different types of pain in *Katipradesha* and *Prushtha* are mentioned. *Katishoola, Trikashoola,* and *Prushthashoola* have been described as the symptoms of *Vataja Arsha. Katigraha* has been mentioned as a symptom of *Vrukkaja Vidradhi.*

2.2. *Sushruta Samhita*

Acharya Sushruta has mentioned *Katishoola* as a symptom of *Vataja Arsha, Vankshanotha Vidradhi,*[5] *Bhagna, 7th stage of Sarpa visha, Akshepaka* and an indirect reference can be drawn from *Dalhana* commentary about *Pakwashayagata Vata* that along with *Trika Vedana* there will be *Jangha, Trika*, and *Prushtha Vedana*.

2.3. *Ashtanga Samgraha* and *Ashtanga Hridaya*

In *Ashtanga Samgraha* and *Ashtanga Hridaya, Acharya Vagabhatta* has described *Katishoola* as a symptom of *Vataja Jwara* and Madhyama Margashrita Vyadhi.[6] He also mentioned *Katishoola* as a symptom of *Pakwashayagata Vata*. The reference of *Katitoda* and *Katibheda* as a *Poorvarupa* of *Vatarakta* can also be found.

2.4. *Madhava Nidana*

Madhava Nidana provides a detailed description of *Vatavyadhi,* including all the symptoms described by *Acharya Charaka, Sushruta*, and *Vagabhatta. Acharya Madhavakara* described that *Katishoola* manifests as a symptom in various diseases such as *Amavata*,[7] *Samgraha Grahani, Vataja Arsha, Vatanubandhi Raktarsha*, and *Anaha*.

2.5. *Kashyapa Samhita*

Acharya Kashyapa has mentioned *Asthi* and *Majja* as the sites of *Vata dosha*. This indicates that *Prushtha* is also one of the *sthanas* of *Vata dosha*. Hence, when *Vata dosha* gets vitiated in the *Prushtha* region, or the vitiated *Vata dosha* affects the *Prushtha* region, it causes *Katishoola*. *Acharya Kashyapa* has also described *Katishoola* as one of the complications that occurs due to *Dushprajata* and has prescribed *Swedana* treatment for it.[8]

2.6. *Bhela Samhita*

The classification of *Vatavyadhi* into two groups – *Sarvanga and Ekanga* can be found in *Bhela Samhita*. All the pain-dominant diseases of the *Prushtha and Kati* regions are enlisted in *Ekanga Vatarogas*.[9] *Acharya Bhela* has described *Mandagni* and hindered the movement of *Vata* as the main causes of *Katishoola*. He also mentioned *Katishoola* as a complication of many diseases, such as *Vataja Kasa*. The reference to *Yapana Basti* as the treatment modality of *Katishoola* can be found in *Bhela Samhita*.

2.7. *Sharangdhara Samhita*

In *Sha.Pu.Kha.7 Acharya Sharangdhara* has mentioned *Katishoola* as one of the *Vata Nanatmaja Vyadhi*.[10] *Aadhmalla* has described that the *Stambha* (stiffness) in *Katipradesha* causes a specific type of pain, i.e., *Vedana vishesha,* and named it *Katishoola*. In addition, he also mentioned various treatments for *Katishoola* in detail.

2.8. *Bhava Prakasha*

The reference to *Katishoola in Bhavaprakasha* can be found in *Mahdyama Khanda* chapter 24/115. *Bhavamishra* has described *Katishoola* as a separate disease in *Amavata Rogadhikara* and referred to it as *Trikashoola* and has mentioned the involvement of *Vata dosha* in its occurrence. He has specified treatments such as *Baluka Sweda*, formulations such as *Trayodashanga Guggulu*,[11] and *Rasnasaptaka Kwatha,* along with *Shunthi Churna* to relieve the pain.

2.9. *Harita Samhita*

Acharya Harita has described the *Vata Vikara* and classified them according to five types of *Vata*. He mentioned 16 diseases for each type. *Acharya Harita* mentioned *Katishoola* as a symptom of *Amavata* and *Gridhrasi* and has also mentioned some *yogas* together for *Gridhrasi, Amavata,* and *Katishoola*.[12]

2.10. *Yoga Ratnakara*

In *Yogaratnakara*, terms such as *Katishoola, Kativata*, *and Katipeeda* have been used in "*Asheeti Vataroga Chikitsa*" to denote the backache. In *Yogaratnakara*, the references for *Katishoola* can be found as a symptom of *Vataja Arsha*,[13] *Gudashrita Vata*,[14] and *Pakwashayagata Vata*.[15]

2.11. *Gada Nigraha*

In the introduction of *Vatavyadhi Rogadhikara, Acharya Shodhala* mentioned that *Vatavyadhi* is the root cause of all other diseases. The detailed description of *Katishoola* as a separate disease can only be found in *Gadanigraha* with the name "*Katigraha*" in the "*Chikitsa Khanda Vatarogadhikara*."[16] *Acharya Shodhala* has specifically mentioned the use of *Triyodashang Guggulu* for the treatment of *Katishoola*. He also mentioned other *yogas,* such as *Panchmooli yoga* and *Shunthiyadi payas*. He described the use of *Erand Taila* with *Dashmoola Kwatha or Shunthi Kwatha* in all types of *Katishoola*.

2.12. Some Other References

- In *Rasa Ratna Samucchaya*, *Katishoola* has been mentioned as an invariable symptom in the context of *Amavata*.
- In *Bhrita Nighantu*[17] and *Dhanvantari Nighantu*,[18] it is explained in the context of *Bhagandara* and its management.
- *Bhaishajya Ratnawali* described the treatment aspects and explained, in particular, the use of *Guggulu Kalpana* in *Katishoola*.[19]

2.13. Treatment of *Katishoola*

Katishoola is a *Kshaya-janya Vatavyadhi,* and the line of treatment includes *Ama pachana, Agnivardhana, Vata shaman, Anulomana, Dhatu Poshana*, and *Santarpana*. Hence, all the treatment modalities, whether internal or external, that alleviate the *Vata dosha* shall be used.

2.13.1. Shamana Chikitsa

2.13.1.1. Internal

- *Churna: Rasna Churna, Ashwagandha Churna, Bala Churna, Shatavari Churna, Sudarshana Churna*, and *Ajmoodadi Churna.*
- *Kashaya: Dashmoola Kashaya, Rasnadi Kashaya, Rasnasaptak Kashaya, Shunthyadi Kashaya*, and *Rasna Shunthyadi Kashaya.*
- *Guggulu: Trayodashanga Guggulu, Yograja Guggulu, Simhanada Guggulu*, and *Vatari Guggulu.*
- *Rasa Aushada: Vata Vidhvansana Rasa, Vata Gajankusha Rasa, Yogendra Rasa, Bhrita Vata Chintamani Rasa, Rasraja rasa*, and *Vatari Rasa.*
- *Taila pana: Rasona Taila, Bala Taila, Mahanarayan Taila, Moolaka Taila*, and *Nakuladya Taila.*

2.13.1.2. External

Abhyanga, Nadi Sweda, Mardana, Veshtana (Traction), Lepa, Kati Basti, and *Mud Therapy.*

2.13.2. Shodhana Chikitsa

- *Poorva Karma: Deepana, Ama pachana, Vata Anulomana, Snehana*, and *Swedana.*
- *Pradhana Karma: Mridu Virechana, Niruha Basti*, and *Anuvasana Basti.*
- *Paschata Karma: Samsarjana Krama.*

Indications of various *Basti Kalpana in Katishoola:*

- *Erandamooladi Niruha Nasti*
- *Shampakadi Niruha Basti*
- *Ksheera Basti*
- *Vaitrana Basti*
- *Pippalyadi Anuvasana Basti*
- *Shatyadi Anuvasana Basti*

3. DISCUSSION

As Lumbar Spondylosis is a musculoskeletal disorder, *Katishoola,* when correlated with Lumbar Spondylosis, can be considered a symptom of *Asthigata Vata* or *Sandhigata Vata* considering its peculiar features such as pain, stiffness, and restricted movements. *Katishoola* is a *Vatavyadhi. Vataprakopaka ahara-vihara* leads to an increase in *Vata dosha*. Increased *vata dosha* causes *Kapha dosha kshaya,* which further causes reduced lubrication at the site of lumbar joints. *Kapha dosha* not only lubricates the joints but also provides nourishment to the lumbar joints. Reduction in the lubrication results in painful and restricted joint movement. Hence, the treatment opted for should be such that it pacifies the vitiated *Vata dosha*.

4. CONCLUSION

Katishoola is one of the most common presenting complaints seen in the male and female population, especially after 40 years of age. Nowadays, *Katishoola* is also being noticed in the younger generation. Hence, early diagnosis is necessary to start the effective treatment and provide relief to the patient.

5. ACKNOWLEDGMENT

Nil.

6. AUTHORS' CONTRIBUTIONS

All the authors contributed equally to the design and execution of the article.

7. FUNDING

Nil.

8. ETHICAL APPROVALS

This study does not require ethical approval as it is a review study.

9. CONFLICTS OF INTEREST

Nil.

10. DATA AVAILABILITY

This is an original manuscript and all data are available for only review purposes from principal investigators.

11. PUBLISHERS NOTE

This journal remains neutral with regard to jurisdictional claims in published institutional affiliation.

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How to cite this article:
Shrivastava S, Mishra J, Mishra S, Upadhyay DK. A Review Article on *Katishoola* with Special Reference to Lumbar Spondylosis. IRJAY. [online] 2025;8(5);73-78.
Available from: https://irjay.com
DOI link- https://doi.org/10.48165/IRJAY.2025.80513