

Research Article





# Degenerative disc disease: causes, symptoms, anatomy, market trends, and emerging treatment strategies

#### **Abstract**

Degenerative disk disease (DDD) is a progressive condition characterized by the breakdown of intervertebral disks. This represents a significant concern in spinal health due to its impact on flexibility, mobility, and quality of life. Although the exact causes of this disease remain unknown, its prevalence increases with age, and is influenced by several risk factors, including prior injury, excessive use, and repetitive activities. DDD presents a wide array of symptoms, from back or neck pain to numbness or tingling in the limbs, with a varying degree of pain, highlighting its complex nature. Intervertebral disks are vital to the vertebral column's structure and function and undergo degenerative changes with aging, resulting in hydration loss, disc height reduction, and potential disc herniation. This can cause significant discomfort. Despite the avascular nature of these discs, they serve as shock absorbers and facilitate a range of spinal movements. As of 2021, the global market for DDD treatment was valued at 26.05 billion USD and is projected to reach 45.92 billion USD by 2029. The increasing market size, combined with the launch of innovative treatment products, signifies the growing emphasis on addressing DDD. The high prevalence of DDD-induced low back pain and the higher incidence in low- and middle-income countries underscore the urgent need for effective management strategies. This paper provides a comprehensive overview of DDD, examining its causes, risk factors, symptoms, anatomical aspects, and market trends, aiming to promote understanding and guide future research and treatment approaches.

**Keywords:** degenerative disc disease, intervertebral disc, spinal disorders, low back pain, disc degeneration

Volume 10 Issue 4 - 2023

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Received: August 20, 2023 | Published: September 04, 2023

**Abbreviations:** DDD, degenerative disk disease; MRI, magnetic resonance imaging; CT, computed tomography; LMICs, low- and middle-income countries; HICs, high-income countries

#### Introduction

Degenerative disk disease (DDD) is a chronic condition marked by the gradual deterioration of intervertebral disks which are essential cushioning structures in the spine. As these disks degenerate, symptoms of pain and discomfort become a notable concern in spinal health.<sup>1-3</sup> The spinal disks, which act like shock absorbers between vertebrae, degrade. This impairs flexibility and functionality, hindering comfortable movements such as bending and twisting.<sup>2,3</sup>

Although the chances of DDD increases with age, the etiology surrounding its onset is still unknwon.<sup>4</sup> Most individuals experience some degree of spinal degeneration after the age of 70.<sup>2</sup> However, not all individuals with DDD experience noticeable pain, highlighting symptom variability and the complex nature of this condition.<sup>2,3</sup> Risk factors for DDD include age, previous injuries, repeated actions, and overuse.<sup>1</sup> These are some of the few things which accelerate damage to spinal disks, causing them to degrade.<sup>1-3</sup>

The signs of DDD are varied: pain in the back or neck, paresthesia in the arms or legs,<sup>3</sup> pain spreading to the lower back and buttocks, weak leg muscles, and an increase in pain during actions like bending or lifting. <sup>1-3</sup> By examining DDD's causes, risks, and symptoms, we can better understand how it affects the spine. This understanding allows for the development of more effective strategies that can be used to diagnose, manage, and treat this condition.

# **Anatomy of intervertebral disks**

# Normative anatomy

The intervertebral discs, an essential component of the vertebral column, play a critical role in maintaining its structure and function. These fibrocartilaginous cushions serve as connectors between adjacent vertebral bodies, helping to stabilize and link them together. Firmly anchored to the bodies of neighboring vertebrae, each disc contributes to their strong union. 5.8

Made of three primary components, as shown in Figure 1,7 – the nucleus pulposus, annulus fibrosus, and cartilaginous end-plates – the intervertebral disc exhibits a complex structure.9 The nucleus pulposus, a soft, gel-like center situated at the core, is enveloped by the annulus fibrosus, which consists of concentric layers of pliable fibrocartilage.8 While the annulus fibrosus provides strength and stability to the disc, the nucleus pulposus enables shock absorption and balanced force distribution.<sup>5,9</sup>

The cartilaginous end-plates are on the upper and lower surfaces of each vertebral body, giving a smooth surface for the disc. Additionally, these end-plates facilitate nutrient exchange between the disc and the neighboring vertebral bodies. Although the intervertebral discs are mostly avascular, except for the outer annulus that receives limited blood supply, essential nutrients like glucose and oxygen reach the avascular regions through diffusion.

Regarding their functions, intervertebral discs serve crucial roles in providing structural support and facilitating movement. During weight-bearing activities, they act as cushions, stopping direct contact



and offering padding between vertebrae. Additionally, these discs enable flexibility and motion between neighboring vertebrae, making possible different spinal movements.<sup>5,8</sup> Lastly, they function as shock absorbers, efficiently spreading forces and protecting the vertebral column from everyday impacts.<sup>6</sup>

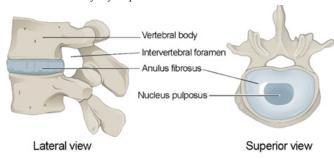


Figure 1 Primary components of intervertebral discs.<sup>7</sup>

The image illustrates the key structures of the intervertebral discs, showcasing both the lateral and superior views. These critical components include the vertebral body, the intervertebral foramen, the anulus fibrosus, and the nucleus pulposus.

# Anatomy of degenerative disc disease

However, as intervertebral discs age, degenerative changes occur. Gradual loss of osmotic pressure in the nucleus pulposus leads to dehydration and a reduction in disc height. In the process of degeneration, nociceptive nuclear material may leak through the outer rim of the annulus fibrosus, causing discogenic pain, a type of pain arising from the intervertebral disc itself. The leaked material can irritate surrounding nerves, causing localized pain in the back or neck. In advanced stages of degeneration, the tearing of the annulus fibrosus can result in a herniated disc.

A herniated disc, as shown in Figure 2,<sup>11</sup> occurs when the gellike substance from the nucleus pulposus leaks through the annulus fibrosus, causing the disc to bulge or rupture. This can cause compression or irritation of nearby spinal nerves, leading to radiating pain, numbness, tingling, or muscle weakness in the limbs.<sup>8</sup> Such herniated discs often cause significant pain and discomfort.



Figure 2 Example of disc problems.11

The image illustrates various types of disc problems that can impact the intervertebral discs. These issues include degenerated discs, bulging discs, herniated discs, thinning discs, and disc degeneration accompanied by the formation of osteophytes.

The cumulative effects of dehydration, disc height reduction, annular tears, and herniation can lead to a loss of structural integrity in the degenerated disc. This can result in decreased stability and impaired function of the affected spinal segment. The disc's ability to cushion and distribute forces between adjacent vertebrae is compromised, affecting the overall mechanical behavior of the spinal column.

# Market size

## Global market size

In 2021, the degenerative disc disease treatment market size reached 26.05 billion USD, and experts project it to grow to 45.92 billion USD by 2029, exhibiting a compound annual growth rate (CAGR) of 7.4% during the forecast period.<sup>5</sup> By 2030, it is estimated that the global degenerative disc disease market will surpass \$4,525.9 million USD, with a current valuation of \$2,235.1 million USD in 2023.<sup>6</sup> These figures indicate a substantial increase in market size, highlighting the growing importance of addressing degenerative disc disease.

Looking specifically at the market in 2022, as shown in Figure 3, <sup>12</sup> the degenerative disc disease treatment sector accounted for 24 billion USD, and experts anticipate a CAGR of 7.2% that would lead to a market size of 49.7 billion USD by 2032. <sup>1</sup> These statistics demonstrate sustained growth and highlight the potential market opportunities within the degenerative disc disease treatment sector.

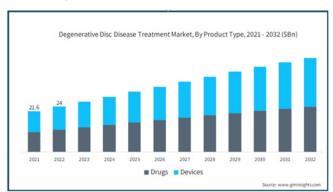


Figure 3 Degenerative disc disease treatment market. 12

The following image shows the degenerative disc disease treatment market based on either drugs and devices. The graph shows the predicted growth of both products in the market within the next decade.

# Market size in the United States

In 2021, the estimated degenerative disc disease treatment market size in the United States was 11.3 Billion USD, as shown in Figure 4.<sup>12</sup> Furthermore, it is estimated that nearly 80% of adults will experience low back pain at some point in their lives, with DDD being a common cause.<sup>5</sup> The high prevalence of low back pain emphasizes the significance of addressing DDD as a healthcare concern in the United States.

Furthermore, a report by Technavio identifies the launch of innovative products as a key trend propelling the growth of the degenerative disc disease market in the United States.<sup>13</sup> This suggests that advancements in treatment options and therapeutic approaches are poised to shape the market landscape in the country, leading to further growth and development opportunities.

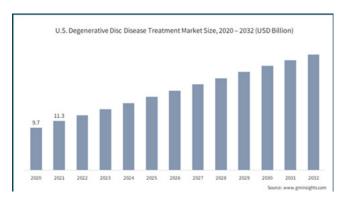


Figure 4 U.S. degenerative disc disease treatment market size.<sup>12</sup>

The image illustrates the market for degenerative disc disease treatment in the United States. It presents a graph that forecasts the growth of various products within this sector over the coming decade.

#### Market size in China

According to a study, approximately 266 million individuals (equivalent to 3.63% of the global population) receive a lumbar degenerative disc disease diagnosis annually, with Europe experiencing the highest estimated incidence (5.7%) and Africa the lowest (2.4%). Notably, low- and middle-income countries (LMICs) account for nearly four times as many cases of degenerative disc disease and low back pain compared to high-income countries (HICs). Although specific data on the market size of DDD in China is currently unavailable, these figures underscore the significant burden of the disease in different regions and emphasize the necessity for effective treatment options.

In conclusion, the global market size for degenerative disc diseases is expected to witness substantial growth in the next decade, with a projected CAGR of approximately 7%.<sup>4</sup> While specific data regarding the market size of DDD in China or the United States is lacking, it is evident that DDD is a prevalent cause of low back pain worldwide. Furthermore, the introduction of innovative products is anticipated to drive growth in the United States market.<sup>5,13,14</sup> These trends, coupled with the increasing prevalence of degenerative disc disease, highlight the significance of continued research and development efforts in addressing this major health issue.

# Market segments and trends

#### Segmentation of market

The market for degenerative disc disease can be divided into several segments, mainly categorized by the indication of the disease. These segments include degenerative disc disease, traumas

Table I Market segments related to degenerative disc disease

& fractures, complicated deformities, and others.<sup>15</sup> Among these segments, degenerative disc disease is expected to dominate the market and hold the largest share in 2022. This dominance can be attributed to the increasing number of disc replacement procedures and the growing demand for artificial discs, indicating a preference for surgical interventions in managing this condition.

The sector focusing on complicated deformities is anticipated to witness significant growth. This growth can be attributed to factors such as the rising rate of the geriatric population and the increasing number of births with abnormalities that cause modifications or misalignments in the spinal column. These factors drive the demand for treatments and corrective measures in managing complex deformities <sup>15</sup>

Furthermore, the traumas & fractures market segment is projected to experience substantial growth between 2022 and 2030. This growth is primarily fueled by the expanding geriatric population and the rising prevalence of bone degenerative disorders like osteoporosis and rheumatoid arthritis. Such conditions make individuals more susceptible to traumas and fractures, thereby increasing the demand for related treatments.<sup>15</sup>

## **Emerging trends**

The global market for degenerative disc disease treatment is expected to witness a Compound Annual Growth Rate (CAGR) of 7.4% during the forecast period of 2021-2029. This growth can be attributed to the increasing geriatric population worldwide and the rising prevalence of age-related diseases, including degenerative disc disease, among the elderly. Additionally, the market growth is further driven by the escalating investments in research and development (R&D) efforts aimed at exploring innovative drugs and therapies. These investments seek to enhance treatment options and address the unmet needs in effectively managing degenerative disc disease.

Key market players are also adopting inorganic growth strategies, such as obtaining product approvals, to expand their market presence and capitalize on the growing demand for degenerative disc disease treatments. These product approvals by market players are expected to drive the global degenerative disc disease treatment market throughout the forecast period.<sup>17</sup>

Advancements in diagnostic techniques, treatment modalities, and emerging technologies represent other promising trends that can significantly impact the market. For instance, Smart Soft Healthcare recently received 510(k) approval from the U.S. Food and Drug Administration (FDA) for their software designed to assist surgeons in planning spinal surgeries with higher precision and accuracy. These advancements contribute to the overall management of degenerative disc disease and lead to improved patient outcomes (Tables 1&2).<sup>17</sup>

Segment	Description
Degenerative Disc Disease	This segment encompasses the degenerative disc disease population, characterized by the gradual deterioration of intervertebral discs, leading to pain and mobility issues. It includes individuals seeking disc replacement procedures and those in need of artificial discs for pain management and functional restoration. The rising prevalence of degenerative disc disease and the growing preference for surgical interventions drive the growth of this segment.
Traumas and Fractures	This segment focuses on those experiencing spinal traumas and fractures often from accidents. It covers conditions including vertebrae fractures and spinal cord injuries. Growth is due to the increasing geriatric population prone to fractures and prevalence of disorders like osteoporosis and rheumatoid arthritis.
Complicated Deformities	This segment encompasses individuals with complex spinal deformities (e.g. scoliosis, kyphosis, etc.). These conditions may result from congenital factors, birth defects, or acquired deformities. The segment is driven by factors like the growing rate of the elderly, who may develop degenerative deformities, and the increase in births with spinal abnormalities needing modification or realignment for functionality.

Table 2 Trends impacting degenerative disc disease treatment market

Trend	Description
Advancements in Diagnostic Techniques	Rapid advancements in diagnostic techniques, such as imaging modalities (MRI, CT scans), genetic testing, and biomarker identification, enable more accurate and early detection of degenerative disc disease. This aids in precise diagnosis, treatment planning, and monitoring of the condition. Additionally, the integration of artificial intelligence (AI) and machine learning (ML) algorithms enhances the interpretation and analysis of diagnostic results, leading to improved patient outcomes.
Advancements in Treatment Modalities	Ongoing research and development in degenerative disc disease focuses on expanding treatment options, including minimally invasive techniques like endoscopic discectomy and laser spine surgery (reducing trauma, faster recovery, improved comfort), regenerative methods like stem cell therapy and tissue engineering (restoring damaged discs, promoting regeneration), and new pharmacological approaches including targeted drug systems and disease-modifying drugs.
Emerging Technologies	Emerging technologies are revolutionizing the treatment of degenerative disc disease. Robotic-assisted surgeries grant surgeons increased precision, dexterity, and visualization during complex procedures, resulting in improved surgical outcomes. Virtual reality (VR) and augmented reality (AR) technologies enable surgeons to simulate and practice surgeries, enhancing their skills and reducing surgical errors. Moreover, the integration of telemedicine and remote patient monitoring allows for remote consultations, follow-ups, and data collection, enabling efficient healthcare for patients with degenerative disc disease.
Adoption of Inorganic Growth Strategies	Key market players are increasingly adopting inorganic growth strategies to strengthen their market position and expand their product portfolios. This includes strategic collaborations, partnerships, mergers, and acquisitions to gain access to complementary technologies, expertise, and geographic markets. Additionally, product approvals by regulatory authorities, such as the FDA, play a crucial role in market penetration and commercialization of innovative treatments for degenerative disc disease. These inorganic growth strategies foster innovation, accelerate market entry, and contribute to the overall growth and development of the degenerative disc disease treatment market.

In summary, the market for degenerative disc disease exhibits various segments based on disease indication, including degenerative disc disease, traumas & fractures, complicated deformities, and others. The largest segment is projected to be degenerative disc disease, primarily driven by the increasing number of disc replacement procedures and the growing demand for artificial discs. Promising trends impacting the market include advancements in diagnostic techniques, treatment modalities, emerging technologies, and the adoption of inorganic growth strategies by key market players. These trends contribute to the comprehensive understanding and assessment of the degenerative disc disease treatment market.<sup>15-17</sup>

#### **Products**

# **Existing products**

Degenerative disc disease (DDD) presents formidable challenges in the realm of medical treatment. Tissue engineering treatments have emerged as potential solutions, with stem cell therapy and growth factor-based therapies being the go-to approaches. These innovative treatments seek to spur tissue regeneration and repair within degenerated discs by introducing fresh cells or growth factors to the affected area. Nonetheless, it is crucial to acknowledge the limitations and potential risks entailed, including the peril of infection or immune rejection.<sup>2</sup>

The landscape of tissue engineering has witnessed remarkable advancements, giving rise to novel techniques like 3D bioprinting and scaffold-based therapies. These cutting-edge methodologies hold immense promise in revitalizing functional spinal discs. Through 3D bioprinting, the precise placement of cells and biomaterials becomes feasible, enabling the creation of intricate structures that faithfully mimic the natural architecture of intervertebral discs. On the other hand, scaffold-based therapies employ biocompatible materials as supportive frameworks to facilitate cell growth and tissue regeneration.<sup>2</sup> While these trailblazing approaches offer distinctive features and potential benefits, their true effectiveness necessitates ongoing research endeavors.

The surgical treatment landscape for degenerative disc disease is divided into two primary categories: traditional surgeries and minimally invasive surgeries. Each category encompasses a variety of approaches tailored to address the symptoms and root causes of this condition. Within this comprehensive overview, we delve deeper into the surgical options, exploring their objectives, methodologies, and applications.

#### Products/Treatments in clinical

Traditional surgeries encompass well-established procedures such as discectomy, laminectomy, and spinal fusion. Discectomy is a venerable surgical technique used to alleviate the symptoms of degenerative disc disease, particularly in cases involving herniated or bulging discs. The crux of discectomy lies in the elimination of the damaged disc and any accompanying bone spurs that exert undue pressure on the spinal cord or adjacent nerve roots. 18 By relieving this compression, discectomy aims to assuage pain and restore normal nerve function.

# Laminectomy

Laminectomy, another time-honored surgical approach, is primarily employed to tackle spinal stenosis. This condition arises from the narrowing of the spinal canal, leading to spinal cord or nerve root compression. Laminectomy entails the removal of a portion of the vertebral bone called the lamina, thereby mitigating constriction and alleviating related symptoms.

# Spinal fusion

Spinal fusion, an all-encompassing traditional surgical procedure, often serves as a recommended course of action for degenerative disc disease, spinal stenosis, and spondylolisthesis. The core objective of spinal fusion lies in stabilizing the spine and reducing pain. This is achieved by fusing two or more adjacent vertebrae together, promoting the growth of new bone and creating a solid, rigid structure. The cessation of movement between affected vertebrae brought about by spinal fusion can relieve pain stemming from damaged discs and restore spinal stability.

# Minimally invasive surgeries

Minimally invasive surgeries have gained traction as alternatives for treating degenerative disc disease. This category encompasses procedures like microdiscectomy and endoscopic techniques. Microdiscectomy represents a minimally invasive surgical approach aimed at addressing degenerative disc disease. By removing a small portion of the herniated disc through a tiny incision, microdiscectomy aims to alleviate pressure on affected nerves while minimizing tissue damage and facilitating speedier recovery.<sup>20</sup> The advantages of microdiscectomy include shorter hospital stays, reduced postoperative discomfort, and quicker return to daily activities as compared to traditional surgeries.

# **Endoscopic procedures**

Endoscopic procedures have risen to prominence as minimally invasive alternatives for treating degenerative disc disease. These procedures involve the utilization of an endoscope, a slender tube fitted with a light and camera, to visualize and treat the affected area with pinpoint accuracy. This approach mitigates tissue damage, minimizes scarring, and expedites recovery time. Endoscopic procedures strive to optimize patient outcomes by reducing the invasiveness of surgery while effectively addressing the underlying issues.

The selection of a specific surgical intervention for degenerative disc disease hinges on a multitude of factors, including symptom severity, the location of the affected disc, and the overall condition of the patient. Traditional surgeries, though more invasive, may be necessary for severe cases or when minimally invasive options are ill-suited. Conversely, minimally invasive surgeries offer advantages such as swifter recovery times, reduced tissue damage, and improved patient outcomes, but their applicability varies depending on individual circumstances. In conclusion, surgical treatments for degenerative disc disease span a gamut of traditional and minimally invasive procedures. These interventions aim to alleviate nerve compression, reduce pain, and enhance overall functionality. By comprehending the intricacies of each surgical option, patients and healthcare professionals can make informed decisions tailored to individual circumstances, with the goal of achieving optimal outcomes and enhancing quality of life.

## Products/Treatments in development

# Hydrafil<sup>TM</sup> injectable gel<sup>21</sup>

A promising experimental treatment for degenerative disc disease (DDD) is Hydrafil<sup>TM</sup>, an injectable gel. This innovative gel has demonstrated its potential in reducing chronic low back pain associated with DDD. In a recent small-scale study, participants who received injections of Hydrafil<sup>TM</sup> into the affected discs experienced significant pain reduction and improved physical function. One key advantage of this treatment is that it can be administered without the need for open surgery. The gel works by restoring the structural integrity of the discs, providing potential relief for individuals suffering from DDD.

# Platelet-based treatments (platelet-rich plasma, platelet lysate, and platelet poor plasma)<sup>22</sup>

This clinical study aims to comprehensively evaluate and compare two platelet-based treatments—platelet-rich plasma, platelet lysate, and platelet poor plasma—with sham procedures for the management of degenerative disc disease. The study follows a single-blind, randomized, and placebo-controlled design, ensuring rigorous scientific standards. Participants will be monitored at regular intervals, with follow-up visits scheduled at 3 and 12 months after the injections. By investigating the efficacy of these platelet-based treatments, researchers seek to provide valuable insights into their potential benefits for individuals with degenerative disc disease.

# NuVasive interbody implants for spinal surgery

The objective of this clinical study is to assess the safety and performance of NuVasive interbody implants in patients undergoing

thoracic and/or lumbar spine surgery for degenerative conditions, including degenerative disc disease. Interbody implants are medical devices specifically designed for thoracic and/or lumbar spine surgery, aiming to address degenerative conditions. These implants are placed between the vertebrae to restore stability, alleviate nerve compression, and promote fusion of the affected spinal segments. By mimicking the natural function of intervertebral discs, interbody implants provide support and maintain appropriate spacing between the vertebrae. They can take various shapes and be made of materials like titanium or other biocompatible substances. Surgeons carefully select and position these implants based on the patient's individual requirements and the surgeon's standard of care. This study will span a 24-month period and evaluate various aspects, including complications, radiographic outcomes, and patient-reported outcomes. By conducting comprehensive assessments, researchers aim to determine the safety, effectiveness, and long-term benefits of utilizing interbody implants for patients with degenerative conditions in the thoracic and/or lumbar spine.23

#### **KUR-113 Bone graft for interbody fusion**

This prospective, controlled, single-blind, and open-label study seeks to evaluate the safety and efficacy of KUR-113 Bone Graft as compared to local autograft for the treatment of degenerative disc disease. The study focuses on individuals requiring single-level interbody fusion. Throughout the study, clinical and radiological assessments will be conducted at multiple time points, extending up to 24 months. By thoroughly examining the outcomes of using KUR-113 Bone Graft in comparison to local autograft, researchers aim to gather valuable evidence regarding its effectiveness and safety as a potential treatment option for individuals with degenerative disc disease.<sup>24</sup>

## Conclusion

Degenerative disc disease (DDD) is a complex and prevalent condition characterized by the progressive deterioration of intervertebral discs, significantly impacting spinal health and patient quality of life. The disease is marked by a multifaceted symptomatology, including pain, discomfort, numbness, and tingling sensations, presenting substantial challenges in diagnosis and treatment. Despite the unclear etiology, aging, prior injury, excessive use, and repetitive activities have been identified as potential risk factors.

Intervertebral discs, crucial for spinal structure and function, undergo degenerative changes leading to hydration loss, disc height reduction, potential disc herniation, and significant discomfort. These changes disrupt the discs' crucial roles in providing structural support, facilitating movement, and acting as shock absorbers.

The escalating global market size for DDD treatment, expected to reach 45.92 billion USD by 2029, underlines the growing recognition of DDD's impact and the need for effective management strategies. Despite the lack of specific data for the United States and China, the high prevalence of DDD-induced low back pain and higher incidence rates in low- and middle-income countries underscores the urgent necessity for accessible and effective treatment options.

This paper's comprehensive review of DDD, examining its causes, risk factors, symptoms, anatomical aspects, and market trends, aims to foster a deeper understanding of the disease and guide future research efforts. The advent of innovative treatment products offers hope for better management strategies, emphasizing the importance of continued research and development efforts in this field. Despite the challenges, substantial progress has been made, and the outlook

for patients with DDD looks promising. However, there is still a need for further research to fully understand the disease's complexities and develop more effective diagnostic and therapeutic strategies.

# **Acknowledgments**

Farid Manshaii extends his gratitude to Dr. Tawil for the guidance provided during the spring quarter of his junior year at UCLA, where he gained substantial knowledge in tissue engineering and entrepreneurship. Additionally, he wishes to express his thanks to Dr. Tawil for assisting in arranging the publication of this paper.

#### Conflicts of interest

Authors declare that there is no conflict of interest.

# **Funding sources**

There is no funding to report for this study.

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