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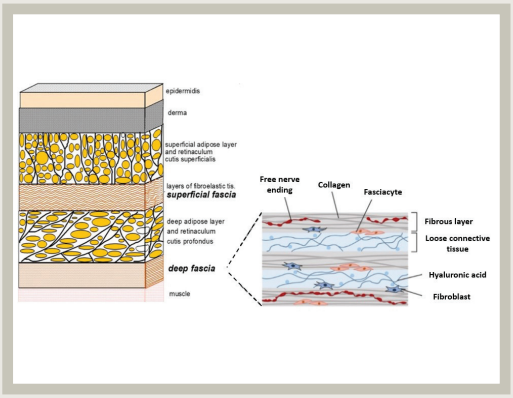

Figure 2. Schematic representation of the fascia from skin to muscle

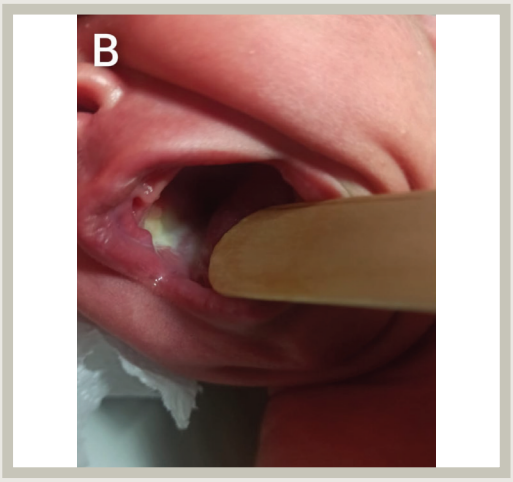

Figure 1. (A) Right facial swelling and erythema. (B) Pus coming from Stenson duct upon massage on parotid gland

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Editorial

Dear Colleagues,

It is our great pleasure to publish the first issue of CSMJ this year. As you well know, CSMJ has been indexed in several indexes including DOAJ, J-Gate, Türk Medline, EBSCO Central & Eastern European Academic Source and Gale on the third year of its' publication. This success has been achieved with your valuable and continuous support.

In this first issue of 2024, you can read the interesting review about the role of fascia in both musculoskeletal function and myofascial pain syndrome. You can read four different original articles in this issue. The first article is an epidemiological research study that evaluated the data of HIV patients during the pandemics. The second original article in this issue is about the evaluation of the association between iron deficiency anemia and febrile seizures in children. This topic has been reported to be controversial and this study has also yielded similar results. The other study aims to establish the quality of life, prevelance of depression in older adults. And the last study is about the comparison of optic nerve sheath diameter by ultrasonography for prediction of increased intracranial pressure in two different anesthesia methods in patients at reverse Trandelenburg position. You can also read an interesting and rare case report about acute suppurative parotitis in a septic neonate.

I think that all the articles and case report will be helpful for both your routine daily practice and also for future studies. We want to continue to discuss different important topics in future issues of CSMJ with your support.

Best regards,

On Behalf of Deputy Editors, Associate Editors, and Editorial Secretary

Merih Çetinkaya

Editor-in-Chief

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The Role of Fascia in Myofascial Pain Syndrome: A Look at Cinderella Tissue

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ABSTRACT

The word "myofascia" refers to the interwoven, indivisible nature of the web of connective tissue (fascia) that surrounds muscle tissue (myo-). The "myo" component of myofascial pain syndrome (MPS) has been covered very well, but the same cannot be said for the "fascial" component. In this article, fascia and its relationship with MPS are discussed.

Keywords: Chronic pain, fascia, myofascial pain, physical medicine and rehabilitation

Introduction

Physiatrists treat various musculoskeletal disorders, emphasizing the importance of understanding their pathophysiology. The fascia, a component of the connective tissues and musculoskeletal system in the human body, could be the key structure and concept needed to understand the processes of various dysfunctions.

Myofascial pain syndrome (MPS) was first described by Simons et al. (1). MPS is a very comprehensive and well-expressed definition. This expression is a term that includes both the muscles and fascia (2). There is no single branch of medicine that deals with muscles, and this has caused muscles to be ignored for years. This being the case, Travel referred to muscles as an orphan organ of medicine in one of his articles (3,4). Musculoskeletal problems and myofascial pain are common conditions that all physicians regularly observe in their daily practice. It is important to be able to detect this disease and be aware of the various treatment options available. The word "myofascia" refers to the interwoven, indivisible nature of the web of connective tissue (fascia) that surrounds muscle tissue (myo-). The "myo" component of MPS has been covered very well, but the same cannot be said for the "fascial" component. Understanding the relationship between deep fascia and epimysium has made fascia a treatment target in MPS treatment (5).

Fascia has been largely neglected in conventional medicine over the past several years, and its contribution to many areas of biomechanics and physiology has been overlooked (6). The first reason for this is the inadequacy of imaging methods that evaluate the fascia. X-rays have traditionally been used to objectively check bones, whereas electromyography is used to study muscles. However, accurately measuring changes in

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fascial tissues in living organisms is challenging. The second reason fascial tissue has been neglected for many years is the dissection method preferred by anatomists. Examining the tissues by dissecting them has made it difficult to evaluate the fascia as a whole. We can determine the number of bones and muscles in the human body, but this is not possible for the fascia. The fascial tissue is a complex structure composed of interconnected bags, string-like condensations, and pockets inside pockets, all linked by septa and layers of connective tissue. Digital modeling using 3D computer systems is necessary to uncover such a network structure. We shall gain further knowledge about fascia in the upcoming years (7). This review aims to provide an understanding of MPS from the perspective of fascia and the fascial system, the importance of which has begun to be understood in recent years.

Definition

The term fascia is frequently used in anatomical contexts, although its precise definition has proved challenging to comprehend. Many anatomical texts have been written about the facia anatomy. However, most anatomy professionals consider fascia only as connective tissue that fills empty spaces in the body (8). In 1983, the International Committee on Anatomical Nomenclature created a system of classification for all structures made of connective tissue. Different definitions have also been provided over the years by the Federative International Committee on Anatomical Terminology in 1998, the British edition of Gray's Anatomy in 2008, and the Fascia Research Congress in 2012. Various perspectives were presented during the 4th International Fascia Research Congress in Washington DC in 2015 (9). Well-known experts in fascial medicine and research presented and discussed the most recent findings in their fields. Finally, a consensus anatomic definition of the fascia was reached: *"…Fascia is a sheath, a sheet, or any other dissectible aggregations of connective tissue that forms beneath the skin to attach, enclose, and separate muscles and other internal organs."*

The functional definition of the fascial system is determined as follows. The fascial system is a three-dimensional network of soft, collagen-rich, loose, and dense fibrous connective tissues that spread throughout the body. The structure consists of multiple components including adipose tissue, adventitia, aponeuroses, deep and superficial fasciae, epineurium, joint capsules, ligaments, membranes, meninges, myofascial expansions, periosteum, retinacula, septa, tendons, visceral fasciae, and all intramuscular and intermuscular connective tissues, encompassing the endo-, peri-, and epimysium. The fascial system surrounds, interweaves, and penetrates all organs, muscles, bones, and nerve fibers, providing the body with a functional framework that enables the coordination of all body systems (9,10).

Architecture of the Fascia

It is crucial to comprehend the fascial system's composition in order to comprehend its architecture and function. It should be noted that fascia is a connective tissue. Fascia layers vary from one another significantly. Each layer is unique in both composition and orientation (11,12). For example, superficial fascia is loosely packed and irregular, whereas deep fascia consists of a well-organized fibrous layer. The classification of the human fascia is schematized in Figure 1.

Superficial Fascia

Superficial fascia is a layer of membranous connective tissue comprising loosely packed intertwined collagen fibers mixed with abundant elastic fibers. It is thicker on the trunk and gradually becomes thinner in the extremities. The retinaculum cutis superficialis, which has thick and vertical collagen septa, connects the superficial fascia to the skin. In addition, it is connected to the deep fascia through the retinaculum cutis profundus, which has loosely oblique and very elastic collagen septa. Deep fat tissue is the region between the superficial fascia and deep fascia, whereas superficial fat tissue is the area between the epidermis and superficial fascia, which contains the superficial retinacula cutis (12). It protects the body against heat loss.

Deep Fascia

Deep fascia is denser than superficial fascia. Collagen bundles are more compact and are regularly arranged. The orientation, composition, and architecture of the deep fascia allow classification as either aponeurotic or epimysial fascia. The deep fascia is more than a tough-barrier structure composed of collagen and elastin. It is a metabolically active

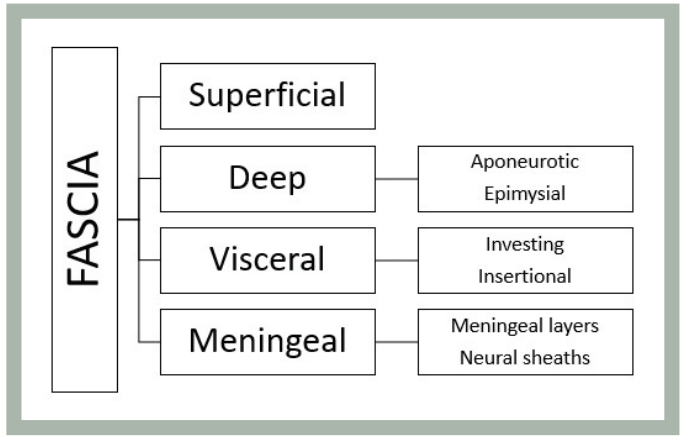

Figure 1. Classification of the human fascia

tissue layer that, in addition to contributing to gliding, also provides protective functions.

The fibrous sheaths that envelop and secure a muscle group or attach a large muscle are known as aponeurotic fascia. The aponeurotic fascia comprises two to three layers of parallel bundles of collagen fibers. Each layer is isolated from the others by a thin layer of loose connective tissue, allowing them to slide over each other independently. This independence gives each layer a distinct impact on the functionality of the tissue.

The epimysial fascia encompasses all thin collagen layers closely attached to the muscle. The epimysical fasciae envelop and stick to the entire muscle and can be a term used to encompass all the intramuscular connective tissue, such as the epimysium, perimysium, and endomysium. Tendons have a compact fibrous structure and can transfer forces between neighboring synergistic muscle fiber bundles, which may be part of the same motor unit. Because of its intimate association with muscle tissue, the epimysial fascia cannot be separated from the muscle. Both epimysial fascia and epimysium proper transmit the force of the muscle to the surrounding areas through myofascial expansions, but they have different thicknesses. The epimysial fascia is thicker (0.5-0.9 mm), whereas the epimysium is thinner (0.1 mm). Both aponeurotic and epimysial fascia transmit the forces of muscle contraction. The perimysium, which surrounds the muscle fiber bundles and continues into the endomysium, which encircles each muscle fiber, is closely related to the epimysium (12). A schematic representation of the fascia from the skin to the muscle is shown in Figure 2.

Connective Tissue

Connective tissue has three main basic components: cells, fibers, and a ground substance (13).

Cell

The metabolic characteristics of biological tissue are provided by the cells. Fibroblasts are the predominant cell type in fascial tissue; they play an important role in mechanotransduction and the secretion of extracellular matrix (ECM) precursors, which preserve the tissue's structural integrity and structure (14). Fibroblasts synthesize collagen fiber types I and III, whereas fasciocytes and hyaluronan (HA)-secreting cells create additional intracellular components, including glycosaminoglycans (GAG). Adipocytes are located in the connective tissue. Fat cells can be categorized as white and brown adipocytes. Adipocytes store energy and serve as crucial insulation, intermediate fillers, and facilitate smooth movement (15).

Fibers

Fibers contribute to the mechanical properties of connective tissue. Fibers can transmit force generated by muscle cells and appear to increase in strength and thickness when subjected to tensile stress. There are two types of fibers in connective tissue: collagen and elastic fibers (16). Collagen is the primary structural protein in connective tissue.

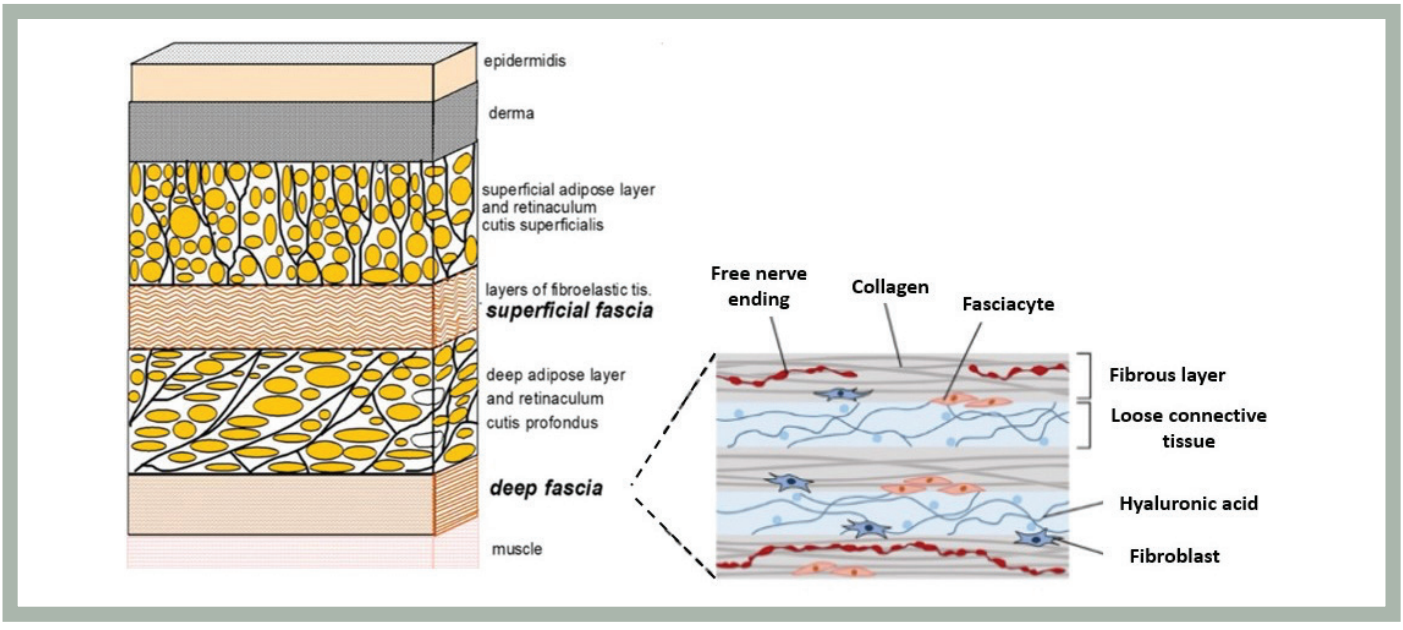

Figure 2. Schematic representation of the fascia from skin to muscle

There are many types of collagen, and almost 90% of the collagen in the muscles is located in the perimysium. Collagen fibers in the deep fascia are aligned parallel to each other, whereas other levels include collagen sequences with varying fiber orientations (17). Elastin fibers are thinner than collagen fibers and form a 3D network around the collagen fibers. Elastin is a protein that gives collagen the ability to stretch and to tolerate tension. Elastic and collagen fibers are not aligned in parallel. They lie on top of each other and/or rotate around each other, thus creating a three-dimensional interactive superstructure and imparting strength and flexibility to the entire tissue matrix (18).

Ground Substance

The ground substance is composed of water and GAGs, which contribute viscosity and plasticity to the tissues. The ground substance itself is a gel-like material including an extrafibrillar matrix, but no collagen or elastin fibers. Collagen and elastin fibers create a 3D network, while the basic substance surrounds and fills the spaces. GAGs are long-chain polysaccharides attached to the core protein of proteoglycans. Various GAG groups have been recognized. The most prevalent compounds are HA, chondroitin sulfate, dermatan sulfate, and heparan sulfate (19).

HA is the most common found GAG in loose connective tissue. HA provides moisture to the skin and facilitates the movement of muscles, tendons, and fascia against each other. HA acts primarily as a lubricant, maintaining normal tissue viscosity and allowing fascial layers to glide over each other (20). HA is widely distributed in the musculoskeletal system, particularly in the spaces between the layers of the aponeurotic fascia, muscles and deep fascia, loose connective tissue that envelops muscle bundles, and intramuscular fascial layers. Furthermore, the perivascular and perineural areas are important for HA. In particular, in the perivascular area around veins and the perineural area surrounding nerves, HA is required to provide appropriate gliding of these structures. Insufficient gliding carries the risk of nerve compression and vascular occlusion (20). Temperature, chemical elements, and pressure can modulate the chemical properties of HA.

Innervation

Proprioceptors, also referred to as mechanoreceptors, are the primary sensory receptors in the musculoskeletal system. Mechanoreceptors are integrated into the fascial system. Research has demonstrated the significance of mechanoreceptors in the layers of fascia, particularly in the highly innervated superficial layers of deep fascia. The facial layers contain free nerve endings and Ruffini and Pacinian corpuscles. The number of free nerve endings, which can also detect temperature, mechanical stimuli, and nociception, is considerably higher than that of other mechanoreceptors (21). The activation of nerve receptors within the fascia may be altered by the viscoelasticity of the tissue. These mechanoreceptors participate in the responses triggered by the viscoelasticity of the surrounding tissue. The dynamic response of mechanoreceptors is shaped by the viscoelasticity of the fascial tissue and HA. Because of the deterioration in the structure of HA and the increase in the densification viscosity, the normal gliding and lubricating effect decreases (21).

Imaging Technique

Another situation that makes understanding the fascial system difficult is the limitation of imaging methods. While bone tissue is evaluated by direct radiography, muscle tissue is evaluated by methods such as EMG. Until recently, there was no imaging method to evaluate the fascial system. Innovations in advanced evaluation technologies, such as tissue imaging, have made it possible to analyze variations in fascial behavior with greater clarity. The fascia can be visualized via computed tomography, magnetic resonance imaging, and ultrasound (US). US is also an advantageous method because it allows both static and dynamic evaluation of fascia (22). There are heterogeneities in fascial measurement protocols with US regarding the selected axis, probe position, and number of measurements taken. Additionally, patient body position also affected fascial thickness and stiffness, further limiting comparisons between studies. Nonetheless, limited studies suggest that US measurements of fascial thickness may have acceptable reliability (23). Ultrasonographic images of the superficial and deep fascia and their location within and under the skin are shown in Figure 3.

A relatively novel imaging method that can be used to assess fascia is elastography. Fascial elasticity was first qualitatively evaluated using axial strain elastography (ASE). Because ASE measurements are user-dependent, shear wave elastography has emerged as a viable objective addition to US and clinical evaluation in the assessment of fascial elasticity in the diagnosis of fascial pathologies (24). Figure 4 shows an example of elastography showing the fascia.

Myofascial Meridians

The effect of muscles is traditionally defined as the movement of a muscle on two bone structures, rather than carrying the load of the body. Nonetheless, some estimates

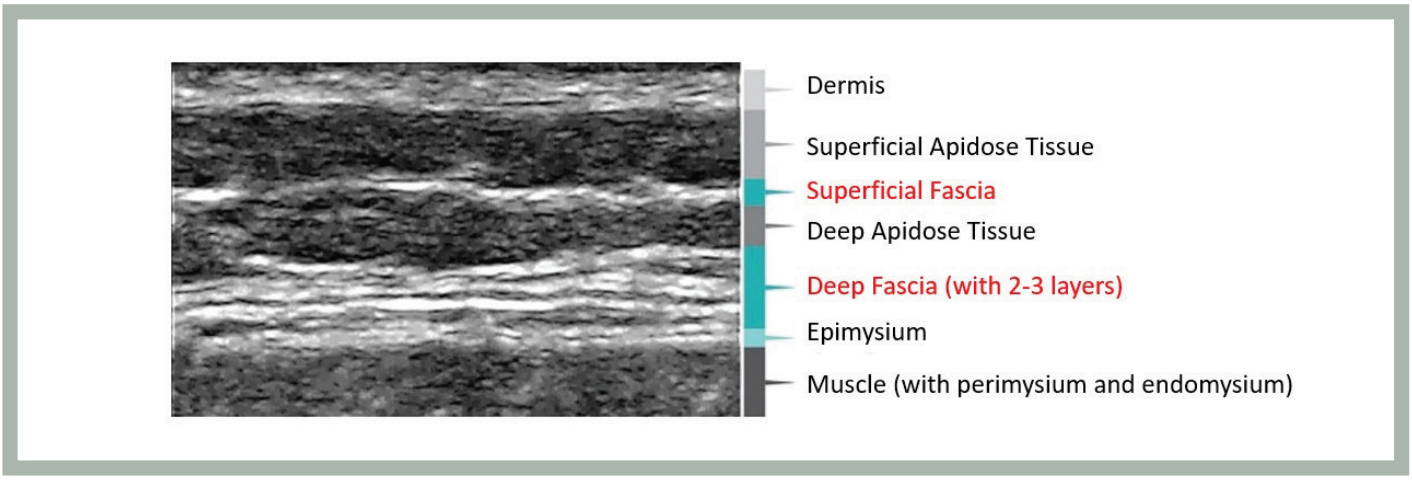

Figure 3. Understanding the fascial anatomy

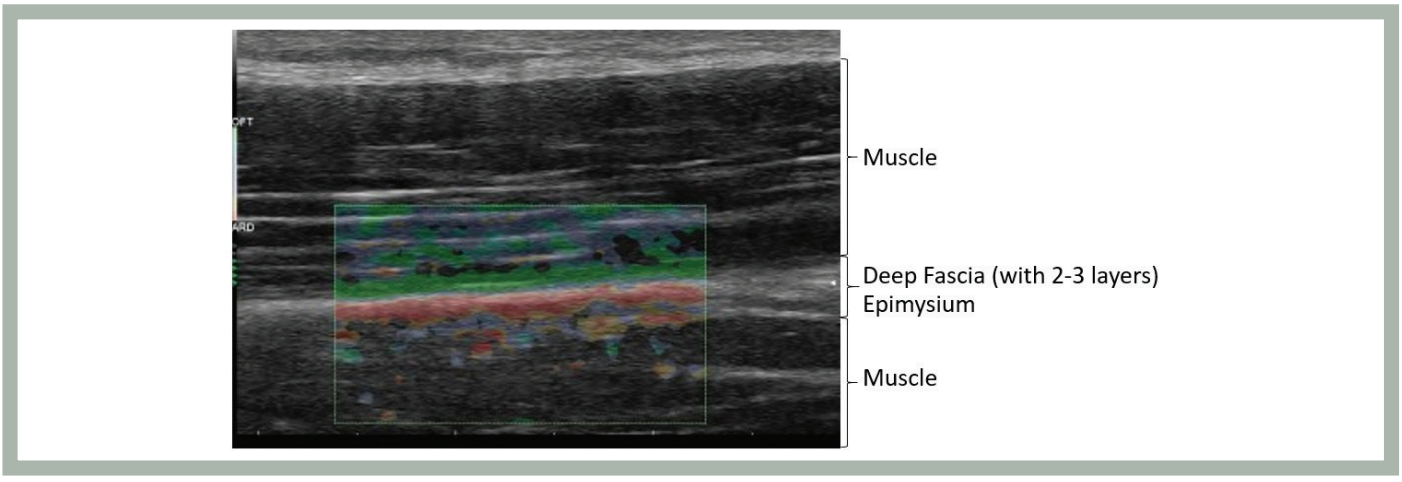

Figure 4. An example of elastography showing deep fascia

claim that 30% of the muscle contractile force is communicated to the perimuscular fascial elements and 70% is delivered to the bone (25).

While the term myofascia refers to the muscle fibers embedded in the fascia, the myofascial chain can be defined as a series of interconnected nerve and muscle pathways. According to this concept, fascia can be viewed as specific traction patterns throughout the body that distribute tension, facilitate movement, and provide stability throughout the body. This theory has helped them discover how two or more distant structures in the body affect each other. Myofascial meridians are anatomical identifiers that are usually defined as continuous bands of fascial tissue that run throughout the body. The term "meridian," in particular, is one of several terminologies used by leading fascia researchers today. However, there are also those who use different terminology. For example, Myers (26), a leading fascia researcher, used the term "trains" to classify these fascia vectors. Terms such as trains, meridians, lines, and chains can be used interchangeably and generally mean the same thing (26). Myers (26) defined 12 myofascial meridians that connect distant parts of the body through fascial tissues. Accordingly, the basic rule for selecting the components of a meridian is a direct linear connection between two muscles (5,26). Proximal and distal fascial connections among different muscles can affect their function. These linkages are known as myofascial chains, which may assist in clarifying referred pain and dysfunction in distant anatomical systems. The significance of myofascial chains was emphasized in a 2016 systematic review. Accordingly, it was concluded that "most skeletal muscles are directly attached to connective tissue" for the three myofascial chains (superficial posterior line, posterior functional line, anterior functional line) (26). The soft tissue components of the included myofascial chains are given in Table 1. Different theories on meridians have been developed by evaluating the cellular and global responses created on

Table 1. Soft tissue components of the included myofascial chains

Myofascial meridians	Soft tissue components
Superficial back line	Plantar fascia Achilles tendon/M. gastrocnemius Hamstrings Sacrotuberous ligament Lumbar fascia/erector spinae
Superficial front line	Toe extensors, M. tibialis anterior, anterior crural department Subpatellar tendon M. rectus femoris/quadriceps M. rectus abdominis M. sternalis/sternocondral fascia M. sternocleidomastoideus
Back functional line	M. vastus lateralis M. gluteus maximus Lumbar fascia M. latissimus dorsi
Front functional line	M. adductor longus M. rectus abdominis M. pectoralis major
Spiral line	Lumbar/erector spinae Sacrotuberous ligament M. biceps femoris M. peroneus longus M. tibialis anterior M. tensor fasciae latae, iliotibial tract M. obliquus abdominis internus/externus M. serratus anterior M. rhomboideus major/minor M. splenius capitis/cervicis
Lateral line	M. peroneus longus/brevis, lateral crural compartment Iliotibial tract M. tensor fasciae latae M. gluteus maximus M. obliquus abdominis internus/externus M. splenius capitis/M. sternocleidomastoideus

the fascia by mechanical stimuli during movement. Some of these theories include piezoelectric effect, viscoelasticity, and mechanoconduction.

Role of Fascia in Myofascial Pain Syndrome

MPS, a common regional pain syndrome, is a clinical disease with sensory-motor and autonomic components. MPS is a soft tissue and muscle-based condition that is often associated with the presence of myofascial trigger points (TP). The clinical symptoms of MPS can occur in acute and chronic forms. Conditions such as previous trauma, poor ergonomics during repetitive activity, psychological factors, structural changes in the spine, hypothyroidism, and vitamin deficiencies are among the important risk factors (27,28). MPS is a common disease and is usually diagnosed through history and physical examination (28,29).

MPS has historically been described as a muscle syndrome, and the contribution of the fascia to MPS has not been sufficiently emphasized. Research conducted recently has found that there are various pathologies in the deep fascia. The basis of fascial pathologies is based on changes in HA. The primary etiology of MPS is prolonged muscle contraction due to repetitive activity. Furthermore, MPS may result from a mismatch in the energy requirements and consumption of muscle tissue and neuromuscular dysfunction (30).

During normal muscle contraction, blood flow through the low-pressure capillary bed is temporarily blocked.

When the muscles relax, normal blood flow resumes. When muscles are constantly in a state of low contraction, intramuscular pressure impairs oxygen diffusion into the muscle and fascia and inhibits oxidative metabolism (31). Chronic hypoxia resulting from capillary occlusion causes lactic acid accumulation, reducing the local pH. Decreased pH leads to the association of HA chains and contributes to the "densification" of the fascia. Stecco et al. (32) suggested that overuse of muscle increases the polymerization of HA and therefore increases viscosity. This may alter local biomechanics by preventing the normal "gliding" of the muscle within the loose connective tissue (32). It has been shown that levels of bradykinin, substance P, serotonin, inflammatory cytokines, and calcitonin gene-related peptides, which contribute to nociception, increase in and around myofascial TPs. It is thought that the release of these mediators is associated with local tissue hypoxia and low pH (10).

Superficial and deep fascia, which are rich in free nerve terminals (Aδ and C), may play an important role in the development of MPS in addition to muscle-related fascial layers such as epimysium, perimysium, and endomysium. The deep fascia is located near the muscle surface and is divided by a transition zone of loose connective tissue. As mentioned before, deep fascia consists of multiple fibrous layers that can slide over each other along thin interfaces of loose connective tissue. The change in the HA chains that fill between the fibrous layers of the deep fascia causes the fascia to thicken and the interfascial slip to decrease (33). The rationale for treating myofascial pain should focus on reducing viscosity by disrupting HA chains.

Fascia-related Treatments

There are many effective treatment options that can be applied to treat MPS, but this article will briefly discuss treatments that target the fascia. With the understanding of the importance of deep fascia for referred pain mechanisms, fascial tissue has become a target in treatment. An important goal of fascia-related pain treatment is to reverse changes in HA. Increased temperature and local alkalization reverse the aggregation of HA fragments. The 3D structure of the HA chains, consisting of intermolecular and intramolecular water bridges, gradually deteriorates when the temperature is increased above 40 °C. Exactly at this temperature, there is a change in the viscosity of the HA solutions. This reduction in viscosity can restore normal gliding and normalize the activation of mechanoreceptors in that area. Manipulation, massage therapy, and osteopathic applications of muscles and their associated fascia increase the local temperature of the tissue (34).

In addition, local anesthetics, dextrose, saline, and dry needling are commonly used injection methods for treating myofascial TPs. These procedures can be performed blindly by manual palpation or with the use of US guidance (10,35). These injection applications are also used to treat deep fascia. When planning fascia injections, it is almost mandatory to use US guidance during administration. Hydrodissection is the process of injecting fluid to dissect the deep fascia under US guidance. Hydrodissection is also used to release nerve compression and treat tendinopathy. Unlike a classic TP injection, an interfascial injection, a larger volume of fluid is injected between the fascial layers. This procedure must be performed under US guidance (36). The mechanism of improvement for interfascial injections is still unknown; however, it is thought to cause changes in ECM viscosity or nociceptor stimulation within the fascia. Myofascial release techniques, manual therapy, extracorporeal shock wave therapy, superficial or deep heat, cannabidiol, and acupuncture applications are also used for treating fascial disorders (10,37).

Conclusion

Recent information has revealed that the fascia is involved in musculoskeletal function and myofascial pain. Understanding the physiology and pathophysiology of the fascial system; knowing myofascial chains and connections will be crucial for the development of appropriate techniques for fascial imaging and for further research targeting the fascial system in MPSs.

Ethics

Authorship Contributions

Concept: M.T.Y., B.T.D., Design: M.T.Y., B.T.D., Data Collection or Processing: M.T.Y., B.T.D., Analysis or Interpretation: M.T.Y., B.T.D., Literature Search: M.T.Y., B.T.D., Writing: M.T.Y., B.T.D.

Conflict of Interest: No conflict of interest was declared by the authors.

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REFERENCES

1. Simons DG, Travell JG, Simons LS. Travell and Simons' myofascial pain and dysfunction: the trigger point manual. 2nd ed. Baltimore (MD): Williams & Wilkins, 1999.
2. Bron C, Dommerholt JD. Etiology of myofascial trigger points. Curr Pain Headache Rep 2012;16:439-444.
3. Shah JP, Thaker N, Heimur J, Aredo JV, Sikdar S, Gerber L. Myofascial trigger points then and now: a historical and scientific perspective. PM R 2015;7:746-761.
4. Simons DG. Orphan Organ. J Musculoskelet Pain 2007;15:7-9.
5. Wilke J, Krause F, Vogt L, Banzer W. What is evidence-based about myofascial chains: a systematic review. Arch Phys Med Rehabil 2016;97:454-461.
6. Schleip R, Jäger H, Klingler W. What is 'fascia'? A review of different nomenclatures. J Bodyw Mov Ther 2012;16:496-502.
7. Findley TW. Fascia science and clinical applications: a clinician/researcher's perspectives. J Bodyw Mov Ther 2012;16:64-66.
8. Bordoni B, Mahabadi N, Varacallo M. Anatomy, Fascia. In: StatPearls. Treasure Island (FL): StatPearls Publishing; July 17, 2023.
9. Adstrum S, Hedley G, Schleip R, Stecco C, Yucesoy CA. Defining the fascial system. J Bodyw Mov Ther 2017;21:173-177.
10. Ganjaei KG, Ray JW, Waite B, Burnham KJ. The fascial system in musculoskeletal function and myofascial pain. Curr Phys Med Rehabil Rep 2020;8:364-372.
11. Benjamin M. The fascia of the limbs and back--a review. J Anat 2009;214:1-18.
12. Stecco C, Macchi V, Porzionato A, Duparc F, De Caro R. The fascia: the forgotten structure. Ital J Anat Embryol 2011;116:127-138.
13. Kamrani P, Marston G, Arbor TC, Jan A. Anatomy, connective tissue. 2023. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024.
14. Langevin HM, Cornbrooks CJ, Taatjes DJ. Fibroblasts form a body-wide cellular network. Histochem Cell Biol 2004;122:7-15.
15. Gomes RN, Manuel F, Nascimento DS. The bright side of fibroblasts: molecular signature and regenerative cues in major organs. NPJ Regen Med 2021;6:43. Erratum in: NPJ Regen Med 2023;8:42.
16. Humphrey JD, Dufresne ER, Schwartz MA. Mechanotransduction and extracellular matrix homeostasis. Nat Rev Mol Cell Biol 2014;15:802-812.
17. Amirrah IN, Lokanathan Y, Zulkiflee I, Wee MFMR, Motta A, Fauzi MB. A comprehensive review on collagen type I development of biomaterials for tissue engineering: from biosynthesis to bioscaffold. Biomedicines 2022;10:2307.
18. Henninger HB, Ellis BJ, Scott SA, Weiss JA. Contributions of elastic fibers, collagen, and extracellular matrix to the multiaxial mechanics of ligament. J Mech Behav Biomed Mater 2019;99:118-126.
19. Mattson JM, Turcotte R, Zhang Y. Glycosaminoglycans contribute to extracellular matrix fiber recruitment and arterial wall mechanics. Biomech Model Mechanobiol 2017;16:213-225.
20. Pratt RL. Hyaluronan and the Fascial Frontier. Int J Mol Sci 2021;22:6845.
21. van der Wal J. The architecture of the connective tissue in the musculoskeletal system-an often overlooked functional parameter as to proprioception in the locomotor apparatus. Int J Ther Massage Bodywork 2009;2:9-23.
22. Pirri C, Pirri N, Guidolin D, Macchi V, De Caro R, Stecco C. Ultrasound imaging of the superficial fascia in the upper limb: arm and forearm. Diagnostics (Basel) 2022;12:1884.
23. Wu J, Zhang YZ, Gao Y, Luo TY. Assessment the reliability of ultrasonography in the imaging of the plantar fascia: a comparative study. BMC Med Imaging 2019;19:62.
24. Zhou J, Lin Y, Zhang J, et al. Reliability of shear wave elastography for the assessment of gastrocnemius fascia elasticity in healthy individual. Sci Rep 2022;12:8698.
25. Stecco C, Pirri C, Fede C, et al. Dermatome and fasciatome. Clin Anat 2019;32:896-902.
26. Myers TW. Anatomy trains: myofascial meridians for manual and movement therapists. 3rd ed. New York: Churchill Livingstone; 2014.
27. Bourgaize S, Newton G, Kumbhare D, Srbely J. A comparison of the clinical manifestation and pathophysiology of myofascial pain syndrome and fibromyalgia: implications for differential diagnosis and management. J Can Chiropr Assoc 2018;62:26-41.
28. Guler K, Guler H, Yildizgoren MT, Seyfettin A, Karazincir S, Turhanoglu AD. Comparison of the efficacy of extracorporeal shock wave therapy and traditional physiotherapy in myofascial trigger points. J PMR Sci 2022;25:197-204.
29. Yildizgoren MT, Bagcier F. Tight fascia and myofascial trigger points can mimic carpal tunnel syndrome. APJP 2023;1-3.
30. Jafri MS. Mechanisms of myofascial pain. Int Sch Res Notices 2014;2014:523924.
31. Shah JP, Danoff JV, Desai MJ, et al. Biochemicals associated with pain and inflammation are elevated in sites near to and remote from active myofascial trigger points. Arch Phys Med Rehabil. 2008;89:16–23.
32. Stecco A, Stern R, Fantoni I, De Caro R, Stecco C. Fascial disorders: implications for treatment. PM R. 2016;8:161
33. Ricci V, Ricci C, Gervasoni F, Cocco G, Andreoli A, Özçakar L. From histoanatomy to sonography in myofascial pain syndrome: a EURO-MUSCULUS/USPRM approach. Am J Phys Med Rehabil 2023;102:92-97.
34. Stecco A, Gesi M, Stecco C, Stern R. Fascial components of the myofascial pain syndrome. Curr Pain Headache Rep 2013;17:352.
35. Cao QW, Peng BG, Wang L, et al. Expert consensus on the diagnosis and treatment of myofascial pain syndrome. World J Clin Cases 2021;9:2077-2089.
36. Tantanatip A, Patisumpitawong W, Lee S. Comparison of the effects of physiologic saline interfascial and lidocaine trigger point injections in treatment of myofascial pain syndrome: a double-blind randomized controlled trial. Arch Rehabil Res Clin Transl 2021;3:100119.
37. Kodama Y, Masuda S, Ohmori T, et al. Response to mechanical properties and physiological challenges of fascia: diagnosis and rehabilitative therapeutic intervention for myofascial system disorders. Bioengineering (Basel) 2023;10:474.

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ORIGINAL ARTICLE

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Evaluation of HIV Patients in the Pandemic

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What is known on this subject?

In this study, we aimed to examine the general characteristics and clinical and laboratory data of human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) cases admitted to an infectious diseases outpatient clinic and to contribute to the scarce epidemiological data in our country.

What this study adds?

In this study, we aimed to examine the general characteristics and clinical and laboratory data of HIV/AIDS cases admitted to infectious diseases outpatient clinics and to contribute to the scarce epidemiological data in our country.

ABSTRACT

Objective: To analyze the overall characteristics and clinical and laboratory data of human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) cases followed up in our clinic during the pandemic.

Material and Methods: Our study included 60 HIV/AIDS patients who were followed up in our center between January 1, 2020 and June 1, 2022. This study was conducted at the Department of Infection Disease, University of Health Sciences Turkey, Kartal Dr. Lütfi Kırdar City Hospital. Retrospective cross-sectional study.

Results: In this study, 57 were male (95%), 3 were female (5%), and the median age was 35 (27-45) years. The median value of HIV-RNA was 168.31 IU/mL. In serological tests, 36% (n=21) of the patients were positive for *Toxoplasma gondii* immunoglobulin G (IgG) antibody, cytomegalovirus (CMV) IgG (n=59) 98%, anti-hepatitis C virus (HCV) (n=2) 3.4%, venereal disease research laboratory (VDRL) (n=10) 17%, and *T. pallidum* antibody (n=15) 25.9%. CD4 T-cell count: 329 cells/µL, 17% CD4, CD8 cell count: 888 cells/µL, 53% CD8, CD4/CD8 ratio: 0.35. The prevalence of serological markers of the patients was as follows: anti-hepatitis A virus IgG was positive in 45 (77.6%), hepatitis B surface antigen 0%, hepatitis B surface antibody 32 (55.2%), hepatitis B core antibody-IgG 17 (29.3%), anti-HCV 2 (3.4%), VDRL 10 (17.2%), anti-*Treponema pallidum* 15 (25.9%), CMV-IgG 59 (98%), and *Toxo*-IgG 21 (36.2%).

Conclusion: In recent years, it has been observed that our patients can express their sexual identities more easily, and therefore, the rate of unknown transmission has decreased.

Keywords: HIV, AIDS, epidemiology

Introduction

The pandemic caused by severe acute respiratory syndrome-coronavirus 2 infection has infected 2.5 million people globally and resulted in more than 165,000 deaths as of 20 April (1).

Human immunodeficiency virus (HIV) is a retrovirus that belongs to the lentivirus subgroup. Following the identification of HIV

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infection in the early 1980s, the pathogen was isolated in 1983 and has been one of the most significant public health problems in the world for more than 40 years (2). The first case was diagnosed in our country in 1985, and the number of cases is increasing day by day in our country as well as in the world. According to the Ministry of Health Public Health data for 2022, there are 30,293 diagnosed patients with HIV in our country (3).

In 2020, the first year of the coronavirus disease-2019 pandemic, there was a sharp decline in the number of HIV diagnoses reported, and in 2021, the number of new HIV diagnoses reported in the World Health Organization European Region was almost 25% below pre-pandemic levels. In 2021, approximately 300 new HIV diagnoses will be made every day in the Eastern Europe/Central Asia Region, including our country (4).

Material and Methods

In this study, we aimed to examine the general characteristics and clinical and laboratory data of HIV/acquired immunodeficiency syndrome (AIDS) cases admitted to infectious diseases outpatient clinics and to contribute to the scarce epidemiological data in our country. Patients who received treatment in our clinic between January 1, 2020 and June 1, 2022 participated in the study. Serum HIV infection markers were detected by an automated electrochemiluminescence immunoassay (Cobas e411, Roche Diagnostics) during the study period. A definite diagnosis of HIV infection was considered as reactive HIV 1/2 antigen/antibodies. This was verified by a confirmatory method (Western blot, lineimmunoassay or indirect immunofluorescence) in the Central Public Health Laboratory. CD4+ T-lymphocyte counts were determined by flowcytometry "flow account" method (Beckman Coulter, United Kingdom). Cases were classified according to the HIV/AIDS case definition first approved by the Centers for Disease Control and Prevention (CDC) in 1993 (5).

This study was approved by the University of Health Sciences Turkey, Kartal Dr. Lütfi Kırdar City Hospital Ethics Committee Commission on 25/01/2023 with the decision number 2022/514/242/18.

Statistical Analysis

Mean, standard deviation, median minimum, maximum, frequency, and ratio values were used to determine the descriptive statistics of the data. The distribution of variables was measured by the Kolmogorov-Smirnov test. Independent samples t-test and Mann-Whitney U test were used to analyze quantitative independent data. Chi-square test was used in the analysis of qualitative independent data, and Fisher's exact test was used when chi-square test conditions were not provided. SPSS 28.0 program was used in the analyses.

Results

At the first examination of HIV/AIDS cases who applied to infectious diseases outpatient clinics during the pandemic, 57 were male (95%), 3 were female (5%), and the median age was 35 (27-45) years. Of the patients, 59 were Turkish nationals (98%) and 1 was a foreign national (2%). The most common transmission method was sexual contact in 58 (96.7%) patients. In two (3.3%) patients,the transmission method was detailed and there was no intravenous drug user. In terms of sexual orientation, 23 (38%) were men who had sexual behavior with men (MSM) and 35 (58%) were men who had heterosexual contact. Comorbidities were diabetes mellitus (DM) in 5 (8%), hypertension (HT) in 5 (8%), hypertriglycaemia in 4 (6%), hypercholesterolaemia in 3 (5%), depression in 3 (5%), malignancy in 2 (3%), syphilis keratitis in 2 (3%), heart disease in 2 (3%), lung disease in 1 (1%), kidney disease in 1 (1%), and hyperthyroidism in 1 (1%). When the patients were classified according to the CDC Surveillance Criteria, 15 patients were in stage 1 (25%), 30 patients were in stage 2 (50%), and 15 patients were in stage 3 (25%). When CDC clinical categories were analyzed, 45 patients were in category A (75%), 11 patients were in category B (18%), and 4 patients were in category C (7%), which means advanced AIDS stage. Laboratory values were found to be within normal limits (Table 1).

The median value of HIV-RNA was 168.31 IU/mL. In serological tests, 36% (n=21) of the cases were positive for *Toxoplasma gondii* immunoglobulin G (IgG) antibody, cytomegalovirus (CMV) IgG (n=59) 98%, anti-hepatitis C virus (HCV) (n=2) 3.4%, venereal disease research laboratory (VDRL) (n=10) 17%, and *T. pallidum* antibody (n=15) 25.9%. Purified protein derivative (PPD) ≥5 mm induration in HIV-positive individuals before treatment for latent tuberculosis was accepted as positive. The results were >5 mm in two of the patients. CD4 T-cell count, 329 cells/µL ,17 % CD4; CD8 cell count, 888 cells/µL, 53% CD8; CD4/CD8 ratio was 0.35 (Table 2).

The prevalence of serological markers of the patients were as follows: anti-hepatitis A virus (HAV)-IgG was positive in 45 (77.6%), anti-hepatitis B surface antigen 0%, anti-hepatitis B surface antibody 32 (55.2%), anti- hepatitis B core antibody-IGg 17 (29.3%), anti-HCV 2 (3.4%), VDRL 10 (17.2%), anti-*Treponema pallidum* 15 (25.9%), CMV- IgG 59 (98%), and *Toxo*-IgG 21 (36.2%) (Table 3).

Table 1. Laboratory values of patients

Laboratory parameters	Min-max	Median	Mean values
Leukocyte (x10^3)	1.77-15.10	6.32	6.46±2.12
Hg (g/dL)	1.37-16.90	14.45	13.59±2.46
Plateletcount (x10^3/L)	0.19-464.00	217.00	221.17±97.53
Lymphocyte (x10^3)	0.00-4.90	1.82	1.98±0.96
Glucose (mg/dL)	67.00-218.00	93.50	96.07±21.94
HbA1c (%)	4.00-11.20	5.50	5.66±1.05
Creatinin (mg/dL)	0.42-1.11	0.80	0.80±0.14
GFR (mL/sec)	72.00-154.00	110.00	110.38±16.40
Cholesterol (mg/dL)	101.00-329.00	157.00	161.93±41.31
HDL (mg/dL)	24.00-74.00	36.00	37.80±10.32
LDL (mg/dL)	45.00-259.00	93.00	101.39±40.54
Triglyceride (mg/dL)	48.00-327.00	108.00	126.24±58.68
ALT (U/L)	10.00-349.00	22.50	42.82±65.74
AST (U/L)	14.00-481.00	23.00	38.07±64.03
ALP (U/L)	12.00-184.00	77.00	78.64±27.49
GGT (mg/dL)	9.00-165.00	23.00	34.68±29.85
LDH (U/L)	144.00-666.00	217.50	227.28±78.12
CK (U/L)	17.00-2675.00	75.00	174.60±385.19
Total bilirubin (mg/dL)	0.11-1.52	0.51	0.58±0.31
Protein (g/dL)	0.16-95.00	79.50	79.40±12.03
Albumine (g/dL)	32.00-56.00	43.00	43.14±5.22

HbA1c: Analysis of glycated hemoglobin, GFR: Glomerular filtration rate, HDL: High density lipoprotein, LDL: Low density lipoprotein, ALT: Alanine amino transferase, AST: Aspartate aminotransferase, ALP: Alkaline phosphatase, GGT: Gamma glutamyl transferase, LDH: Lactatede hydrogenase, CK: Creatine kinase, Min: Minimum, max: Maximum

Table 2. Laboratory values of patients

	Min-max	Median	Mean values (± SD/n %)
PPD (mm)	0.00-25.00	0.00	2.52±5.28
HIV-RNA (x10^3)	9.21-39380.10	168.31	1772.34±6144.14
CD4 T-cell/µL	20.00-1000.00	329.00	351.63±209.58
CD4 %	2.00-47.00	17.00	18.47±9.51
CD8 T-cell/µL	129.00-3920.00	888.00	1054.14±685.93
CD8 %	11.00-81.00	53.00	52.36±13.62
CD4/CD8	0.02-1.68	0.35	0.39±0.27

PPD: Purified protein derivative, HIV: Human immunodeficiency virus, SD: Standard deviation, Min: Minimum, Max: Maximum

Discussion

There were 34,453 HIV (+) individuals and 2,177 AIDS cases in our country from 1985 to 2022. Of these, 81.4% were male and 18.6% were female. If we look at the distribution of cases by mode of transmission, we know that 43.8% of cases are sexually transmitted, and the mode of transmission of 68.5% of these cases is heterosexual sexual intercourse (3).

In the study by Gökengin (6) in 2022, the number of HIV-positive people was 2,971, 82.93% were male and 17.07% were female. 17.94% of the cases were foreign nationals (6).

In our study, 95% were male and 5% were female, and the median age was 35 years (27-45). Similar to the studies conducted in our country, most patient populations consisted of young and male patients (7). Turkish nationals (98%) and 1 person was of foreign nationality (2%). The rates of women

Table 3. Prevalence of serological markers in 60 adult HIV-infected patients

ELISA tests	(n=71)	%
Anti-HAV-IgG	45	77.6%
HBsAg	0	0
Anti-HBs	32	55.2%
Anti-HBc-IgG	17	29.3%
Anti-HCV	2	3.4%
Anti-*Treponema pallidum*	15	25.9%
VDRL	10	17.2%
CMV-IgG	59	98%
Toxo-IgG	21	36.2%

HIV: Human immunodeficiency virus, HAV: Hepatitis A virus, IgG: Immunoglobulin G, HBsAg: Hepatitis B surface antigen, HBs: Hepatitis B surface antibody, HBc: Hepatitis B core antibody, HCV: Hepatitis C virus, VDRL: Venereal disease research laboratory, CMV: Cytomegalovirus

and foreign nationals were found to be lower compared with the studies.

In 2016, in a study conducted with 1,292 HIV-infected individuals in a cohort involving five centers in Turkey, the rate of MSM was 40%. In 2016, when 2,530 cases were examined in a cohort including 33 centers in our country, the rate of MSM patients was reported as 27.5% (8).

The most common way of contamination in HIV infection in the world is through heterosexual sexual contact, and there are reported rates of 79.3%, 81%, 60%, 35.9%, 61.1%, and 63.1% in our country (7,9,10). In our analysis, the heterosexual sexual transmission level was 58%, which is consistent with other studies. Karaosmanoglu et al. (11) reported an MSM rate of 38% in their patient cohort, which is the highest rate reported in our country to present. In our study, MSM was found to be 38%, which is compatible with the studies.

In 2021, more than half of newly diagnosed patients with AIDS have CD4 350/ mm^3 at diagnosis, indicating that they are likely to have lived with undetected HIV for up to 8 or 10 years (4). In our study, CD4 T-cell count was 329 cells/µL, 17% CD4, CD8 T-cell count was 888 cells/µL, 53% CD8, and the CD4/CD8 ratio was 0.35. This is thought to be due to the difficulties in applying to the hospital and having examinations due to the pandemic.

While the rate of patients diagnosed with AIDS and advanced stage (CD4-cell count below 200) was 40% according to the CDC diagnostic criteria, 18% in our study and 7% in the AIDS phase were observed in Çerçi et al. (7). With increased awareness and new treatment options, it has become easier for patients to receive an early diagnosis (9).

When the comorbidities were analyzed, DM and HT were the most common diseases. The prevalence of diabetes in HIV-infected patients has been found to be higher than that in the general population in many studies (12). The prevalence of DM in HIV-infected patients has been reported to be between 2% and 14% (13).

In the Turkish Prevalence Study of DM, HT, Obesity, and Endocrinological Diseases, the prevalence of diabetes in the general population in Turkey was found to be 7.2%, and the prevalence of diabetes in our HIV-diagnosed patients was found to be quite similar to many studies in the literature. Publications are reporting that the prevalence of HT in AIDS patients is higher than in the normal population as well as those reporting that it is consistent with the normal population. In a large cohort, the prevalence of HT was reported to be 8.5%, and the prevalence of 8% in our study was similar to that in other studies (14).

Every patient with a positive HIV diagnosis should be screened for opportunistic infections and other sexually transmitted diseases before treatment. The most common opportunistic infection in HIV patients is TB, and Kurtaran et al. (15) found a rate of HIV-TBC co-infection of 5.7% in their study. Different algorithms are used according to the prevalence of TB and the level of development of countries. It is one of the leading causes of death in HIV/AIDS patients (16).

Globally, it is estimated that approximately 30% of HIV-infected people have a (usually latent) infection with *Mycobacterium tuberculosis*; this rate varies from 14% in Europe to 46% in Southeast Asia. In the 2017 Global Tuberculosis Report, HIV prevalence in newly diagnosed and relapsed tuberculosis (TB) cases in Turkey ranged from 0% to 4.9% (17). No patients with TB were detected in our study. Among patients with CD4 T-cell counts below 200/mL, positive induration of ≥5 mm was detected in two patients in response to PPD, and expanded tests were performed among these individuals.

Because the transmission routes for HIV infection and syphilis are similar, co-infection with syphilis is commonly observed in individuals infected with HIV. Lesions caused by syphilis also increase the risk of HIV transmission. HIV infection can lead to the suppression of the host immune system, which can also affect the clinical course of syphilis (18). *T. pallidum* and HIV are sexually transmitted disease agents that can infect the same host together.

The prevalence of syphilis in HIV-infected patients was 12.9% in the study by Aydin et al. (19), Sarigül et al. (20), who reported the rate of association with syphilis as 25% (18).

In our study, the VDRL test was 17% and syphilis antibody positivity was 25.9%. CMV, the virus infects 60% to 70% of adults in industrialized countries and up to 100% in developing countries. It can be life-threatening for immunocompromised individuals such as HIV-infected persons, organ transplant recipients, or newborn infants. In our study, CMV IgG was 98% (21).

Hepatitis has been diagnosed as a major worldwide public health problem, with a high prevalence and burden of morbidity and mortality and poor diagnostic and therapeutic techniques. Hepatitis patients are affected by HIV, hepatitis B, and hepatitis C with different transmission efficiencies (22).

The prevalence of HCV among HIV-infected participants in this study was 41%. As reported in other parts of the world, a study confirms that HCV is a major threat to people living with HIV/AIDS in China (23). In the report by Lee et al. (24), HAV seropositivity was found to be 21.2%.

Wooten and Karris (25) reported that the prevalence of HAV infection tends to be higher (15.1-96.3%) in HIV-infected individuals than in non-infected individuals.

In the study conducted by Aydin et al. (26) in our country, hepatitis B 6.2% and hepatitis C 0.9 and the rate of hepatitis C was 3% in the study that research in Turkey conducted by Kaptan et al. (27). In our study, hepatitis B was observed in 29%, hepatitis C in 3.4%, and HAV in 77.6%.

Toxoplasmosis is usually asymptomatic in non-immunized persons, and latent infection may persist for the lifetime of the host. *Toxoplasmosis* in HIV/AIDS patients was first reported in 1983. In patients with AIDS, the parasite can reactivate and cause disease, usually when the CD4 count falls below 100 cells/L. It is the most common central nervous system infection in AIDS patients (28). *T. gondii* IgG seroprevalences reported in studies conducted in HIV-infected patients in various countries around the world were between 5.4% and 93.3%, and in our study, *T. gondii* IgG antibody positivity was 36% (29). Although the rates of reaching and staying in treatment of HIV-diagnosed patients in our country are high, the rates of diagnosis are not at the desired level (6).

Conclusion

To control the HIV epidemic and prevent new cases, each country needs to know their patient population well and determine the transmission methods and risk factors. In our country, it is necessary to organize vaccination programs in line with our local epidemiological data to inform about protective sexual behavior and to raise awareness about vaccination.

Ethics

Ethics Committee Approval: This study was approved by the University of Health Sciences Turkey, Kartal Dr. Lütfi Kırdar City Hospital Ethics Committee Commission on 25/01/2023 with the decision number 2022/514/242/18.

Informed Consent: Retrospective study.

Authorship Contributions

Surgical and Medical Practices: S.D.K., B.K., M.E.I., Concept: S.D.K., B.K., M.E.I., Design: S.D.K., B.K., M.E.I., Data Collection or Processing: S.D.K., B.K., M.E.I., Analysis or Interpretation: S.D.K., B.K., M.E.K., Literature Search: S.D.K., B.K., M.E.I., Writing: S.D.K., B.K., M.E.I.

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REFERENCES

1. Johns Hopkins University-Coronavirus Resource Center. COVID-19 casesupdate. Available from: https://coronavirus.jhu.edu/map.html. Accessed July 15, 2020.
2. Raubinger S, Lee FJ, Pinto AN. HIV: the changing paradigm. Intern Med J 2022;52:542-549.
3. T.C. Sağlık Bakanlığı Halk Sağlığı Genel Müdürlüğü. HIV/AIDS İstatistik. Available from: https://hsgm.saglik.gov.tr/depo/birimler/bulasici-hastaliklar-ve-erken-uyari-db/Dokumanlar/Istatistikler/hiv-aids-2023.pdf. Accessed Nov 29, 2022.
4. World Health Organization. Number of deaths due to HIV/AIDS. Available from: https://www.who.int/data/gho/data/indicators/indicator-details/GHO/number-of-deaths-due-to-hiv-aids. Accessed July 19, 2022.
5. Centers for Disease Control and Prevention. 1993 revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. MMWR Recomm Rep 1992;41:1-19.
6. Gökengin D. HIV infection in Turkey: how close are we to the target? Klimik Derg 2018;31:4-10.
7. Çerçi P, İnkaya AÇ, Alp Ş, Tümer A, Ünal S. Evaluation of 255 HIV/AIDS cases: Hacettepe Cohort, Ankara, Turkey. Mikrobiyol Bul 2016;50:94-103.

8. Erdinç FŞ, Dokuzoğuz B, Ünal S, et al. Changing trends in the epidemiology of Turkey [Abstract]. In: 30th IUSTI Europe Conference (15-17 September 2016, Budapest, Hungary) Abstract Book. UK: International Union Against Sexually Transmitted Infections. 2016:115-116.
9. Ozdemir B, Yetkin MA, Bastug A, et al. Evaluation of epidemiological, clinical, and laboratory features and mortality of 144 HIV/AIDS cases in Turkey. HIV Clin Trials 2018;19:69-74.
10. Ertunc B, Kaya S, Koksal I. Clinico-epidemiological analysis of HIV/AIDS patients. Eurasian J Med 2016;48:157-161.
11. Karaosmanoglu HK, Aydin OA, Nazlican O. Profile of HIV/AIDS patients in a tertiary hospital in Istanbul, Turkey. HIV Clin Trials 2011;12:104-108.
12. Duncan AD, Goff LM, Peters BS. Type 2 diabetes prevalence and its risk factors in HIV: A cross-sectional study. PLoS One 2018;13:e0194199.
13. Capeau J, Bouteloup V, Katlama C, et al. Ten-year diabetes incidence in 1046 HIV-infected patients started on a combination antiretroviral treatment. AIDS 2012;26:303-314.
14. Data Collection on Adverse Events of Anti-HIV drugs (D:A:D) Study Group; Smith C, Sabin CA, Lundgren JD, et al. Factors associated with specific causes of death amongst HIV-positive individuals in the D:A:D Study. AIDS 2010;24:1537-1548. Erratum in: AIDS 2011;25:883.
15. Kurtaran B, Nazik S, Ulu A, et al. Evaluation of Hiv Infection and tuberculosis concomitance. Mediterr J Infect Microb Antimicrob 2015;4:4
16. Nationwide Shortage of Tuberculin Skin Test Antigens: CDC Recommendations for Patient Care and Public Health Practice. MMWR Morb Mortal Wkly Rep 2019;68:552-553.
17. Republic of Turkey Ministry of Health. Tuberculosis report 2018 in Turkey. Available from: https://hsgm.saglik.gov.tr/depo/birimler/tuberkuloz-db/Dokumanlar/Raporlar/Tu_rkiye_de_Verem_Savas_2018_Raporu_kapakl_.pdf. Accessed Jan 5, 2019.
18. Dinç HÖ, Alkan S, Özbey D, et al. Evaluation of Syphilis Coinfection in HIV-infected individuals. Klimik Dergisi 2020;33:292:296.
19. Aydin ÖA, Karaosmanoğlu HK, Sayan M, İnce ER, Nazlıcan Ö. Seroprevalence and risk factors of syphilis among HIV/AIDS patients in Istanbul, Turkey. Cent Eur J Public Health 2015;23:65-68.
20. Sarigül F, Sayan M, İnan D, et al. Current status of HIV/AIDS-syphilis co-infections: a retrospective multicentre study. Cent Eur J Public Health 2019;27:223-228.
21. Fülöp T, Larbi A, Pawelec G. Human T cell aging and the impact of persistent viral infections. Front Immunol 2013;4:271.
22. Lawal MA, Adeniyi OF, Akintan PE, Salako AO, Omotosho OS, Temiye EO. Prevalence of and risk factors for hepatitis B and C viral co-infections in HIV infected children in Lagos, Nigeria. PLoS One 2020;15:e0243656.
23. Falade-Nwulia O, Seaberg EC, Snider AE, et al. Outcomes of acute hepatitis B virus (HBV) in HIV infection with and without HBV-active antiretroviral therapy. AIDS 2021;35:991-993.
24. Lee YL, Lin KY, Cheng CY, et al. Evolution of hepatitis A virus seroprevalence among HIV-positive adults in Taiwan. PLoS One 2017;12:e0186338.
25. Wooten D, Karris MY. The As and Bs of HIV and hepatitis co-infection. Trop Med Infect Dis 2019;4:55.
26. Aydin OA, Yemisen M, Karaosmanoglu HK, et al. Low prevalence of hepatitis C virus infection among HIV-positive patients: data from a large-scale cohort study in Istanbul, Turkey. Hepat Mon 2014;14:e18128.
27. Kaptan F, Örmen B, Türker N, et al. Retrospective evaluation of 128 cases infected with human immunodeficiency virus. Turkiye Klinikleri J Med Sci 2011;31:525-533.
28. Aberg JA, Gallant JE, Ghanem KG, et al. Primary care guidelines for the management of persons infected with HIV: 2013 update by the HIV medicine association of the Infectious Diseases Society of America. Clin Infect Dis 2014;58:e1-34.
29. Akanmu AS, Osunkalu VO, Ofomah JN, Olowoselu FO. Pattern of demographic risk factors in the seroprevalence of anti-Toxoplasma gondii antibodies in HIV infected patients at the Lagos University Teaching Hospital. Nig Q J Hosp Med 2010;20:1-4.

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Evaluation of the Relationship Between Iron Deficiency Anemia and Febrile Seizures

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What is known on this subject?

The most common neurologic problem in children is febrile convulsion. This occurs in children between the ages of 6 and 72 months. The most common micronutrient deficiency is iron deficiency anemia, which is more common in children aged 6 to 24 months. The age range of the two groups covers each other.

What this study adds?

The study highlights that iron deficiency anemia is more common in patients undergoing febrile seizure.

ABSTRACT

Objective: Febrile convulsions are the most common neurologic problems in children. We investigated whether iron deficiency anemia affects febrile convulsions.

Material and Methods: This study was conducted as a retrospective cross-sectional study with 100 children aged between 6 months and 78 months who visited the Gaziantep University Şahinbey Practice and Research Hospital, Pediatric Emergency Department and Pediatric Outpatient Clinic between January 2016 and September 2019. Participants were examined in two groups in terms of the presence or absence of iron deficiency anemia.

Results: 50% (n=50) of the individuals included in the study had febrile seizures (FS) (case group), and 50% (n=50) did not have FS (control group). The rate of iron deficiency anemia was 22% (n=11) in the case group and 16% (n=8) in the control group.

Conclusion: We observed that the low hemoglobin level was more evident in children with febrile convulsions, but the difference was not statistically significant. It was determined that 22% of patients with FS had iron deficiency anemia, but there was not any notable difference from the control group.

Keywords: Anemia, febrile seizures, iron deficiency, pediatrics

Introduction

Seizures that occur in children six months to 6 years, are not associated with a central nervous system infection, have no history of febrile seizures (FS), and occur due to a high body temperature when no other cause for the seizure is found are defined as FS (1). The most common type of seizure in childhood and infancy is FS (2). In studies, the frequency of FS varies between 2 and 10% (3).

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Although the etiopathogenesis of FS is still not clear, recent studies have provided important insights into the genetic basis. On the other hand, studies have shown that iron and zinc deficiency, central thermoregulation disorders, an increase in excitatory amino acids, humoral immune system disorders, prenatal maternal problems, and growth and developmental delays may play a role in the etiology (4).

Our study aimed to determine whether iron deficiency anemia plays a role in the etiology of FS.

Material and Methods

The study included 100 patients aged between 6 and 78 months who presented to the Pediatric Emergency Department and the Polyclinic for Child Health and Diseases of the Şahinbey Research and Practice Hospital between January 2016 and September 2019. In the case group, 50 patients with FS were selected, and in the control group, 50 patients with high fever but without seizures were selected. Patients in the case group must be in the specified age group, must have no intracranial pathology and/or central nervous system infection, the seizure must not recur within 24 h, must be of the generalized type, must have no history of febrile convulsions in the child, must have no pathological neurological findings (such as cerebral palsy, mental motor retardation), and must have no electrolyte disturbance that could cause a seizure. Patients with complicated FS were not included in the study. The control group was selected from patients of the same age group who had a body temperature above 38 °C, were seizure-free, and had no known chronic disease. Prior to the study, approval was obtained from the Gaziantep University Clinical Research Ethics Committee, dated December 25, 2019, with decision number 2019/483. The study was conducted in accordance with the principles of the Declaration of Helsinki. This article is derived from the dissertation entitled "Evaluation of the Relationship Between Failure to Thrive or Anemia and Febrile Convulsion".

Laboratory parameters such as serum iron, ferritin, complete blood count, and total iron binding capacity (TIBC) were retrieved from the archive. Laboratory tests were performed in the biochemistry laboratory of Şahinbey Research and Practice Hospital. At our center, approximately 1 mL of venous blood was used to determine hematological parameters such as hemoglobin (HBG), hematocrit (HTC), mean red cell hemoglobin (MCH), mean red cell hemoglobin concentration (MCHC), mean red cell volume (MCV), and red blood cell count (RBC) as part of the complete blood count. The blood was placed in an EDTA-containing hemogram tube and automatically analyzed with the Cellpack kit using the optical or impedance method on a SYSMEX brand device (Sysmex Turkey Diagnostic Systems Limited Company, İstanbul, Turkey). For the measurement of serum iron, TIBC and ferritin, approximately 2.5 cm^3 of venous blood was placed in a plain dry tube and centrifuged at 4000 rpm for 10 min to separate serum. Subsequently, the electrochemiluminescence method was analyzed using a Beckman Coulter device (Beckman Coulter Diagnostics, Brea, California, USA) and a Beckman kit.

Statistical Anaysis

Statistical Package for Social Sciences (SPSS) version 22 was used to analyze the data. In addition to descriptive statistics, chi-square, Student's t-test, and Kruskal-Wallis analyses were performed. In descriptive statistics, numbers and percentages were used to describe nominal variables, and mean, standard deviation, and lowest and highest values were used to describe numerical variables. The 0.05 level was considered significan.

Results

One hundred children, the youngest at the age of 6 months and the oldest at the age of 78 months, were included in the study. The mean age of the children was 34.45±19.45 months (minimum: 6, maximum: 78); the mean age of the case group was calculated as 30.88±20.86 months (lowest age: 6, highest age: 78), and the mean age of the control group was calculated as 39.12±18.49 months (lowest age: 8, highest age: 76). While 50% (n=25) of the case group were male and 50% (n=25) were female, 68% (n=34) of the control group were male and 32% (n=16) were female.

Ferritin, iron, TIBC, HBG, HTC, MCV, MCH, MCHC, and RBC did not differ significantly between the study groups (p=0.360, p=0.313, p=0.362, p=0.164, p=0.185, p=0.242, p=0.976, p=0.651 and p=0.859, respectively) (Table 1).

The number of children with iron deficiency anemia in the case group was higher than that in the control group, but this difference was not significant (p=0.444). Iron deficiency anemia was present in 22% of the case group (n=11) and 16% of the control group (n=8) (Figure 1).

Discussion

The most common neurologic problem in childhood is FS, which is also the most frequent seizure in childhood (2). They usually have a benign course; however, it is essential to investigate the underlying causes in terms of etiology, as they may recur and develop into epilepsy in the future (2).

Anemia caused by iron deficiency is the most frequent lack of micronutrients, accounting for 50% in developing countries and 30% worldwide. Iron deficiency anemia is more common

in children aged 6 months to 2 years, which is the age range in which FS is most common (5,6,7). Iron deficiency anemia occurs in 46-66% of children under the age of 4 years in developing countries (8). Because it is an avoidable reason, the frequency of iron deficiency anemia can be reduced through good nutrition and iron supplements (7). Iron deficiency slows down the metabolism of neurotransmitters, such as aldehyde oxidase and monoamine, which can change a child's seizure threshold (9). In addition, the production of cytochrome c oxidase, an indicator of neuronal metabolic activity, decreases in anemia caused by iron deficiency (10). Iron deficiency anemia affects the growing brain by changing the neuronal development mechanisms of the hippocampus, impairing energy metabolism function, delaying myelin development, blunting auditory and visual action potentials, and causing alterations in synaptic neurotransmitter systems (including dopamine, gamma-aminobutyric acid, norepinephrine and glutamate) (11,12). Iron deficiency, which is easily treatable, is considered a risk factor for febrile convulsions in children (13).

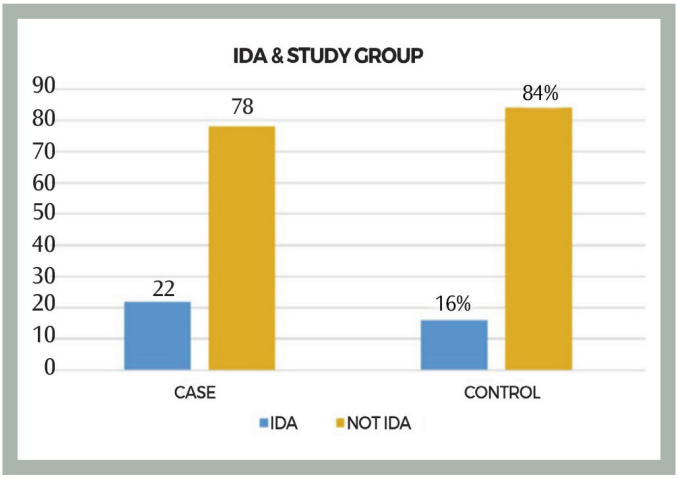

Figure 1. Distribution of Iron deficiency anemia by study groups (%)

In the study conducted by Gupta et al. (14) 2015 in Bhopal, 70 children suffering from FS were compared with 100 children in the control group, and it was found that the serum HGW amount of the children with seizures (<11 g/dL) was lower than the control group (12±0.37). In a study carried out by Fallah et al. (15) in Iran, it was found that the HGB level (11.46±1.18 g/dL) was lower in children with febrile convulsions than the control group (11.9±0.89 g/dL) (15). Similarly, in a study carried out by Sultan et al. (16) in 2013 in Pakistan, 68% of 31 children with FS were found to have low HGB, while 31 children who had fever but no seizures were found to have low HGB of 32%, and this difference was found to be statistically significant. In a study conducted by Omran et al. (17) in Iran in 2009, the average HGB was (11.75±1.15 g/dL) in the case group and (11.99±1.94 g/dL) in the control group; however, this difference was not significant. In our study, the mean serum HGW was found to be lower in children with febrile convulsions (11.50±1.78) than in the control group (11.94±1.30). Although this difference is not statistically significant, we believe that there might be a difference when studies with larger series are conducted (p=0.164).

In the study carried out by Ahmed (18) on Egyptian children, it was found that the mean HGB and HTC were significantly lower in cases with simple FS than in the control group. In a study by Srinivasa and Reddy (19) in India, the mean HGB and MCV values in children with FS were lower than those in the control group. Likewise, Aziz et al. (20) reported significantly lower HTC, MCV, and MCHC values in

Table 1. Distribution of blood values of individuals included in the study according to study groups

Blood value	Group				p value
	Case		Control		
	Average + SD	Minimum-maximum	Average + SD	Minimum-maximum	
Ferritin	36.62±41.71	2.30-214.20	43.62±45.30	2.20-223.70	0.360
Iron	56.32±28.88	9.80-119.00	50.36±29.93	12.00-171.00	0.313
TIBC	388.27±88.72	187.00-579.00	372.76±0.45	88.00-527.00	0.362
HBG	11.50±1.78	5.60-18.20	11.94±1.30	9.00-15.90	0.164
HTC	34.92±4.96	21.10-55.70	36.04±3.31	29.40-46.20	0.185
MCV	73.18±9.65	34.20-86.90	70.03±5.60	58.90-86.30	0.242
MCH	24.41±3.31	13.50-30.10	24.43±4.02	2.30-29.20	0.976
MCHC	32.87±1.76	26.50-36.20	33.01±1.32	30.10-35.80	0.651
RBC	4.73±0.54	3.36-6.46	4.75±0.44	4.05-6.23	0.859

TIBC: Total iron binding capacity, HBG: Hemoglobin, HTC: Hematocrit, MCV: Mean red cell volume, MCH: Mean red cell hemoglobin, MCHC: Mean red cell hemoglobin concentration, RBC: Red blood cell count, SD: Standard deviation

children with FS compared with the control group. In our study, although the mean levels of HTC, MCV, and MCHC in the serum of children with FS were lower than those in the control group, no statistical difference was demonstrated. We believe that a large series of studies is needed to prove the difference.

The relationship between FS and iron deficiency anemia was first investigated by Pisacane et al. (21) in this study, published in 1996, it was found that the rate of iron deficiency anemia was higher in children with FS than in the control group. The study by Fallah et al. (22) found a higher rate of iron deficiency anemia in children with FS than in the control group (22% vs. 10%) and in the study by Gupta et al. (14) (30.5% vs. 50.5%). It was found in the study by Vaswani et al. (23) (34.68% vs. 15.3%), Hartfield et al. (24) (16% vs. 5%), and Zareifar et al. (25) (56.6% vs. 24.8%). A high prevalence was also found in the study by Kumari et al. (26) (63.6% vs. 24.7%). Daoud et al. (13) a study in Jordan showed that the rate of iron deficiency anemia was higher in children with febrile convulsions than in children with fever but no convulsions, but this was not statistically significant. On the other hand, a study conducted by Talebian et al. (27) found that the rate of iron deficiency anemia was significantly lower in children with FS (13.3% vs. 20%) than in children with fever and without seizures. The study by Kobrinsky et al. (28) in Fargo and the studies by Derakhshanfar et al. (29), Bidabadi and Mashouf (30), and Abaskhanian et al. (31) in Iran found that the rate of iron deficiency anemia was lower in children with FS than in children with fever and without seizures. In our study, the rate of iron deficiency anemia was higher in the FS group (22%) than in the control group (16%), but not significant (p=0.444).

Assessment of anemia and planning of its treatment in patients admitted to hospital with FS may be important for prognosis. Comparison of seizure frequency during follow-up of patients treated for anemia with those who did not receive treatment may be important in clarifying the etiology.

Conclusion

We believe that iron deficiency anemia is more common in patients undergoing FS, but studies with a larger number of participants are needed to demonstrate a statistically significant association.

Ethics

Ethics Committee Approval: Gaziantep University Clinical Research Ethics Committee, dated December 25, 2019, with decision number 2019/483.

Informed Consent: Informed consent was obtained from the patient's relatives.

Authorship Contributions

Surgical and Medical Practices: H.C., M.K., Concept: H.C., Design: H.C., Data Collection or Processing: H.C., O.G., Analysis or Interpretation: H.C., M.K., M.T.T., Literature Search: H.C., Writing: H.C.

Conflict of Interest: No conflict of interest was declared by the authors.

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REFERENCES

1. Millar JS. Evaluation and treatment of the child with febrile seizure. Am Fam Physician 2006;73:1761-1764.
2. Dubé CM, Baram TZ. Febrile Seizures. In: Shorvon S, Pedley TA (eds). The Epilepsies 3: Blue Books of Neurology Series. Saunders, Philadelpia. 2009;33:17-26.
3. Özmen M. Konvülzyonlar. Apak S (ed). Pediatrik epileptoloji ve antikonvülziv ilac tedavisi İstanbul: Sanal Matbaacılık, 1986;93-107.
4. Commission on Epidemiology and Prognosis, International League Against Epilepsy. Guidelines for epidemiologic studies on epilepsy. Epilepsia 1993;34:592-596.
5. Florentino RF, Guirric RM. Prevalence of nutritional anaemia in infancy and childhood with emphasis on developing countries. In: Stekel A, (ed). Iron nutrition in infancy and childhood. New York: Raven Press, 1984;61-74.
6. Stoltzfus R. Defining iron-deficiency anemia in public health terms: a time for reflection. J Nutr 2001;131:565S-567S.
7. WHO. Iron deficiency anaemia. Assessment Prevention Control. A Guide for Program Managers. Available from: https://cdn.who.int/media/docs/default-source/2021-dha-docs/ida_assessment_prevention_control.pdf?sfvrsn=fb8c459c_1&download=true.
8. Steering Committee on Quality Improvement and Management, Subcommittee on Febrile Seizures American Academy of Pediatrics. Febrile seizures: clinical practice guideline for the long-term management of the child with simple febrile seizures. Pediatrics 2008;121:1281-1286.
9. Lozoff B, Beard J, Connor J, Barbara F, Georgieff M, Schallert T. Long-lasting neural and behavioral effects of iron deficiency in infancy. Nutr Rev 2006;64:S34-43; discussion S72-91.
10. de Deungria M, Rao R, Wobken JD, Luciana M, Nelson CA, Georgieff MK. Perinatal iron deficiency decreases cytochrome c oxidase (CytOx) activity in selected regions of neonatal rat brain. Pediatr Res 2000;48:169-176.

11. Madan N, Rusia U, Sikka M, Sharma S, Shankar N. Developmental and neurophysiologic deficits in iron deficiency in children. Indian J Pediatr 2011;78:58-64.
12. Yadav D, Chandra J. Iron deficiency: beyond anemia. Indian J Pediatr 2011;78:65-72.
13. Daoud AS, Batieha A, Abu-Ekteish F, Gharaibeh N, Ajlouni S, Hijazi S. Iron status: a possible risk factor for the first febrile seizure. Epilepsia 2002;43:740-743.
14. Gupta S, Agarwal N, Maheshwari M. Iron deficiency as a risk factor for febrile seizures-a case control study. PJSR 2015;8:37-40.
15. Fallah R, Tirandazi B, Ferdosian F, Fadavi N. Iron deficiency and iron deficiency anemia in children with first attack of seizure and on healthy control group: a comparative study. Iran J Child Neurol 2014;8:18-23.
16. Sultan A, Fayaz M, Khan AN, Fayaz A. Relationship between anaemia and simple febrile convulsions. J Ayub Med Coll Abbottabad 2013;25:156-158.
17. Omran MS, Tamaddoni A, Nasehi MM, Babazadeh H, Navaei RA. Iron status in febrile seizure: a case-control study. Iran J Child Neurol 2009;3:39-42.
18. Ahmed BA. Iron deficiency as a risk factor for simple febrile seizures. Med J Cairo Univ 2013;81:51-54.
19. Srinivasa S, Reddy SP. Iron defeiciency anaemia in children with simple febrile seizures-A cohort study. Curr Pediatr Res 2014;18:95-98.
20. Aziz KT, Ahmed N, Nagi AG. Iron deficiency anaemia as risk factor for simple febrile seizures: a case control study. J Ayub Med Coll Abbottabad 2017;29:316-319.
21. Pisacane A, Sansone R, Impagliazzo N, et al. Iron deficiency anaemia and febrile convulsions: case-control study in children under 2 years. BMJ 1996;313:343.
22. Fallah R, Tirandazi B, Akhavan Karbasi S, Golestan M. Iron deficiency and iron deficiency anemia in children with febrile seizure. Iran J Ped Hematol Oncol 2013;3:200-203.
23. Vaswani RK, Dharaskar PG, Kulkarni S, Ghosh K. Iron deficiency as a risk factor for first febrile seizure. Indian Pediatr 2010;47:437-439.
24. Hartfield DS, Tan J, Yager JY, et al. The association between iron deficiency and febrile seizures in childhood. Clin Pediatr (Phila) 2009;48:420-426.
25. Zareifar S, Hosseinzadeh HR, Cohan N. Association between iron status and febrile seizures in children. Seizure 2012;21:603-605.
26. Kumari PL, Nair MK, Nair SM, Kailas L, Geetha S. Iron deficiency as a risk factor for simple febrile seizures--a case control study. Indian Pediatr 2012;49:17-19.
27. Talebian A, Momtazmanesh N, Moosavi SGH, Khojasteh MR. The relationship between anemia and febrile seizure in children under 5 years old. Iran J Pediatr 2006;16:79-82.
28. Kobrinsky NL, Yager JY, Cheang MS, Yatscoff RW, Tenenbein M. Does iron deficiency raise the seizure threshold? J Child Neurol 1995;10:105-109.
29. Derakhshanfar H, Abaskhanian A, Alimohammadi H, ModanlooKordi M. Association between iron deficiency anemia and febrile seizure in children. Med Glas (Zenica) 2012;9:239-242.
30. Bidabadi E, Mashouf M. Association between iron deficiency anemia and first febrile convulsion: a case-control study. Seizure 2009;18:347-351. Erratum in: Seizure 2021;85:155.
31. Abaskhanian A, Vahid Shahi K, Parvinnejad N. The association between iron deficiency and the first episode of febrile seizure. J Babol Univ Med Sci 2009;11:32-36.

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Quality of Life, Prevalence of Depression, Independence in Activities of Daily Living Among Individuals Aged 65 and Over Living in the City Center of Bitlis

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What is known on this subject?

The increase in the elderly population worldwide also reveals the importance of elderly people having a long and healthy life. The important factors of a long and healthy life include quality of life, independence in daily living activities and active life, and depression, which is one of the increasing problems of mental health in the elderly.

What this study adds?

Quality of life, independence status, and depression in the elderly are affected by many variables.

ABSTRACT

Objective: This study aimed to determine the quality of life, prevalence of depression, and level of independence in activities of daily living among individuals aged 65 and over and to examine related factors.

Material and Methods: This was a cross-sectional study. Three hundred and fifty-four individuals aged 65 and over were included in the study. In the study, socio-demographic questions, "World Health Organization Quality of Life-Old Module (WHOQOL-OLD)", "Katz Index of Independence in Activities of Daily Living", and "Yesavage Geriatric Depression Scale" were used.

Results: The rate of dependence on activities of daily living among the elderly who participated in the study was 27.7%. The level of definitive depression in the elderly was 55.1%. Considering the WHOQOL-OLD total scores, educational level, nutrition, health assessment, pain, physical activity, leisure time, and use of mobile phones significantly affected the quality of life ($p<0.05$). The difference between age groups, marital status, people with whom they share the same house, pain status, and dependence on daily living activities was significant ($p<0.05$). The difference between age groups, gender, chronic disease status, health assessment, pain, sleeping pattern, physical activity, leisure time, and depression was significant ($p<0.05$).

Conclusion: Quality of life, dependency status, and depression in the elderly are affected by many variables, and comprehensive and cross-sectoral studies are required.

Keywords: Quality of life, activities of daily living, geriatric psychiatry, elderly

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This study was derived from Fatma Söylemez's doctoral thesis titled "Quality of Life, Depression Frequency, İndependence in Daily Life Activities and Related Factors Among 65 Age and Over İnviduals Living in Bitlis Province Center".

This study was presented and published as an online oral presentation at the "Academic Geriatrics Society E-Congress 2020" congress.

Introduction

The number and rate of the population over 60 is increasing daily; it is expected to double from 12% to 22% in 2050 compared to 2015 (1). The data of the Turkish Statistical Institute show that while the population aged 65 and over was 8.5% in 2017 in Turkey, it will increase to 9.9% in 2022 (2). The quality of life and drawbacks of the elderly population should be examined because of the increase in older individuals in the world and Turkey and the problems experienced in old age. Increasing age increases the risk of chronic disease and dependence. Diseases such as hearing, vision, and movement-related losses, dementia, cardiovascular diseases, stroke, chronic respiratory diseases, diabetes, and osteoarthritis in individuals over 60 years of age can cause disability and death. In addition, older individuals show more depression symptoms than younger individuals. This situation is seen in 1 out of 10 older people, poses a risk for depression, and negatively affects the quality of life of the elderly (3). The World Health Organization reports that the prevalence rate of depression in individuals over 60 is 5.7% worldwide (4). Depression in the elderly: It may be related to situations such as loneliness, loss of a spouse, and dependence on daily activities (5,6). The presence of depression in an individual's history and family history may also pose a risk of depression in old age. This depression should not be confused with the sadness and mourning of individual experiences due to crises and stress. Untreated depression not only impairs the quality of life of the elderly individual but can also lead to dire consequences such as suicide if it becomes chronic in the individual (7). In the "Turkey Healthy Aging Action Plan and Implementation Program 2021-2026", it is expected that physiological changes with age will cause some adverse effects on quality of life. However, it is emphasized that treating chronic diseases, eliminating social and economic negativities, gaining healthy lifestyle behaviors for the elderly, and making the environment of elderly individuals healthy and safe are essential to prevent the dependence of the elderly and to enable them to live a better quality of life (8).

This study aims to determine the quality of life, prevalence of depression, and level of independence in activities of daily living in older people aged 65 years and over living in the city center of Bitlis and to identify the related factors.

Research Questions

1. What is the quality of life of individuals aged 65 years and over living in Bitlis city center?

2. What is the frequency of depression in individuals aged 65 years and over living in Bitlis city center?

3. What is the level of independence in daily life activities of individuals aged 65 years and over living in Bitlis city center?

4. Do socio-demographic characteristics affect the quality of life, frequency of depression, and level of independence in daily life activities of elderly individuals?

Material and Methods

This cross-sectional study was conducted on individuals aged 65 years and over in the city center of Bitlis from March to May 2018. The number of elderly individuals aged 65 and over, who were 3012 registered in the existing family health centers (FHC) at the time of the study, was obtained from the Provincial Directorate of Health, and the sample size was calculated as 338 people at a confidence interval of 95%. The sample size was weighted according to the population registered in 9 FHCs in the center of Bitlis. Despite the possibility of missing or incorrectly filled questionnaires, an additional two people were included in the study for each FHC, and 354 elderly individuals were reached. Participation in the study was based on volunteerism, and a face-to-face survey technique was used. Institutional permission was obtained from the Provincial Directorate of Health of Bitlis, and ethics committee approval was obtained from the Bitlis Eren University Ethics Committee with the decision dated 13.12.2017 and numbered 2017/12-IX.

Socio-demographic questions for individuals over the age of 65, "World Health Organization Quality of Life-Old Module (WHOQOL-OLD)", "Katz Index of Independence in Activities of Daily Living", and "Yesavage Geriatric Depression Scale" were used in the questionnaire form used to collect the data.

World Health Organization Quality of Life-Old Module

"WHOQOL-OLD" was developed as a result of research with the participation of 22 countries to be used in epidemiological studies in elderly groups, supported by the "World Health Organization Quality of Life Group" The Turkish validity and reliability study was performed by Eser et al. (9) in 2010. The Cronbach's alpha value is 0.85. Twenty-four and one hundred twenty points are obtained from this five-point Likert-type scale. The higher the score obtained from the scale, the better the individual's quality of life (9).

Katz Index of Independence in Activities of Daily Living

The Katz index of Independence in Activities of Daily Living was developed by Katz et al. (10) to determine the independence of older individuals in activities of daily living. A Turkish validity and reliability study of the scale was

conducted by Arik et al. (11) in 2015. The Cronbach's alpha value is 0.83. It has six items rated 1 point if the individual is independent in some activities for various activities of daily living and 0 if he/she is dependent. A total of 6 points indicate independence, and 0 points indicate complete dependence (11).

Geriatric Depression Scale

The geriatric depression scale was developed by Yesavage et al. (12) in 1983 to assess depressive status in elderly groups. The Turkish validity and reliability study was conducted by Ertan (13) in 1997. While each answer in favor of depression is evaluated as 1 point, the other answers are evaluated as 0 points. The scores obtained from this scale, which consists of 30 questions, range from 0 to 30. The scale is scored asfollows: 0-10 points for "no depression", 11-13 points for "probable depression", and ≥14 points for "definitive depression" (13).

Statistical Analysis

The dependent variables were WHOQOL-OLD total score, independence index, and geriatric depression scale scores. In contrast, the independent variables were age, gender, educational background, people with whom they share the same house, number of chronic diseases, nutritional status, sleeping pattern, and mobile phone use. The data were analyzed using SPSS 16.0. In the Shapiro-Wilk test, it was observed that the data were not suitable for normal distribution ($p<0.05$). WHOQOL-OLD total score, independence index, and geriatric depression scale scores were not normal distrubation ($p<0.05$). Chi-square test, Fisher's exact test, Mann-Whitney U test, Kruskal-Wallis analysis of variance, and Mann-Whitney U test with Bonferroni correction as a post-hoc test were used for statistical analysis. The significance value was set as $p<0.05$ during the assessment.

Results

As seen in Table 1, 65.2% of the study group were aged between 65 and 74 years, 59.6% were female, and 56.2% were married. 67.8% of the participants were illiterate. 5.6% stated that they were employed, and 29.7% were retired. 48.9% of the participants stated that they lived with their partners.

Furthermore, 65.5% of individuals over 65 stated that they had a regular diet, and 47.2% stated that they slept regularly. 64.1% of the sample group rated their health as moderate. 43.5% of the elderly stated that they regularly did physical activity. 20.3% of the participants stated that they had no chronic diseases. 60.7% of the individuals in the sample group stated that they used mobile phones, and 28% stated that they spent their leisure time.

When the WHOQOL-OLD total score was examined according to some characteristics of the participants, the difference between the WHOQOL-OLD total score was not significant in terms of age groups, gender, people with whom they share the same house, and the number of chronic diseases ($p>0.05$). The WHOQOL-OLD median total score of the participants who had a primary school and higher education stated that they had a regular diet, evaluated their health as excellent and moderate, and did not suffer from pain was significantly higher when compared with the other groups ($p<0.05$). The WHOQOL-OLD median total score of those who performed physical activity, spent their leisure time, and used mobile phones was significantly higher than that of the other groups ($p<0.05$) (Table 2).

Table 1. Distribution of socio-demographic characteristics of the participants

	n	%
Gender		
Male	143	40.4
Female	211	59.6
Marital status		
Married	199	56.2
Single or widow	155	43.8
Age group		
65-74	231	65.2
75-84	88	24.9
85 and above	35	9.9
Educational background		
Illiterate	240	67.8
Literate	63	17.8
Primary school and higher	51	14.4
Number of children		
No children	6	1.7
1-3	18	5.1
4-6	92	26.0
7-9	161	45.5
10 and more	77	21.8
Monthly income		
Low	117	33.1
Middle	205	57.9
High	32	9.0
People with whom participants share the same house		
Alone	22	6.2
With their partner	173	48.9
With their children or relatives	159	44.9
Total	354	100.0

Table 2. Comparison of WHOQOL-OLD total score in terms of some characteristics of the participants

Some characteristics	WHOQOL-OLD total score Min-med-max	p
Age group		
65-74	39-70-105	0.064*
75-84	37-71-104	
85 and above	39-60-100	
Gender		
Male	42-71-104	0.087**
Female	37-69-105	
Educational background		
Illiterate	37-66.5-105	**<0.001***
Literate	42-71-104	
Primary school and higher[a]	54-80-104	
People with whom participants share the same house		
Alone	53-73.5-104	0.120*
With their partner	42-70-104	
With their children or relatives	37-69-105	
Number of chronic diseases		
None	39-69.5-104	0.994*
1	39-70-105	
2	37-70-100	
3 and more	42-70-101	
Nutritional status		
Regular	41-71-104	**0.001****
Irregular	37-65-105	
Health assessment status		
Good	50-75-104	**0.001***
Moderate[b]	42-72-105	
Poor	37-60.5-98	
Presence of pain		
Yes	37-67-105	**0.001****
No	37-74-102	
Status of doing physical activity		
Yes	42-73-105	**0.001****
No	37-67.5-104	
Status of spending leisure times		
Yes	41-74-104	**0.001****
No	37-68-105	
Status of using mobile phone		
Yes	39-72-104	**0.001****
No	37-65-105	

**Kruskal-Wallis test, **Mann-Whitney U test, [a]'Primary school and higher' different from illiterate and literate, [b]'Moderate' different from good and poor. WHOQOL-OLD: World Health Organization Quality of Life-Old Module, Min-med-max: Minimum, median, maximum*

Table 3. Comparison of dependence status of the participants in terms of some characteristics of them

Some characteristics	Dependence status				p****
	Dependent		Independent		
Age group	n	%	n	%	
65-74[a]	42	18.2	189	81.8	**<0.001**
75-84[b]	35	39.8	53	60.2	
85 and above[c]	21	60.0	14	40.0	
Gender					
Male	43	30.1	100	69.9	0.409
Female	55	26.1	156	73.9	
Marital status					
Married	42	21.1	157	78.9	**0.002**
Single or widow	56	36.1	99	63.9	
Educational background					
Illiterate	73	30.4	167	69.6	0.22
Literate	15	23.8	48	76.2	
Primary school and higher	10	19.6	41	80.4	
People with whom participants share the same house					
Alone	5	22.7	17	77.3	**0.008**
With their partner	36	20.8	137	79.2	
With their children or relatives[d]	57	35.8	102	64.2	
Presence of pain					
Yes	75	31.8	161	68.2	**0.015****
No	23	19.5	95	80.5	

****Pearson chi-square, [a, b, c]: '65-74', '75-84', '85 and above' are different from each other. [d]: 'With their children or relatives' different from 'alone' and 'with their partner'

Table 3 shows that the difference between the dependence status of the participants according to gender and educational background was insignificant (p>0.05). The dependence rate was 18.2% in the age group of 65-74 years, 39.8% in the age group of 75-84 years, and 60% in the age group of ≥85, and all the groups differed from each other (p<0.001). The rate of dependence was significantly higher in those who were single or widowed (36.1%), those living with their children or relatives (35.8%), and those suffering from pain (31.8%) (p<0.05) (Table 3).

Table 4 compares some characteristics and depression status of the participants. 47.2% of the individuals in the age group of 65-74 years, 65.9% of the individuals in the age group of 75-84 years, 80.0% of the individuals aged 85 and over were at the level of definitive depression, and the difference between the age groups was significant (p=0.001). Those who were female, had three or more chronic diseases, assessed their health as poor, suffered from pain, had irregular sleeping patterns, did not perform physical activity, and did not spend their leisure time had a significantly higher rate of definitive depression than the other groups (p<0.05) (Table 4).

Discussion

There was no significant difference in the WHOQOL-OLD total scores of the participants with regard to age group, gender, people with whom they share the same house, and number of chronic diseases. Similarly, many studies examining how a healthy lifestyle affects the quality of life in the elderly have reported no significant difference between the quality of life and age groups and gender (14,15). An international study reported no correlation between living alone or with someone and quality of life, which is compatible with this study (15). Another international study stated that quality of life scores decreased significantly in patients suffering from 5 or more diseases (16). Living with their partner or with someone for the elderly can be effective in meeting their needs and leading a regular life. The reason why there was no significant

difference between the people with whom they shared the same house and the quality of life in the present study may be due to the scarcity of elderly individuals living alone. Among the individuals over 65 who participated in the study, those with a higher educational level had a higher quality of life scale score. Likewise, a study conducted in Brazil on the elderly group indicated that the quality of life was enhanced in groups with higher educational levels (17). The quality of life of the group who stated that they ate regularly, assessed their health as excellent and moderate, and did not have pain was higher. It has been reported in the literature that positive nutritional behaviors are the most crucial factor in terms of quality of life in advanced ages (18), and a conscious, healthy, and balanced diet enhances the quality of life (19). A study conducted with data obtained from cities selected from 20 countries found that satisfaction with health status significantly enhanced

Table 4. Comparison of depression status according to some characteristics of the participants

Some characteristics	Depression status						p*
	No depression		Probable depression		Definitive depression		
Age group	n	%	n	%	n	%	
65-74[a]	87	37.6	35	15.2	109	47.2	**0.001**
75-84[b]	20	22.7	10	11.4	58	65.9	
85 and above[c]	4	11.4	3	8.6	28	80.0	
Gender							
Male	57	39.8	20	14.0	66	46.2	0.011
Female	54	25.6	28	13.3	129	61.1	
People with whom participants share the same house							
Alone	6	27.3	4	18.2	12	54.5	0.449
With their partner	61	35.2	19	11.0	93	53.8	
With their children or relatives	44	27.7	25	15.7	90	56.6	
Number of chronic disease							
None[d]	39	54.1	4	5.6	29	40.3	**<0.001**
1	38	34.6	16	14.5	56	50.9	
2	27	24.8	20	18.3	56	50.9	
3 and more[e]	7	11.1	8	12.7	48	76.2	
Health assessment							
Good[a]	23	56.1	6	14.6	12	29.3	**<0.001**
Moderate[b]	78	34.4	37	16.3	112	49.3	
Poor[c]	10	11.6	5	5.8	71	82.6	
Presence of pain							
Yes	57	24.2	31	13.1	148	62.7	**<0.001**
No	54	45.8	17	14.4	47	39.8	
Sleeping pattern							
Regular	70	41.9	22	13.2	75	44.9	**<0.001**
Irregular	41	21.9	26	13.9	120	64.2	
Physical activity							
Yes	66	42.9	23	14.9	65	42.2	**<0.001**
No	45	22.5	25	12.5	130	65.0	
Status of spending leisure times							
Yes	46	46.5	20	20.2	33	33.3	**<0.001**
No	65	25.5	28	11.0	162	63.5	

**Pearson chi-square, [a, b, c]: '65-74', '75-84', '85 and above' are different from each other, [d, e]: 'None' and '3 and more' different from others*

quality of life (20). A study conducted in Chile reported that the quality of life decreased significantly in individuals who described themselves as sick (21). In a study conducted in 2018 in Turkey, it was stated that pain caused problems in sleep, memory, and concentration in elderly individuals and decreased quality of life (22). A study conducted in a nursing home in İstanbul reported an increased quality of life in elderly individuals who did not experience pain (23). The quality of life was higher in the elderly who were physically active, spent their leisure time, and used mobile phones. International studies have found that physical activity positively affects the quality of life, and there is a significant correlation between physical activity and quality of life (15,24). The results of this study indicated that physical activity positively affects the quality of life, which is consistent with the literature. Physical activity reduces inactivity in the elderly in daily life, increases their well-being, and may enhance their quality of life.

A study conducted in Japan on elderly individuals over the age of 60 reported a positive correlation between spending leisure time and quality of life (24). Spending leisure time with elderly individuals may cause them to realize that their productivity continues and enhance their quality of life. A study conducted in 11 cities in the Black Sea, Central Anatolia, and Mediterranean regions demonstrated that information and communication technology can enhance the quality of life of elderly individuals (25). The present study was conducted in a province in eastern Turkey, and the use of mobile phones by elderly individuals living in this city, which has both climatic and geographical difficulties, can be very beneficial in terms of socialization and reaching needs.

There was no significant difference between the dependence status of individuals over 65 in the sample group according to gender and educational background. In a study conducted in Turkey, no correlation was found between gender and independence in activities of daily living (26), which is compatible with the present study. A study conducted in a nursing home in Kayseri reported that 9.8% of the illiterate elderly were dependent, and there was no dependence on the elderly with higher education (26). In this study, the dependence rate increased significantly in the groups with increasing age. Likewise, an international study indicated that as age increased, dependence and restriction in activities of daily living increased (27). Similar to this study, studies conducted in Karaman and Spain reported that married older people showed lower levels of dependence than their single counterparts (28,29). In this study, the dependence rate was significantly higher in the elderly living with their children or relatives. In an international meta-analysis study, it was reported that living with people other than children and their partners was a risk factor for independence in activities of daily living (27). In a study conducted in Turkey, which supports this study, it was stated that pain has a negative effect on activities of daily living (30). Accompanying pain in health problems that cause dependence on activities of daily life may cause a high dependence rate in elderly individuals.

In this study, the level of depression increased with increasing age. Those who were female, had three or more chronic diseases, assessed their health as poor, had pain, irregular sleeping patterns, did not do physical activity, and stated that they did not spend their leisure time had a significantly higher level of depression than the other groups. In studies conducted in Turkey and abroad, similar to our study, the rate of depression increases significantly as the age group increases (31,32). A previous study reported no significant correlation between depression and age (33). As age progresses, physical health may deteriorate, resulting in a negative effect on mental health and an increase in the rates of depression. Similar to the present study, the results of a study on older people living in their homes and nursing homes in Bolu indicated that the mean score of depression in women was 10.21 and 6.69, in men and the difference was significant (34). Although national and international studies support the results of this study (31,35,36), in some studies, no significant difference was found between gender and depression (32,33,37). The fact that depression was higher in women in this study can be explained by the longer life expectancy in women than in men, and chronic diseases are more common; therefore, depression accompanies diseases. Similar to the present study, although studies have reported a significant difference in depression in patients with chronic diseases compared with those without chronic disease (32,36), there are also studies reporting no difference (31,35). Chronic diseases may negatively affect daily life in the elderly, sometimes cause problems in vital activities, and therefore may increase the rates of depression. Studies conducted in Turkey and South Africa reported that those who assessed their health as poor had a significantly higher risk of depression (31,38). The fact that individuals consider their health negatively may also have negatively impacted their mental health. In some national and international studies, similar to this study, it was stated that pain was associated with an increase in the level of depression (35,39). Pain may be associated with fatigue, sleep disorders, and memory and concentration problems in elderly individuals, and depression may accompany these conditions. Similar studies have reported that sleep disorders may impair mental health, and depression may cause sleeplessness (38,39). While there are

studies stating that high physical performance is associated with low depression symptoms (39) and supporting the present study, there are also studies in which the difference is not significant (33). National and international studies have reported that increasing leisure activities significantly reduces depressive symptoms (40). The fact that the elderly are engaged in hobbies during their leisure time can make them feel good regarding mental health.

Study Limitations

The limitations of this study are that it covers a provincial center, is conducted within a certain period of time, and cannot be generalized to the whole country. In addition, the limitations of the study are that the data were obtained through a questionnaire based on verbal statements.

Conclusion

Efforts to protect and improve the health of the elderly should be carried out more effectively, and health and social services for the elderly should be increased. Public health interventions and policies planned for these purposes should be implemented comprehensively. "Lifelong Learning" programs and effective preventive health services should be offered to the elderly, physical activity should be encouraged, leisure time activities should be increased, and hobby centers should be established. Care should be taken to diagnose and treat mental health issues in elderly individuals.

Ethics

Ethics Committee Approval: Institutional permission was obtained from the Provincial Directorate of Health of Bitlis, and ethics committee approval was obtained from the Bitlis Eren University Ethics Committee with the decision dated 13.12.2017 and numbered 2017/12-IX.

Informed Consent: Written and verbal consent was obtained from older who agreed to participate in the research.

Authorship Contributions

Concept: F.S., A.Ö., Design: F.S., Data Collection or Processing: F.S., A.G., Analysis or Interpretation: F.S., A.G., A.Ö., Literature Search: F.S., A.G., Writing: F.S., A.G., A.Ö.

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REFERENCES

1. World Health Organization (WHO). Ageing. Available from: https://www.who.int/health-topics/ageing#tab=tab_1. Accessed Sept 7, 2022.
2. Türkiye İstatistik Kurumu (TÜİK). İstatistiklerle Yaşlılar, 2022. [cited Available from: https://data.tuik.gov.tr/Bulten/Index?p=%C4%B0statistiklerleYa%C5%9Fl%C4%B1lar-2022-49667&dil=1. Accessed Sept 6, 2023.
3. World Health Organization (WHO). Integrated care for older people Guidelines on community-level interventions to manage declines in intrinsic capacity (2017). Available from: https://www.who.int/publications/i/item/9789241550109. Accessed 29, Nov 2022.
4. World Health Organization (WHO). Depression. Available from: https://www.who.int/news-room/fact-sheets/detail/depression. Accessed 29, Nov 2022.
5. Beğer T, Yavuzer H. Yaşlılık ve yaşlılık epidemiyolojisi. Klinik Gelişim 2012;25:1-3.
6. Kalkan M. Yaşlılık: Tanımı Sınıflandırılması ve Genel Bilgiler. In: Ersanlı K, Kalkan M, editors. Psikolojik, Sosyal ve Bedensel Açıdan Yaşlılık. 1st ed. Pegem Akademi Yayınları; 2008:1-17.
7. Özer S. Sık Rastlanan Psikiyatrik Sorunlar. Available from: https://gebam.hacettepe.edu.tr/yaslilikta_kaliteli_yasam_son.pdf. Accessed 12, Nov 2022.
8. TC. Sağlık Bakanlığı. Türkiye Sağlıklı Yaşlanma Eylem Planı ve Uygulama Programı 2021-2026. Available from: https://ekutuphane.saglik.gov.tr/Home/GetDocument/653. Accessed 18 Aug 2023.
9. Eser S, Saatli G, Eser E, Baydur H, Fidaner C. Yaşlılar için Dünya Sağlık Örgütü Yaşam Kalitesi Modülü WHOQOL-OLD: Türkiye alan çalışması Türkçe sürüm geçerlilik ve güvenilirlik sonuçları. Türk Psikiyatri Dergisi 2010;21:37-48.
10. Katz S, Downs TD, Cash HR, Grotz RC. Progress in development of the index of ADL. Gerontologist 1970;10:20-30.
11. Arik G, Varan HD, Yavuz BB, et al. Validation of Katz index of independence in activities of daily living in Turkish older adults. Arch Gerontol Geriatr 2015;61:344-350.
12. Yesavage JA, Brink TL, Rose TL, et al. Development and validation of a geriatric depression screening scale: a preliminary report. J Psychiatr Res 1982-1983;17:37-49.
13. Ertan T. Reliability and validity of the geriatric depression scale and the self rating depression scale in Turkish population over years of age (Medical Specialization Thesis). İstanbul: İstanbul Univ; 1996.
14. Güngör Tavşanlı N, Özçelik H, Karadakovan A. Examine of quality of life of elderly indivudals suffering pain. Ağrı 2013;25:93-100.
15. Haider S, Luger E, Kapan A, et al. Associations between daily physical activity, handgrip strength, muscle mass, physical performance and

quality of life in prefrail and frail community-dwelling older adults. Qual Life Res 2016;25:3129-3138.

16. Viana DA, Andrade FCD, Martins LC, Rodrigues LR, Dos Santos Tavares DM. Differences in quality of life among older adults in Brazil according to smoking status and nicotine dependence. Health Qual Life Outcomes 2019;17:1.
17. Varela FRA, Ciconelli RM, Campolina AG, et al. Quality of life evaluation of frail elderly in Campinas, São Paulo. Rev Assoc Med Bras 2015;61:423-430.
18. Aksoydan E. Yaşlılık ve Beslenme. 1st ed. Ankara, Klasmat Matbaacılık. 2008:3-45.
19. Aslan P. Yaşlılıkta Sağlıklı ve Bilinçli Beslenme. Available from: https://gebam.hacettepe.edu.tr/yaslilikta_kaliteli_yasam_son.pdf. Accessed 12, Nov 2022.
20. Low G, Molzahn AE, Schopflocher D. Attitudes to aging mediate the relationship between older peoples' subjective health and quality of life in 20 countries. Health Qual Life Outcomes 2013;11:146.
21. Urzúa A, Bravo M, Ogalde M, Vargas C. Factores vinculados a la calidad de vida en la adultez mayor. Rev Med Chile 2011;139:1006-1014.
22. Durduran Y, Okka B, Şafak Ş, Karaoğlu N, Uyar M. Yaşlılıkta yaşam kalitesi değerlendirilmesi: kamu hastanesine başvuranlar örneği. Genel Tıp Derg 2018;28:113-120.
23. İlhan N, Arpacı S, Havaoğlu D, Kalyoncuoğlu H, Sarı P. Quality of life and factors affecting the quality of life of elderly nursing home residents. Clin Exp Health Sci 2016;6:56-65.
24. Sampaio PY, Ito E. Activities with higher influence on quality of life in older adults in Japan. Occup Ther Int 2013;20:1-10.
25. Kalınkara V, Başıbüyük GÖ, Ay F. Yaşlıların geronteknolojik ürünleri kabule yönelik tutumları. Yaşlı Sorunları Araştırma Dergisi 2016;9:1-19.
26. Göçer Ş, Günay O. Kayseri'de Bir Huzurevinde Yaşayan Yaşlıların Günlük Yaşam Aktiviteleri ve Depresif Belirti Düzeyleri. Euras J Fam Med 2018;7:116-124.
27. van der Vorst A, Zijlstra GA, Witte N, et al. Limitations in activities of daily living in community-dwelling people aged 75 and over: a systematic literature review of risk and protective factors. PLoS One 2016;11:e0165127. Erratum in: PLoS One 2017;12:e0170849.
28. Cingil D, Bodur S. Karaman il merkezinde yaşayan yaşlıların bağımlılık düzeyleri, demografik ve medikal özelliklerinin incelenmesi. Atatürk Üniversitesi Hemşirelik Yüksekokulu Dergisi 2008;11:33-39.
29. Millán-Calenti JC, Tubío J, Pita-Fernández S, et al. Prevalence of functional disability in activities of daily living (ADL), instrumental activities of daily living (IADL) and associated factors, as predictors of morbidity and mortality. Arch Gerontol Geriatr 2010;50:306-310.
30. Babacan Gümüş A, Keskin G, Orgun F. Pain and living activities in elderly at a nursing home: an investigation in terms of depression, anxiety and somatization. Turk J Geriatr 2012;15:299-305.
31. Altay B, Üstün G. Risk of depression in hospitalized elderly patients at a university hospital and the effects of some socio-demographic characteristics. Acıbadem Üniversitesi Sağlık Bilimleri Dergisi 2012;3:108-116.
32. Liu PC, Chung MS. The prevalence and correlates of depression of the elderly in local community centers in Nantou, Taiwan. Taiwan J Psychiatry 2019;33:110-113.
33. Mohd Aznan MA, Mohamad CM, Nur Suriati S, et al. Prevalence of depressive symptoms among elderly and its predictors: a cross sectional study in community Felda Bukit Goh, Kuantan Pahang. J Fam Med Forecast 2019;2:1-6.
34. Tarsuslu Şimşek T, Tütün Yümin E, Sertel M, Öztürk A, Yümin M. The Effect of Depression on Life Satisfaction and Health Related Quality of Life in The Elderly Men and Women. F Ü Sağ Bil Tıp Derg 2010;24:147-153.
35. Babatsikou F, Konsolaki E, Notara V, Kouri M, Zyga S, Koutis C. Depression in the elderly: a descriptive study of urban and semi-urban Greek Population. Int J Caring Sci 2017;10:1286-1295.
36. Saltan A. The investigation of the relations between depression and pain, sociodemographics knowledge in the elderly people. J DU Health Sci Inst 2017;7:67-72.
37. Nascimento PPP, Batistoni SST, Neri AL. Frailty and depressive symptoms in older adults: data from the FIBRA study – UNICAMP. Psicologia: Reflexão e Crítica 2016;29:1-11.
38. Padayacheya U, Ramlalla S, Chipps J. Depression in older adults: prevalence and risk factors in a primary health care sample. South African Family Practice 2017;59:61-66.
39. Silva MR, Ferretti F, Pinto SS, Tombini Filho OF. Depressive symptoms in the elderly and its relationship with chronic pain, chronic diseases, sleep quality and physical activity level Br J Pain. São Paulo 2018;1:293-298.
40. Poelke G, Ventura MI, Byers AL, Yaffe K, Sudore R, Barnes DE. Leisure activities and depressive symptoms in older adults with cognitive complaints. Int Psychogeriatr 2016;28:63-69.

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Optic Nerve Sheath Diameter Changes During Laparoscopic Cholecystectomy in the Reverse Trendelenburg Position: Total Intravenous Anesthesia vs. Desflurane

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What is known on this subject?

Sonographically determined optic nerve sheath diameter (ONSD) has been proposed as a straightforward and non-invasive technique for detecting elevated intracranial pressure (ICP). Several studies have measured ONSD in different positions by comparing other anesthesia methods. However, studies on the reverse Trendelenburg position are limited.

What this study adds?

Ultrasonographically assessed ONSD as a representative metric for ICP is evaluated to assess the effects of desflurane and propofol-based total intravenous anesthesia in patients undergoing elective laparoscopic procedures in the reverse Trendelenburg position.

ABSTRACT

Objective: We aimed to compare the impacts of total intravenous anesthesia (TIVA) and desflurane on optic nerve sheath diameter (ONSD) among patients undergoing elective laparoscopic surgery in the reverse Trendelenburg position.

Material and Methods: In this prospective randomized trial, individuals aged 18 to 65 scheduled for laparoscopic cholecystectomy were recruited and randomly divided into either the TIVA or desflurane group. ONSD was assessed at four distinct time points: before anesthesia administration (T0), 5 min after carbon dioxide insufflation in the reverse Trendelenburg position (T1), 5 min after pneumoperitoneum termination in the reverse Trendelenburg position (T2), and post-extubation (T3). The primary outcome was the mean ONSD measurement at each of these time points within the TIVA and desflurane groups throughout the surgery.

Results: No statistical difference was found in the mean ONSD values between the groups at all four points. However, the mean change in ONSD between T0 and T1 points and T1 and T2 points was significantly lower in the TIVA group (p=0.025, p=0.006, respectively) than in the desflurane group.

Conclusion: Our findings imply that TIVA may be more appropriate for patients undergoing surgery in the reverse Trendelenburg position because of minor changes in ONSD.

Keywords: Ultrasonography, reverse trendelenburg position, pneumoperitoneum, optic nerve sheath diameter

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Introduction

Laparoscopic surgery has gained popularity as the preferred approach for numerous treatments recently (1). Nevertheless, laparoscopic procedures necessitate the creation of an artificial pneumoperitoneum, which might result in physiological alterations such as an increase in intracranial pressure (ICP) (2). While laparoscopy might lead to a major negative impact on cerebrovascular condition due to increased ICP, the ideal approach for monitoring ICP, which is invasive, has a risk of serious complications such as bleeding or infection (3). Sonographically measured optic nerve sheath diameter (ONSD) has been proposed as a straightforward and non-invasive technique for detecting elevated ICP (3,4).

Total intravenous anesthesia (TIVA) is commonly acknowledged for its capacity to lower ICP by diminishing both cerebral blood flow (CBF) and cerebral blood volume (CBV) (5). In contrast, inhalational anesthetics have a dose-dependent effect of increasing CBF by stimulating cerebral vasodilatation, which in turn may lead to an increase in ICP (6,7,8). Moreover, the patients' positions are changed to ease the surgical technique, which also affects ICP. Several studies have measured ONSD in different positions by comparing other anesthesia methods (9,10,11,12,13,14,15). However, studies on the reverse Trendelenburg position are limited (11). To the best of our knowledge, no study has compared ONSD measurements between desflurane and TIVA administration in the reverse Trendelenburg position.

Ultrasonographically assessed ONSD as a representative metric for ICP was evaluated to assess the effects of desflurane- and propofol-based TIVA in patients undergoing elective laparoscopic procedures in the reverse Trendelenburg position.

Material and Methods

Participants

This prospective randomized controlled trial was conducted at University of Health Sciences Turkey, Kartal Dr. Lütfi Kırdar City Hospital following approval from the Ethics Committee of the University of Health Sciences Turkey, Kartal Dr. Lütfi Kırdar City Hospital (approval number: 2019/514/148/19, date: 27/02/2019). All participants provided written informed consent. This study adhered to the ethical principles outlined in the Declaration of Helsinki-2013 and followed guidelines for good clinical practice.

Between March and July 2019, a total of eighty-six patients, classified as American Society of Anesthesiologists (ASA) class I to II and aged between 18 and 65 years, were enrolled in the study. Two patients with previous cerebrovascular incidence with hydrocephalus and intracranial hemorrhage, two patients with glaucoma, one patient with body mass index >30, one patient who refused to participate, and two patients due to other reasons were excluded from enrollment.

Anesthesiologist randomly assigned patients to the desflurane or TIVA groups 1 h before surgery. After randomization, participants were divided into two groups: desflurane group, which received desflurane inhalation and remifentanil infusion (n=39); and TIVA group, which received propofol and remifentanil infusion for anesthesia maintenance during surgery (n=39). Two patients in the TIVA group were excluded due to operation cancelation (Figure 1).

Anesthetic and Surgical Techniques

In the operating room, patients were monitored using pulse oximetry, electrocardiography, and non-invasive blood pressure monitors. Following 3 min of preoxygenation, patients in the desflurane group received 2 mg/kg of propofol for anesthesia induction, followed by maintenance with 4-6% desflurane and 0.05-0.15 mcg/kg/min IV remifentanil. Patients

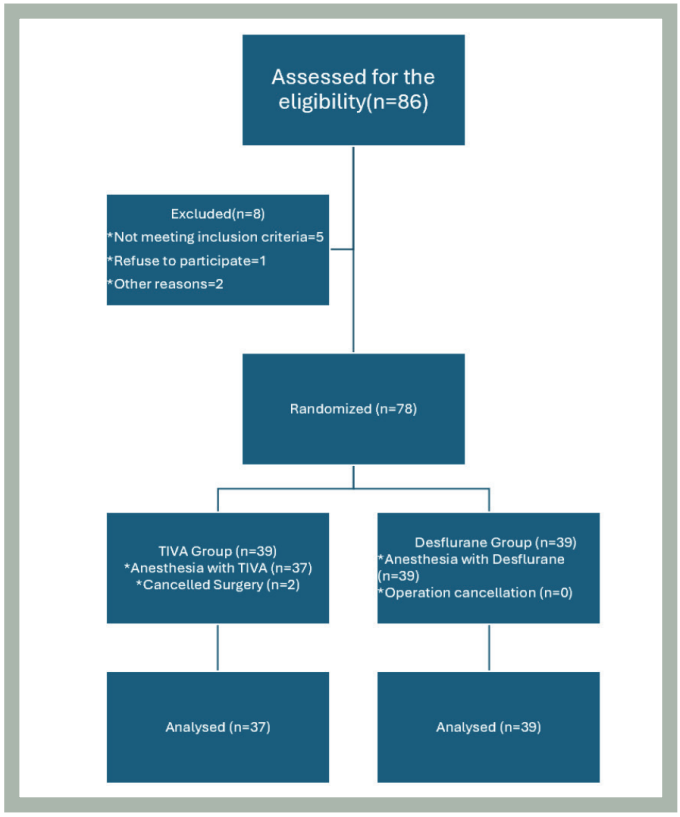

Figure 1. Consort flow diagram
TIVA: Total intravenous anesthesia

in the TIVA group received continuous infusions of propofol and remifentanil via a target-controlled infusion pump. Propofol dosage was adjusted within a range of 2-5 mcg/mL, whereas remifentanil dosage was adjusted within a range of 2-5 ng/mL. Both groups received 0.6 mg/kg of rocuronium for muscle relaxation followed by intubation. Mechanical ventilation was maintained in a volume-controlled mode with a tidal volume of 6 mL per kilogram of ideal body weight.

The respiratory rate was adjusted to maintain SPO_2 between 97-100% and end-tidal carbon dioxide ($etCO_2$) partial pressure at 35±5 mmHg. Positive end-expiratory pressure (PEEP) was maintained between 3 and 5 cmH_2O. All patients were kept normothermic, and their depth of anesthesia was monitored using a bispectral index score monitor set at 40-60 to ensure comparable levels of anesthesia between the two groups. Throughout the procedure, carbon dioxide pneumoperitoneum was maintained at an intra-abdominal pressure of 15±5 mmHg in patients positioned in the reverse Trendelenburg position.

No patients were excluded from the study because of a lack of experiencing unstable vital signs, change into open abdominal surgery, or technical challenges of measurement of ONSD.

Measurements

An experienced anesthesiologist, unaware of the patient's group, used a 7.5-MHz linear probe to evaluate ONSD using ultrasonography. After applying ultrasonic gel, the linear probe was positioned and affixed onto the patient's closed eyelids using transparent Tegaderm. The optic disk vitreous body, and hypoechoic ONS were examined by carefully adjusting the angle of the probe (Figure 2). The ONSD was measured vertically 3 mm posterior to the optic disk in both eyes' sagittal and transverse planes using electronic calipers. For analysis, the mean of the four measurements was used. Each measurement was completed within a 1-min timeframe. Four measurements were taken at specific time points: before anesthesia administration (T0), 5 min after carbon dioxide insufflation in the reverse Trendelenburg position (T1), 5 min after pneumoperitoneum termination in the reverse Trendelenburg position (T2), and post-extubation (T3). $EtCO_2$, mean arterial pressure (MAP), heart rate, and peak airway pressure (PAP) were systematically monitored and recorded at each of the four specified time intervals.

Figure 2. D1: Distance behind the eyeball, D2: ONSD
ONSD: Optic nerve sheath diameter

The primary outcome was the measurement of mean ONSD at each observed time point in the TIVA and desflurane groups during surgery. The secondary outcome was the calculation of changes in mean ONSD and diameter trends in the observed time in the two groups.

We hypothesize that ONSD significantly increases due to the pneumoperitoneum effect, and that TIVA results in a lesser increase in ONSD compared with desflurane anesthesia.

Statistical Analysis

A previous study documented a mean ONSD of 4.7 mm and a maximum ONSD value of 5.1 mm in patients receiving volatile anesthetics (8). According to this study, detecting a mean difference in ONSD between two independent groups with a type I error of 0.05, a power of 80%, and an effect size of 0.6 necessitated a sample size of 36 patients per group.

The normality of continuous data was assessed using the Shapiro-Wilk test. Continuous data are presented as mean ± standard deviation or median (interquartile range), whereas categorical data are presented as frequency (%). Data were compared using independent two-sample t-tests, Mann-Whitney U tests, chi-square tests, or Fisher's exact tests as appropriate. A p value <0.05 was considered statistically significant.

Changes in ONSD over time were evaluated using repeated measures ANOVA with Bonferroni correction, where an adjusted p value of 0.0125 was considered statistically significant in post-hoc tests. All analyses were conducted using SPSS software version 26.0 (IBM Corp., Armonk, NY, USA).

Results

Seventy-six patients in the two groups were analyzed; the median age, height, and weight were similar. There were more women than men in both groups, and the number of

ASA-II patients was higher than that of ASA-I patients in both groups, but no significant difference was detected between the groups. The number of patients with hypertension was similar, whereas the number of patients with diabetes was higher in the TIVA group, but no significant difference was found. The duration of operation and anesthesia were similar in both groups (Table 1).

The ONSD measurements were similar in the two groups; no statistical difference was detected in any of the four measurements. The sheath diameter changes between T0 and T1 points and between T1 and T2 points were significantly lower in the TIVA group than in the desflurane group (p=0.025, p=0.006, respectively). Other measurement differences between observation points were similar in both groups, and no statistically significant difference was detected (Table 2).

When the groups were evaluated independently, a significant increase in ONSD was found between T0 and T1 points, a substantial decrease between T1 and T2 points, and between T1 and T3 points in both groups separately, whereas no significant difference was found in other comparisons (p<0.00, p<0.001, p<0.001, respectively) (Figure 3).

Table 1. Characteristics of the patients

Variables	TIVA group (n=37)	Desflurane group (n=39)	p value
Age (years)	55 (53-61.5)	54.7 (49-57)	0.075
Height (cm)	162.8 (157-169)	164 (158-170)	0.544
Weight (kg)	76 (71-81.3)	77.3 (70.6-82)	0.317
Gender (male/female)	8 (10.5%)/29 (38.2%)	13 (17.1%)/26 (34.2%)	0.376
ASA ASA-I ASA-II	 11 (14.5%) 26 (34.2%)	 10 (13.2%) 29 (38.2%)	0.887
Hypertension	13 (17.1%)	14 (18.4%)	0.945
Diabetes mellitus	14 (18.4%)	9 (11.8%)	0.250
Duration of operation (min)	35 (22.5-35)	35 (25-35)	0.991
Duration of anesthesia (min)	45 (32.5-45)	45 (35-45)	0.991

Data are shown as median (IQR) or number (%, frequency). IQR: Interquartile range, TIVA: Total intravenous anesthesia, ASA: American Society of Anesthesiologists

Table 2. Comparison of mean ONSD values and changes between the two groups

Variables	TIVA group (n=37)	Desflurane group (n=39)	p
ONSD T0 (mm)	4.7±0.4	4.6±0.33	0.208
ONSD T1 (mm)	4.96±0.33	4.98±0.41	0.811
ONSD T2 (mm)	4.7±0.35	4.6±0.4	0.58
ONSD T3 (mm)	4.68±0.37	4.74±0.4	0.883
ONSD difference			
T0-T1 (mm)	0.31±0.24	0.46±0.31	**0.025**
T1-T2 (mm)	0.35±0.22	0.40±0.32	**0.006**
T2-T3 (mm)	0.20±0.19	0.24±0.16	0.466

Data are shown as mean ± standard deviation. Before anesthesia administration (T0), 5 minutes after carbon dioxide insufflation in the reverse Trendelenburg position (T1), 5 minutes after pneumoperitoneum termination in the reverse Trendelenburg position (T2), and post-extubation (T3). TIVA: Total intravenous anesthesia, ONSD: Optic nerve sheath diameter

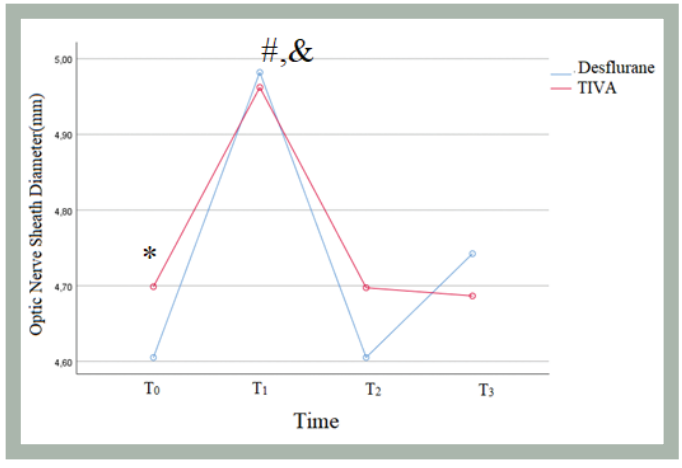

Figure 3. Linear mean ONSD trend of Desflurane and TIVA groups
T_0: Before anesthesia administration, T_1: 5 minutes after carbon dioxide insufflation in the reverse Trendelenburg position, T_2: 5 minutes after the termination of pneumoperitoneum in the reverse Trendelenburg position, T_3: After extubation, ONSD: Optic nerve sheath diameter, TIVA: Total intravenous anesthesia
**: Mean difference between T_0 and T_1, p<0.001*
#: Mean difference between T_1 and T_2, p<0.001
&: Mean difference between T_1 and T_3, p<0.001

The MAP measurements were higher in the TIVA group at time T0, higher in the desflurane group at time T1, and similar in both groups at T2 and T3. However, no statistically significant difference was observed. The value of $EtCO_2$ was higher in the TIVA group at all three time points. However, at T2, the difference between the TIVA and desflurane groups was statistically significant (p=0.02). PAP was equal in both groups at T1, higher in the desflurane group at T2, and higher in the TIVA group at T3, and no statistically significant difference was found for all three measurements (Table 3).

Discussion

Our study revealed significantly less sheath diameter change in the TIVA group. In addition, for the values measured at different time points during follow-up, as expected, there was an increase in the mean ONSD value with insufflation, followed by a decrease and return to baseline values. At the termination of the pneumoperitoneum, the observed value of $EtCO_2$ was higher in the TIVA group, which was an unexpected result.

This study assessed the differences in the mean ONSD measurements of the TIVA and desflurane groups during laparoscopic cholecystectomy. In contrast to our hypothesis, we found no significant variations in ONSD measurements between the two groups. These findings contrasted from the results of the study conducted during robot-assisted laparoscopic prostatectomy. Which revealed significantly lower ONSD measurements during propofol anesthesia compared with sevoflurane anesthesia 60 min after pneumoperitoneum and the Trendelenburg position (9).

Table 3. Comparison of mean arterial pressure, end-tidal CO_2, and peak airway pressure between two groups

Variables	TIVA group (n=37)	Desflurane group (n=39)	p
MAP T0 (mmHg)	113±16	110±13	0.087
MAP T1 (mmHg)	97±17	98±22	0.067
MAP T2 (mmHg)	93±16	93±13	0.416
MAP T3 (mmHg)	101±14	101±13	0.465
$EtCO_2$ T1 (mmHg)	33±4	31±3	0.109
$EtCO_2$ T2 (mmHg)	35±4	34±3	**0.02**
$EtCO_2$ T3 (mmHg)	34±5	32±3	0.097
Peak T1 (cmH_2O)	24±4	24±4	0.287
Peak T2 (cmH_2O)	19±4	20±4	0.083
Peak T3 (cmH_2O)	21±5	20±5	0.793

Data are shown as mean ± standard deviation. Before anesthesia administration (T0), 5 minutes after carbon dioxide insufflation in the reverse Trendelenburg position (T1), 5 minutes after pneumoperitoneum termination in the reverse Trendelenburg position (T2), and post-extubation (T3). MAP: Mean arterial pressure, TIVA: Total intravenous anesthesia

Farling et al. (10) indicated a significant decrease in ICP after 2 hours of continuous propofol administration in head-injured patients. However, in our study, the surgical duration was less than 2 hours for all cases. Even if there was less change in ONSD in the TIVA group, this might be the reason for not seeing the ONSD decreasing effect of propofol and finding similar measurements between the desflurane and TIVA groups. Another reason for the similar measurements could be the preventive effect of the reverse trendelenburg position in ICP increase.

Demirgan et al. (11) stated that adopting the reverse Trendelenburg position before pneumoperitoneum prevented an increase in ONSD. These results slightly differ from one animal study that showed the reverse Trendelenburg position does not counteract the elevation in ICP observed with insufflation (12). Sahay et al. (2) noted that placing patients' heads down or heads up after pneumoperitoneum significantly increased their ICPs, although this increase was less for patients placed in reverse Trendelenburg position. However, we could not observe whether reverse trendelenburg had any preventive effect because the positioning of the patient and intra-abdominal pressure were standardized in our study.

The average ONSD value remained below 5 mm in both groups, indicating that increased ICP may be excluded as a possibility. Intracranial hypertension is characterized by an ICP exceeding 20 mmHg (13). In a prior study, Tayal et al. (14) demonstrated that an ONSD of 5.00 mm correlated with computed tomography findings indicative of elevated ICP. They also reported a sensitivity of 100% for an ONSD of 5 mm in predicting an ICP exceeding 20 mmHg.

The result of lower changes in mean ONSD in the TIVA group during the insufflation and termination of carbon dioxide correlated with the study that TIVA is more effective than inhalation of sevoflurane in reducing the rise in ICP and preserving cerebral autoregulation (15). Additionally, the research of Petersen et al. (6) showed the significantly higher carbon dioxide reactivity observed during anesthesia with volatile agents may elucidate the higher change observed in the desflurane group. After the end of the pneumoperitoneum period, ONSD measurements returned to the basal values, which showed the reversible effect of CO_2 insufflation.

In our study, the degree of reverse trendelenburg and hemodynamics of the patients were kept constant throughout. The MAP and PAP were comparable. Different ventilation modes have been observed to affect oxygenation and ventilation during laparoscopic procedures, consequently

influencing ICP through the aforementioned mechanisms. Therefore, we monitored these factors, and to minimize bias, we adjusted the respiration rate to maintain $EtCO_2$ of 35±5 mmHg. PEEP values were maintained between 3 and 5 cmH_2O to minimize the airway pressure difference between individuals, which finally affected the intrathoracic pressure and ICP. We observed significantly higher $EtCO_2$ values in the TIVA group at just one observation period, which could be explained by the decreased carbon dioxide reactivity with propofol-based anesthesia (6).

Study Limitations

The intra- and interobserver variation in the measurement of ONSD might have been observed in our study as a limitation. To mitigate this bias, we enlisted a single experienced anesthesiologist to conduct the measurements four times, averaging the results each time. We measured ONSD before induction and 5 min after carbon dioxide insufflation and positioning. Because of the short operation time and technical necessities, we could not observe the effect of anesthetic agents and the impact of pneumoperitoneum alone without the position. When the human brain detect increases in ICP, compensatory mechanisms are activated. The Monroe-Kellie doctrine upholds the dynamic equilibrium among arterial and venous blood, parenchymal tissue, and cerebrospinal fluid, which is essential for preserving cerebral autoregulation and averting an elevation in ICP. This concept might elucidate the observation that none of the patients in either group exhibited ONSD values exceeding the mean value of 5.0 mm, which is another limitation of this study. Similarly, the short operation time and relatively healthy (ASA I-II) patient group also limited the evaluation of possible compensatory mechanisms in ICP. According to the exclusion criteria, patients enrolled in our study did not present with any pre-existing cerebral disease. Therefore, this study did not evaluate the effect of ICP on individuals with cerebral disease. Patients with pre-existing cerebral ischemia or elevated ICP may exhibit varying outcomes in terms of ONSD.

Conclusion

In summary, carbon dioxide pneumoperitoneum during laparoscopic cholecystectomy increases ONSD. However, the change in ONSD values was significantly lower in the TIVA group than in the desflurane group, indicating that propofol-based anesthesia may mitigate ICP fluctuations during laparoscopic cholecystectomy. These results suggest that TIVA is a preferable anesthetic choice for patients undergoing surgery in the reverse Trendelenburg position.

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Ethics

Ethics Committee Approval: University of Health Sciences Turkey, Kartal Dr. Lütfi Kırdar City Hospital (approval number: 2019/514/148/19, date: 27/02/2019).

Informed Consent: All participants provided written informed consent.

Authorship Contributions

Surgical and Medical Practices: S.S., E.H.Ü., M.K.B., M.A.Y., Concept: S.S., E.H.Ü., T.K., M.A.Y., Y.Y., K.T.S., Design: S.S., T.K., Y.Y., M.K.B., K.T.S., Data Collection or Processing: S.S., E.H.Ü., M.K.B., M.A.Y., Analysis or Interpretation: S.S., T.K., Y.Y., E.H.Ü., K.T.S., Literature Search: S.S., T.K., Y.Y., E.H.Ü., K.T.S., Writing: S.S., E.H.Ü., M.A.Y., K.T.S.

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REFERENCES

1. Gonzalez R, Smith CD, McClusky DA 3rd, et al. Laparoscopic approach reduces likelihood of perioperative complications in patients undergoing adrenalectomy. Am Surg 2004;70:668-674.
2. Sahay N, Sharma S, Bhadani UK, et al. Effect of pneumoperitoneum and patient positioning on intracranial pressures during laparoscopy: a prospective comparative study. J Minim Invasive Gynecol 2018;25:147-152.
3. Sezen O, Saracoglu KT, Şimşek T, Cevik B, Aydoğmuş E. The effect of positive end-expiratory pressure on optic nerve diameter in patients undergoing craniotomy operation. Ann Clin Anal Med 2021;12:199-203.
4. Kristiansson H, Nissborg E, Bartek J Jr, Andresen M, Reinstrup P, Romner B. Measuring elevated intracranial pressure through noninvasive methods: a review of the literature. J Neurosurg Anesthesiol 2013;25:372-385.
5. Hans P, Bonhomme V. Why we still use intravenous drugs as the basic regimen for neurosurgical anaesthesia. Curr Opin Anaesthesiol 2006;19:498-503.
6. Petersen KD, Landsfeldt U, Cold GE, et al. Intracranial pressure and cerebral hemodynamic in patients with cerebral tumors: a randomized prospective study of patients subjected to craniotomy in propofol-fentanyl, isoflurane-fentanyl, or sevoflurane-fentanyl anesthesia. Anesthesiology 2003;98:329-336.
7. Petersen KD, Landsfeldt U, Cold GE, et al. ICP is lower during propofol anaesthesia compared to isoflurane and sevoflurane. Acta Neurochir Suppl 2002;81:89-91.
8. Chui J, Mariappan R, Mehta J, Manninen P, Venkatraghavan L. Comparison of propofol and volatile agents for maintenance of anesthesia during elective craniotomy procedures: systematic review and meta-analysis. Can J Anaesth 2014;61:347-356.
9. Yu J, Hong JH, Park JY, Hwang JH, Cho SS, Kim YK. Propofol attenuates the increase of sonographic optic nerve sheath diameter during robot-assisted laparoscopic prostatectomy: a randomized clinical trial. BMC Anesthesiol 2018;18:72.
10. Farling PA, Johnston JR, Coppel DL. Propofol infusion for sedation of patients with head injury in intensive care. A preliminary report. Anaesthesia 1989;44:222-226.
11. Demirgan S, Özcan FG, Gemici EK, et al. Reverse Trendelenburg position applied prior to pneumoperitoneum prevents excessive increase in optic nerve sheath diameter in laparoscopic cholecystectomy: randomized controlled trial. J Clin Monit Comput 2021;35:89-99.
12. Halverson A, Buchanan R, Jacobs L, et al. Evaluation of mechanism of increased intracranial pressure with insufflation. Surg Endosc 1998;12:266-269.
13. Rajajee V, Vanaman M, Fletcher JJ, Jacobs TL. Optic nerve ultrasound for the detection of raised intracranial pressure. Neurocrit Care 2011;15:506-515.
14. Tayal VS, Neulander M, Norton HJ, Foster T, Saunders T, Blaivas M. Emergency department sonographic measurement of optic nerve sheath diameter to detect findings of increased intracranial pressure in adult head injury patients. Ann Emerg Med 2007;49:508-514.
15. Sujata N, Tobin R, Tamhankar A, Gautam G, Yatoo AH. A randomised trial to compare the increase in intracranial pressure as correlated with the optic nerve sheath diameter during propofol versus sevoflurane-maintained anesthesia in robot-assisted laparoscopic pelvic surgery. J Robot Surg 2019;13:267-273.

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CSMJ

Acute Suppurative Parotitis in a 22-Day-Neonate with Sepsis: A Rare Case Report

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What is known on this subject?

Acute suppurative parotitis (ASP) in the neonatal period is a rare phenomenon characterized by swelling, pain, and erythema over the parotis gland.

What this case report adds?

Although rare, ASP should be suspected in patients diagnosed with late-onset sepsis with erythematous preauricular mass with or without any predisposing factors.

ABSTRACT

Acute neonatal suppurative parotitis is a very rare condition that causes parotid swelling and purulent exudation into the oral cavity through the Stenson duct. The prognosis is usually excellent, but may be complicated by sepsis, meningitis, and abscesses. A case of sepsis and unilateral suppurative parotitis in a 22-day-old male infant successfully treated with intravenous antibiotics is presented here. Although rare, acute suppurative parotitis can be discovered in neonates, especially in 2-4 weeks of age, and is mostly caused by *Staphylococcus aureus*. Prompt diagnosis, appropriate intravenous antibiotics, and adequate hydration should be initiated immediately to prevent complications.

Keywords: Newborn, parotitis, inflammation, sepsis

Introduction

Acute suppurative parotitis (ASP) is very rare in the neonatal period, with a prevalence of between 3.8 and 14/10,000 newborn emergency department admissions (1,2). Dehydration, prematurity, low birth weight, immune system defects, trauma, and ductal obstruction are risk factors for neonatal ASP (1,3). Hydration, drawing specimens for pus, blood, and if necessary, cerebrospinal fluid (CSF) cultures, and immediate empirical antibiotic therapy covering possible agents are important in the treatment and prevention of complications (4). Herein, we present the case of a 22-day-old neonate who developed severe late-onset sepsis and right ASP.

Case Report

The male infant was born at 37 weeks of gestation, weighing 3300 g, via normal vaginal delivery to a primiparous 24-year-old mother. Exclusively breastfed neonate was brought to the emergency department at 22 days of age with complaints of high fever, uncontrollable crying, and facial swelling on the right side for the previous 24 h. There was no history of trauma or infection/abscess formation in the mother's nipples or areola. The rectal body temperature was 38.2 °C, respiratory rate was 50 beats/min, arterial blood pressure was 97/66 mmHg, and heart rate was 166 breaths/min. The patient weighed 3200 g and appeared lethargic, dehydrated,

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with decreased peripheral perfusion, depressed neonatal reflexes, and a prolonged capillary refill time of 7 s. The right preauricular region and the right side of the cheek were swollen, tender, and erythematous (Figure 1A). When the right parotid gland was compressed, pus was released into the oral cavity via the Stenson duct (Figure 1B). Laboratory tests revealed a white blood cell count of 18,660/mm^3, 61% neutrophil predominance, hemoglobin level of 14.1 g/dL, thrombocyte count of 254,000/mm^3, and C-reactive protein level of 0.48 mg/dL (normal range 0-0.3). Serum biochemistry was normal, with amylase levels of 4 IU/L (normal range, 28-100 IU/L). Blood gas analysis revealed pH: 7.28, pCO_2: 45.3, lactate: 6.0, HCO_3: 19.4, base excess: 4.4, and urinalysis of the catheterized specimen was normal. The examination of the CSF was normal. Ultrasonographic (US) examination revealed an enlarged, hypoechoic, and hypervascularized right parotid gland with adjacent millimetric lymph nodes (Figure 2A, B). On the second day of treatment, the patient still had signs of severe sepsis and high fever. Magnetic resonance imaging (MRI) of the parotid gland was performed to exclude any abscess formation/congenital tumor or malformations of the venous and lymphatic system that were secondarily infected. It revealed an enlarged gland with no evidence of mass or abscess formation after gadolinium administration (Figure 2C, D). The neonate was diagnosed with ASP and late-onset neonatal sepsis. Warm compresses were applied to the gland, along with intravenous hydration, analgesics, vancomycin, and cefotaxime. After three days of intravenous antibiotics, the patient's condition improved, and the swelling disappeared. Blood, urine, and CSF cultures remained sterile. However, *Staphylococcus aureus* was isolated from the pus culture and was sensitive to vancomycin treatment; therefore, no change in antibiotic treatment was needed.

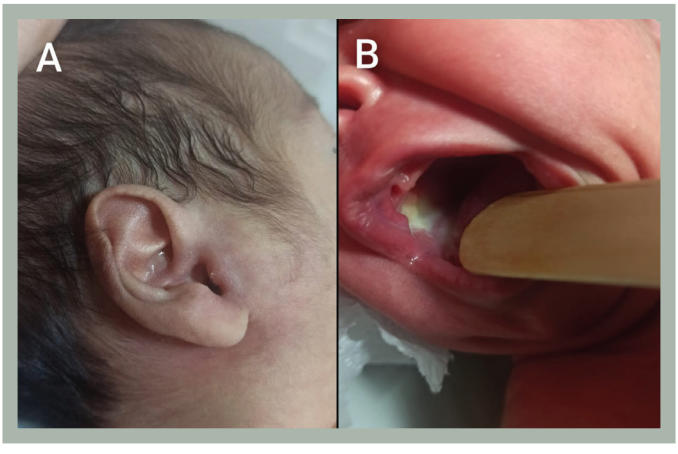

Figure 1. (A) Right facial swelling and erythema. (B) Pus coming from Stenson duct upon massage on parotid gland

Pre-discharge ultrasound of the parotid gland was normal, with improvement of parotid edema. Immunoglobulin levels and lymphocyte subsets were also within age-appropriate ranges. The patient was discharged after 10 days of intravenous antibiotics. The family of our patient provided written informed consent for publication of their child's information.

Discussion

In infants, suppurative infection of the salivary glands is extremely rare, with the parotid gland being the most commonly affected gland (1). Paouris et al. (3) reported only 65 cases of neonatal ASP in the English literature between 1970 and 2020. Prematurity, male gender, dehydration, immune deficiency, trauma, ductal occlusion by tumor, sialolithiasis, breastfeeding in the case of mastitis, or consumption of contaminated formula are risk factors (2,4). Dehydration leads to decreased salivation, impaired salivary flow resulting in salivary stasis, and increased bacterial ascent from the oral cavity to the salivary gland (5).

Infection ascending from the oral cavity through the Stenson duct is the most common route of colonization; hematogenous bacterial germination is less common. The most common organism isolated from pus specimens is *Staphylococcus aureus*. Other Gram-positive microorganisms

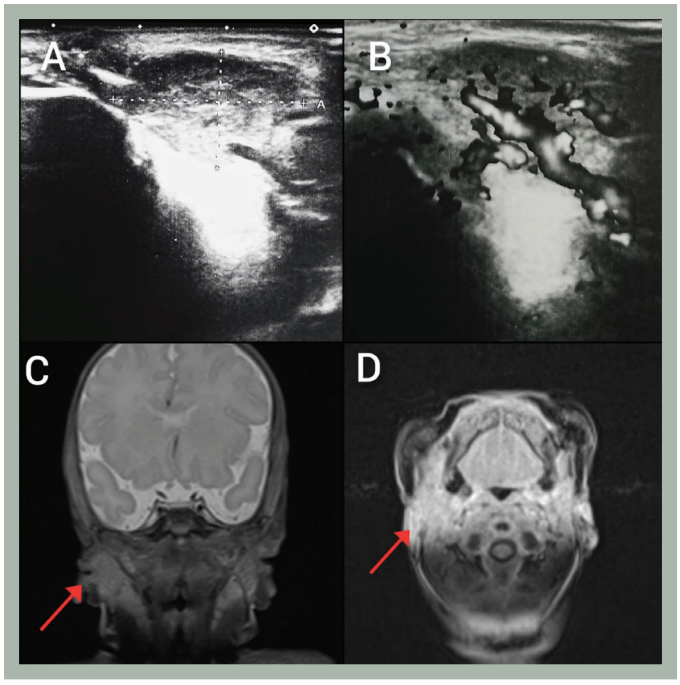

Figure 2. (A and B) Diffuse enlarged (22.3x13.7 mm in diameter), edematous and hypervascularized right parotid gland on ultrasound images. (C and D) Magnetic resonance images with gadolinium administration of the right parotid gland, showing enlarged gland (arrows), with no evidence of mass or abscess formation

such as *Streptococcus viridans, Streptococcus pyogenes,* and *Streptococcus agalactiae,* Gram-negative organisms including *Escherichia coli, Klebsiella, Pseudomonas,* and *Moraxella catarrhalis,* and anaerobic species such as *Bacteroides melaninogenicus, Fusobacterium nucleatum, Peptostreptococcus,* and *Prevotella* spp. can be isolated (4,6,7). Similar to most literature, *Staphylococcus aureus* was isolated from the pus culture of our patient, whereas cultures of blood, urine, and CSF remained sterile.

The diagnosis of the disease is primarily based on the clinical picture, although laboratory tests and imaging studies may also be helpful. Diagnostic criteria are parotid enlargement with or without redness, purulent exudation from Stensen's duct, and the isolation of pathogenic bacteria from pus culture (8). Approximately 50% of neonates with ASP are afebrile, and the condition is typically unilateral, and bilateral involvement is extremely rare. Laboratory tests are typically non-specific. Because of immature salivary isozyme activity in neonates, serum amylase levels are elevated in only 10%-20% of cases (6). The current case was febrile, with impaired peripheral perfusion, depressed neonatal reflexes, and increased lactate on blood gasses; however, no bacteremia or meningitis was detected, laboratory evaluation was non-specific, and the infant gradually improved during the first three days of intravenous antibiotic treatment.

Ultrasound and MRI can be helpful to confirm the diagnosis and exclude other differential diagnoses. US examination, which is non-invasive, cost-effective, and easily accessible, is considered the gold standard for ASP diagnosis. On US, an enlarged and hypervascularized parotid gland, as well as the detection of hypoechoic areas and lymph nodes within and adjacent to the gland, are important indicators of ASP (3). MRI can be used to assist with differential diagnoses and to demonstrate the extent of the disease. In the differential diagnosis, Stenson's duct abnormality or occlusion, sialolith, abscess formation, and parotid gland neoplasms such as hemangiomas, lymphangiomas, lipomas, neurofibromas, and rhabdomyosarcoma should be considered (4).

Although the prognosis tends to be excellent, complications may include abscess formation requiring surgical drainage, facial nerve palsy, septicemia, deep neck infection with mediastinitis, osteomyelitis of the mandible or temporomandibular joint, thrombophlebitis of the jugular vein, meningitis, respiratory distress requiring mechanical ventilation, and even death (5). Antimicrobial treatment should include *Staphylococcus* spp. and anaerobes and Gram-negative spp. Rarely, surgery may be required for abscesses or in patients who do not respond to medical treatment (4,5).

Ethics

Informed Consent: The family of the patient provided written informed consent for publication of their child's information.

Authorship Contributions

Surgical and Medical Practices: M.Ö., D.E., Concept: M.Ö., Design: M.Ö., Data Collection or Processing: M.Ö., D.E., Analysis or Interpretation: M.Ö., D.E., Literature Search: M.Ö., Writing: M.Ö., D.E.

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REFERENCES

1. Sabatino G, Verrotti A, de Martino M, Fusilli P, Pallotta R, Chiarelli F. Neonatal suppurative parotitis: a study of five cases. Eur J Pediatr 1999;158:312-314.
2. Decembrino L, Ruffinazzi G, Russo F, Manzoni P, Stronati M. Monolateral suppurative parotitis in a neonate and review of literature. Int J Pediatr Otorhinolaryngol 2012;76:930-933.
3. Paouris D, Dallos T, Pitiriga V. Polymicrobial acute suppurative parotitis in a 33-day-old infant: a case report and review of the literature. Clin Pediatr (Phila) 2022;61:802-807.
4. Özdemir H, Karbuz A, Ciftçi E, Fitöz S, Ince E, Doğru U. Acute neonatal suppurative parotitis: a case report and review of the literature. Int J Infect Dis 2011;15:e500-e502.
5. D'Souza JN, Geary C, Mukerji S. Neonatal parotid gland enlargement: is it suppurative parotitis? A case report. Am J Case Rep 2012;13:41-43.
6. Spiegel R, Miron D, Sakran W, Horovitz Y. Acute neonatal suppurative parotitis: case reports and review. Pediatr Infect Dis J 2004;23:76-78.
7. Gupta A, Kingdon T, McKernan A. Neonatal parotitis: a case report. Clin Pract Cases Emerg Med 2021;5:218-221.
8. Donovan ST, Rohman GT, Selph JP, Rajan R, Stocks RM, Thompson JW. Methicillin-resistant Staphylococcus aureus as a cause of neonatal suppurative parotitis: a report of two cases and review of the literature. Ear Nose Throat J 2013;92:269-271.