

High Glycemic Index Foods Increase Oxidative Stress and Cause Chronic Musculoskeletal Pain

Adinda^{1*}, Legiran², Arwan Bin Laeto³

¹Master of Biomedical Sciences Program, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

²Department of Anatomy, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

³Department of Physiology, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

*E-mail: adiinda@gmail.com

Abstract

Chronic musculoskeletal pain is a widespread condition that impacts quality of life and poses significant health care challenges. Recent research shows that dietary factors, especially the consumption of high glycemic index (GI) foods, play an important role in exacerbating musculoskeletal pain through metabolic and inflammatory pathways. High GI foods cause a rapid spike in blood glucose, which causes increased production of reactive oxygen species (ROS) resulting in oxidative stress. Oxidative stress disrupts normal cellular function, increases the production of pro-inflammatory cytokines, and exacerbates chronic inflammation, a major driver of musculoskeletal pain. This review discusses the mechanisms by which high GI foods increase oxidative stress and contribute to the onset and persistence of chronic musculoskeletal pain and discusses oxidative damage increasing degradation of musculoskeletal tissue, delaying recovery, and worsening pain perception. Previous studies linking high GI diets to increased oxidative stress and the incidence of musculoskeletal pain provide evidence of the potential for dietary modification as a non-invasive therapeutic strategy. In conclusion, reducing foods with a high glycemic index and adopting a diet rich in antioxidants and low glycemic index to reduce oxidative stress and inflammation is very necessary. Understanding the impact of diet on oxidative stress offers a promising avenue for the prevention and treatment of chronic musculoskeletal pain. Further research is needed to strengthen this association and develop targeted dietary interventions for CMP patients.

Keywords: Chronic Musculoskeletal Pain, Glycemic Index, Oxidative Stress

1. Introduction

The glycemic index (GI) is a classification system that ranks carbohydrates based on their effect on blood glucose levels after consumption. Foods with a high glycemic index are foods that cause a rapid increase in blood sugar due to their rapid digestion and absorption process.^{1,2} Foods with a GI score of 70 or more are considered high GI, while those between 56-69 are medium GI, and 55 or below is classified as low GI.^{3,4} The main focus of this discussion is on foods with a high glycemic index, which are generally found in processed carbohydrates. One food with a high glycemic index is white rice, which is the

main staple food for most people in Asia, especially Indonesia.^{5,6}

High GI foods are broken down quickly by the body, causing a sharp spike in blood glucose levels followed by a rapid drop, which can result in a cycle of hunger and overeating.^{2,7,8} Frequent consumption of high GI foods is known to cause metabolic disorders, increase insulin resistance, and encourage the development of various health problems, including inflammation and oxidative stress.⁹ This contributes to chronic diseases that are often ignored but whose impact greatly affects the quality of life of sufferers, starting from disrupting psychological, mood, and emotional aspects,

namely chronic musculoskeletal pain (CMP).^{2,8,10-15}

Chronic musculoskeletal pain (CMP) is a persistent pain condition lasting at least 3 months that affects the muscles, bones, ligaments, and tendons and significantly affects the quality of life of the affected person.^{16,17} CMP is prevalent in a large proportion of the global population and affects all levels of age and gender. Recent research has identified many chronic musculoskeletal disorders that affect the productive age, namely teenagers to young adults due to lack of knowledge about unergonomic work positions, busy working hours, exposure to pollution which triggers increased accumulation of oxidants, and poor diet.^{15,18-20}

Recent research shows that diet has a very important contribution to the emergence of disease, this is related to the accumulation and formation of AGES, AGEs can trigger an increase in ROS production which then causes oxidative stress conditions.²¹ Oxidative stress occurs when there is an imbalance between the formation of species. Reactive oxygen (ROS) and the body's capacity to neutralize or repair the damage it causes. This imbalance is closely related to inflammation, as ROS can trigger pathways that promote inflammation, such as the NF- κ B pathway. This activation promotes the release of inflammatory cytokines such as TNF- α and IL-6, which further trigger inflammation. In turn, inflammation can intensify ROS production, creating a dangerous cycle in which oxidative stress and inflammation mutually exacerbate each other. Research by Chanika et al explains that there is a relationship between levels of oxidative stress and chronic musculoskeletal diseases, such as fibromyalgia.²² Oxidative stress conditions can also aggravate complaints in sufferers with chronic musculoskeletal pain, where oxidative

damage and inflammation contribute to tissue damage and persistent pain.^{15,23-26}

2. Discussions

2.1. High GI Foods, Oxidative Stress and Inflammation

Consuming foods with a high glycemic index (GI) can quickly result in blood sugar levels called hyperglycemia. A continuous high glycemic index diet pattern can result in chronic hyperglycemia, this condition can cause the formation and accumulation of advanced glycation end products (AGEs). Advanced glycation end products (AGEs) are proteins or lipids that undergo glycation after exposure to sugar. AGEs are inhomogeneous and chemically diverse compounds that are formed both exogenously and endogenously through various pathways in the human body so that AGEs do not necessarily depend on age, gender, and cell physiological factors. Because abundant sources of exogenous AGEs are food and cigarette smoke. The formation of AGEs can occur during food processing processes such as frying, grilling, grilling, and heating at thermal temperatures of 120°C-180°C. Foods rich in sugar that go through a thermal process will experience a Maillard reaction and cause the formation of AGEs more rapidly.²⁷

The AGEs that are formed can accumulate in the bloodstream and digestive system which can then disrupt the balance of the intestinal microbiota and the normal function of enzymes. The accumulation of AGEs in the digestive system can also trigger inflammation and the body's pro-inflammatory response. Apart from that, AGEs can also accumulate in the musculoskeletal system, such as muscle and bone tissue. Research by Cavati et al explains the relationship between AGEs and levels of oxidative stress and bone fragility. This explains that AGEs that are accumulated and left untreated have been shown to have an

impact on the health of the musculoskeletal system.²⁸ In addition, AGEs are responsible for the development of other chronic musculoskeletal diseases such as osteoarthritis, which is currently a common disorder that causes disability in elderly people. High levels of endogenous AGEs may also have an impact on the development of rheumatoid arthritis, where the accumulated AGE compounds can increase the stiffness of collagen tissue in bones, leading to increased bone fragility and risk of fracture.²⁹

Several animal and human studies have reviewed the potential pro-inflammatory effects of AGEs on overall health. Poulsen et al. (2013) found that animals fed a diet high in AGEs showed increased expression of receptors for advanced glycation end products (RAGE) in various tissues.³⁰ Likewise, Van Puyvelde et al (2014) showed a significant correlation between dietary AGE intake and increased inflammation and oxidative stress. In humans, the adoption of a low-AGE diet has been associated with a reduction in inflammatory markers.³¹

2.2. Oxidative Stress Impairs Musculoskeletal Recovery and Increases Pain Sensitivity

A diet containing a lot of sugar such as a high glycemic index promotes the formation of AGEs, which have been shown to accumulate in connective tissue, cartilage, and joints. This accumulation causes hardening and degradation of the tissue which worsens pain and limits mobility.²⁹

The pathological effects of AGEs are related to their ability to increase the production of reactive oxygen species (ROS), resulting in a state of oxidative stress and inflammation by binding to cell surface receptors or cross-linking with body proteins and changing their structure and function. AGEs, through oxidative stress, cause the activation of several stress-induced

transcription factors with the production of proinflammatory and inflammatory mediators, such as cytokines and acute phase proteins. In addition, under conditions of high blood glucose spikes, insulin spikes trigger inflammatory pathways and encourage the release of pro-inflammatory cytokines, such as IL-6 and TNF- α . These cytokines increase sensitivity to pain by sensitizing pain receptors and can delay the healing of damaged tissue. Taken together, these events lead to the development of chronic diseases, particularly of the musculoskeletal system.^{23,32}

Furthermore, oxidative stress interferes with the body's ability to heal muscles, tendons, and other connective tissues effectively after injury, for example after activity, work, and exercise. This happens because oxidative stress is related to decreased production of the hormone melatonin so sufferers experience difficulty sleeping or insomnia and lack of time to rest which increase the body's burden in dealing with fatigue and cell recovery.^{14,33}

In individuals with chronic musculoskeletal pain, AGEs not only promote tissue degradation but also create a feedback cycle that exacerbates pain and inflammation. This can result in greater pain sensitivity, reduced tissue flexibility, and impaired recovery from physical strain or injury. Moreover, the symptoms of musculoskeletal pain do not reflect the tissue damage that has occurred, so often sufferers will complain that pain that previously appeared gradually and was neglected can suddenly become very severe suddenly when the tissue damage has damaged the sufferer's mobility so immediate action is needed to prevent it. Disability and further injury.^{13,18,21} Therefore, it can be concluded that a high GI diet can trigger oxidative stress conditions and result in longer tissue recovery times and increased sensitivity to pain.^{30,34}

2.3. Studies on Diet and Pain Thresholds in Chronic Musculoskeletal Pain

Several studies have shown that diet can significantly influence pain threshold and pain experience in individuals with CMP and other chronic pain conditions. Research has shown that a diet high in refined carbohydrates, sugar, and processed foods is associated with a lower pain threshold, meaning that individuals experience more intense pain. In contrast, an anti-inflammatory diet rich in whole grains, healthy fats (such as omega-3 fatty acids), and antioxidants (found in fruits and vegetables) has been associated with a higher pain threshold and better pain management.^{11,12,25}

In one study, participants who followed a diet low in processed sugar and high in anti-inflammatory nutrients reported reduced levels of pain and improved function compared with those who continued to follow a high GI diet. These findings suggest that by reducing the intake of high-GI foods and focusing on an anti-inflammatory dietary pattern, individuals with CMP can potentially increase pain sensitivity and improve musculoskeletal recovery.²⁴

2.4. Future Studies on Dietary Interventions and Musculoskeletal Health

Although several studies have shown that high glycemic index (GI) diets and increased oxidative stress contribute to chronic pain, there are still key gaps that need to be addressed to develop effective nutritional approaches. Although it is known that high GI diets can intensify inflammation and oxidative stress, the precise biochemical processes linking glycemic load to increased pain sensitivity are not fully understood. For example, further research is needed to clarify how quickly reactive oxygen species (ROS) are produced after blood sugar spikes and how these ROS affect pain receptors. Likewise, the role of advanced glycation end products (AGE)

in tissue damage, especially in chronic pain conditions such as CMP, requires further exploration.

3. Conclusion

Diet has a major impact on the body's sensitivity to pain and the body's ability to heal pain. A diet with a high glycemic index contributes to increased inflammation, and oxidative stress through the rapid formation of AGEs, all of which impair recovery and increase sensitivity to pain. On the other hand, adopting an anti-inflammatory diet with lower sugar intake can reduce pain, support tissue repair, and improve outcomes for individuals with CMP and other musculoskeletal conditions.

1. Sindi E, Nurizki F, Indah E, Nur Y. Gambaran Indeks Glikemik Dan Beban Glikemik Bahan Makanan Pada Penderita Diabetes Melitus Tipe 2. 2024;3(2):52–6.
2. Wronka M, Krzemińska J, Młynarska E, Rysz J, Franczyk B. The Influence of Lifestyle and Treatment on Oxidative Stress and Inflammation in Diabetes. *Int J Mol Sci.* 2022;23(24).
3. Rimbawan AS. Indeks Glikemik Pangan. Penebar Swadaya, Jakarta.; 2004.
4. Kaye Foster-Powell, Susanna HA Holt, Janette C Brand-Miller. Foster-Powell 2002. *Am J Clin Nutr.* 2002;76(5):5–56.
5. Dwiningsih Y, Alkahtani J. Glycemic Index of Diverse Rice Genotypes and Rice Products Associated with Health and Diseases *Advance Sustainable Science , Engineering and Technology (ASSET)* Glycemic Index of Diverse Rice Genotypes and Rice Products Associated with Health and Disease. *Adv Sustain Sci Eng Technol.* 2023;5(1)
6. Sivakamasundari SK, Priyanga S, Moses JA, Anandharamakrishnan C. Impact of

- processing techniques on the glycemic index of rice. *Crit Rev Food Sci Nutr.* 2022;62(12):3323–44.
7. Wolever TMS, Gibbs AL, Chiasson JL, Connelly PW, Josse RG, Leiter LA, et al. Altering source or amount of dietary carbohydrate has acute and chronic effects on postprandial glucose and triglycerides in type 2 diabetes: Canadian trial of Carbohydrates in Diabetes (CCD). *Nutr Metab Cardiovasc Dis.* 2013;23(3):227–34.
 8. Pasmans K, Meex RCR, van Loon LJC, Blaak EE. Nutritional strategies to attenuate postprandial glycemic response. *Obes Rev.* 2022;23(9):1–11.
 9. Anderson C, Milne GL, Park YMM, Sandler DP, Nichols HB. Dietary glycemic index and glycemic load are positively associated with oxidative stress among premenopausal women. *J Nutr.* 2018;148(1):125–30.
 10. Vlachos D, Malisova S, Lindberg FA, Karaniki G. Dietary Interventions for Optimizing Postprandial Hyperglycemia in Patients with T2 Diabetes: A Review. *Nutrients.* 2020;12(1561):1–13.
 11. Bin Arif A, Budiyanoto A, Hoerudin Balai Besar Penelitian dan Pengembangan Pascapanen Pertanian Jalan Tentara Pelajar No dan. Glicemic Index of Foods and Its Affecting Factors. *J Litbang Pert.* 2013;32(2):91–9.
 12. Wang Y, Cheng H, Wang T, Zhang K, Zhang Y, Kang X. Oxidative stress in intervertebral disc degeneration: Molecular mechanisms, pathogenesis and treatment. *Cell Prolif.* 2023;56(9):1–20.
 13. Krishnan KS, Raju G, Shawkataly O. Prevalence of work-related musculoskeletal disorders: Psychological and physical risk factors. *Int J Environ Res Public Health.* 2021;18(17).
 14. Norwitz NG, Sethi S, Palmer CM. Ketogenic diet as a metabolic treatment for mental illness. *Curr Opin Endocrinol Diabetes Obes.* 2020;27(5):269–74.
 15. Elma Ö, Yilmaz ST, Deliens T, Coppieters I, Clarys P, Nijs J, et al. Do nutritional factors interact with chronic musculoskeletal pain? A systematic review. *J Clin Med.* 2020;9(3):1–23.
 16. WHO. Musculoskeletal Conditions. World Health Organization. 2019.
 17. Perrot S, Cohen M, Barke A, Korwisi B, Rief W, Treede RD. The IASP classification of chronic pain for ICD-11: Chronic secondary musculoskeletal pain. *Pain.* 2019;160(1):77–82.
 18. Aprianto B, Hidayatulloh AF, Zuchri FN, Seviana I, Amalia R. Faktor risiko penyebab musculoskeletal disorders (msds) pada pekerja: a systematic review. *J Kesehat Tambusai.* 2021;2(2):16–25.
 19. Statistik Kecelakaan Kerja Eropa Eurostat (ESAW).
 20. Ayudea A, Engka A, Sumampouw OJ, Kaunang W. Postur Kerja dan Keluhan Muskuloskeletal pada Nelayan di Desa Borgo Satu Kecamatan Belang. *J KESMAS.* 2022;11(4):44–51.
 21. Adinda, Legiran ABL. Diet Indeks dan Beban Glikemik Tinggi serta Resiko Terhadap Gangguan Muskuloskeletal. *Plex Med Journal.* 2024;3(4):146–53.
 22. Assavarittirong C, Samborski W, Grygiel-Górniak B. Oxidative Stress in Fibromyalgia: From Pathology to Treatment. *Oxid Med Cell Longev.* 2022;2022.
 23. Jomova K, Raptova R, Alomar SY, Alwasel SH, Nepovimova E, Kuca K, et al. Reactive oxygen species, toxicity, oxidative stress, and antioxidants: chronic diseases and aging. Vol. 97, *Archives of Toxicology.* Springer Berlin

- Heidelberg; 2023. 2499–2574 p.
24. Towery P, Guffey JS, Doerflein C, Stroup K, Saucedo S, Taylor J. Chronic musculoskeletal pain and function improve with a plant-based diet. *Complement Ther Med*. 2018;40(June):64–9.
 25. Mendonça CR, Noll M, Castro MCR, Silveira EA. Effects of nutritional interventions in the control of musculoskeletal pain: An integrative review. *Nutrients*. 2020;12(10):1–17.
 26. Reynolds A, Mann J, Cummings J, Winter N, Mete E, Te Morenga L. Carbohydrate quality and human health: a series of systematic reviews and meta-analyses. *Lancet*. 2019;393(10170):434–45.
 27. Twarda-clapa A, Olczak A, Białkowska AM, Koziolkiewicz M. Advanced Glycation End-Products (AGEs): Formation, Chemistry, Classification, Receptors, and Diseases Related to AGEs. *Cells*. 2022;11(8).
 28. Cavati G, Pirrotta F, Merlotti D, Ceccarelli E, Calabrese M, Gennari L, et al. Role of Advanced Glycation End-Products and Oxidative Stress in Type-2-Diabetes-Induced Bone Fragility and Implications on Fracture Risk Stratification. *Antioxidants*. 2023;12(4).
 29. Verzijl, Nicole PhD; Bank, Ruud A. PhD; TeKoppele, Johan M. PhD; DeGroot JP. AGEing and Osteoarthritis: A Different Perspective. *Curr Opin Rheumatol*. *Curr Opin Rheumatol* 1. :5(5):p 616-622,.
 30. Poulsen MW, Hedegaard R V., Andersen JM, de Courten B, Bügel S, Nielsen J, et al. Advanced glycation endproducts in food and their effects on health. *Food Chem Toxicol*. 2013;60:10–37.
 31. Vlassara H, Cai W, Tripp E, Pyzik R, Yee K, Goldberg L, et al. Oral AGE restriction ameliorates insulin resistance in obese individuals with the metabolic syndrome: a randomised controlled trial. *Diabetologia*. 2016;59(10):2181–92.
 32. O.A. C, S.-C. L, C.-T. H, T.-C. H. Macrophages in oxidative stress and models to evaluate the antioxidant function of dietary natural compounds. Vol. 25, *Journal of Food and Drug Analysis*. 2017. p. 111–8.
 33. Bonanni R, Cariati I, Tancredi V, Iundusi R, Gasbarra E, Tarantino U. Chronic Pain in Musculoskeletal Diseases: Do You Know Your Enemy? *J Clin Med*. 2022;11(9).
 34. Maino Vieytes CA, Taha HM, Burton-Obanla AA, Douglas KG, Arthur AE. Carbohydrate Nutrition and the Risk of Cancer. *Curr Nutr Rep*. 2019;8(3):230–9.