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Literature Review

The Efficacy of Mediterranean Diet for Erectile Dysfunction in Diabetes Mellitus Patients

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Abstract

Male infertility affects millions globally, with 12-15% of Indonesian couples facing conception challenges, 50% of which are attributed to male factors. Despite extensive research, 70% of male infertility cases remain idiopathic. Diabetes, a prominent factor in male infertility, affects 9.3% of the global population, with projections estimating 700 million cases by 2045. Recent studies suggest the Mediterranean diet positively impacts semen parameters, particularly in diabetic individuals. This review aims to explore the Mediterranean diet's effects on fertility in male diabetic patients. The literature review employed three databases, focusing on in-vitro, in-vivo, pre-clinical, and clinical studies from 2014-2024. Diabetes, a chronic disease characterized by abnormal blood sugar levels, affects insulin production or effectiveness, leading to complications if left uncontrolled. Erectile dysfunction (ED), prevalent in diabetic men, is attributed to nerve and blood vessel damage from high blood sugar levels. Treatments for ED include PDE5 inhibitors, but alternative plant-based therapies are being explored. Platelet-rich plasma (PRP) has shown promise in animal studies but lacks human trial data. The Mediterranean diet, rich in plant-based foods and healthy fats, may help prevent sexual function deterioration in diabetic individuals. Comprehensive nutrition education and government efforts are crucial in promoting healthy lifestyles and ensuring access to fresh foods. In conclusion, the Mediterranean diet shows promise as a dietary intervention for improving male fertility in diabetic populations. Further research is warranted to confirm these findings and to explore the mechanisms underlying the effects of the Mediterranean diet on male fertility.

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1. Introduction

Male infertility, defined as the inability of a male to impregnate a fertile female after at least one year of unprotected intercourse, is a prevalent and distressing condition affecting couples worldwide. It is estimated that approximately 180 million individuals worldwide suffer from some form of infertility, with male factors contributing to nearly 50% of cases.[1] In Indonesia, it is estimated that 12-15% of couples experience difficulties in conceiving a child, with male factors accounting for approximately 50% of these cases. Despite advances in medical science, the etiology of male infertility remains elusive in around 70% of cases, highlighting the complexity of this condition.[2]

One significant factor that has been implicated in male infertility is diabetes mellitus (DM), a chronic metabolic disorder characterized by elevated blood sugar levels. The global prevalence of DM has reached alarming levels, with an estimated 463 million individuals diagnosed with the condition in 2019. In Indonesia, the prevalence of type 2 DM among individuals aged 15 years and above is reported to be over 10.9%, posing a substantial public health challenge. Diabetes mellitus has been associated with various complications, including cardiovascular disease, neuropathy, nephropathy, and retinopathy. Of particular concern is the impact of DM on male reproductive health, specifically its association with erectile dysfunction (ED), a common and distressing condition that significantly affects the quality of life of affected individuals.[3,4]

Recent research has suggested that dietary interventions, such as the Mediterranean diet, may have a positive impact on semen parameters and fertility in diabetic males. The Mediterranean diet is characterized by high consumption of fruits, vegetables, whole grains, and olive oil, moderate consumption of fish and poultry, and low consumption of red meat and processed foods. Studies have shown that adherence to the Mediterranean diet is associated with improved glycemic control, lipid profile, and cardiovascular health, all of which are important considerations in the context of male infertility associated with diabetes.[4]

Despite the potential benefits of the Mediterranean diet, there is a noticeable gap in research regarding its effects on male fertility, particularly in diabetic populations. This review aims to address this gap by providing a comprehensive overview of the current literature on the impact of the Mediterranean diet on male fertility, with a specific focus on individuals with diabetes mellitus. By synthesizing and analyzing existing evidence, this review seeks to elucidate the potential mechanisms underlying the effects of the Mediterranean diet on male fertility and to provide insights for future research and clinical practice.

2. Review

The search method of this literature review was done in several databases such as Pubmed, Scopus, Cochrane, Web of Science, CINAHL, and Proquest using keywords (“Diabetes mellitus”) AND (“Erectile dysfunction”) AND (“Mediterranean Diet”. The types of studies are in-vitro, in-vivo, pre-clinical, and clinical studies that assess the effect of mediterranean diet in treating erectile diabetes on diabetes mellitus patients from 2014 - 2024. We are also focusing on the study that discusses the concept of diabetes mellitus, erectile dysfunction, studies explaining the concept and the correlation of diabetes mellitus and erectile dysfunction, and mediterranean diet. The author was last searched on 10th April 2024.

DIABETES MELLITUS

Pathophysiology

Diabetes mellitus (DM) poses a significant global health burden. This chronic disease, characterized by abnormal blood sugar levels, affects a vast number of people. In 2019, a staggering 9.3% of the global population, translating to 463 million individuals, had been diagnosed with DM. Even more concerning is the projected rise to 10.9%, or roughly 700 million people, by 2045.[5] Indonesia reflects this trend, with Basic Health Research (RISKESDAS) data from 2018 revealing that over 10.9% of the population above 15 years old has type 2 DM.[6] These statistics highlight the critical need for increased awareness and education regarding diabetes prevention and management.

Insulin, a key hormone, plays a central role in regulating blood sugar levels within the body. Disruptions in either the production or effectiveness of insulin define the two main types of DM. Type 1 DM is characterized by insufficient or absent insulin production. This typically occurs in childhood due to an autoimmune attack that destroys insulin-producing pancreatic beta cells.[7] In contrast, type 2 DM is characterized by the presence of insulin; however, the body's cells

become resistant to its effects, rendering it ineffective in lowering blood sugar.[8]

Both type 1 and type 2 DM can lead to serious complications if left uncontrolled. In type 1 DM, the absence of insulin disrupts the body's ability to regulate blood sugar. The liver continues to produce glucose, but with limited glycogen stores for storage. This uncontrolled gluconeogenesis, coupled with the inability of fat and muscle cells to take up available blood sugar due to a lack of functional glucose transporter 4 (GLUT4), leads to elevated blood sugar levels.[9] This creates a situation where the body's cells are starved for glucose while blood sugar remains excessively high. Furthermore, unopposed glucagon secretion, a hormone that normally works in conjunction with insulin to regulate blood sugar, further disrupts blood sugar control. These combined factors can lead to a dangerous condition called ketoacidosis, characterized by the production of ketone bodies due to excessive lipolysis.[10] Without insulin to inhibit this process, ketone levels can become dangerously elevated. Management of type 1 DM relies solely on exogenous insulin injections to address the absolute deficiency. Even with the best efforts at controlling blood sugar, chronically elevated glucose and lipids can damage tissues and lead to various medical complications.

Type 2 DM presents a different scenario. While insulin is present, the body's cells become resistant to its effects. Despite this resistance, the pancreas often continues to produce insulin, leading to high insulin levels in the blood.[8] Similar to type 1 DM, uncontrolled type 2 DM can also lead to complications. However, the specific mechanisms differ. The liver retains its capacity for glycogen production, and lipolysis remains controlled due to the presence of insulin. However, plasma lipoprotein levels are often elevated, potentially due to factors like poor nutrition and obesity. Ketoacidosis is uncommon in type 2 DM but can occur under specific circumstances like metabolic stress or pancreatic failure, which further reduces insulin production and secretion.[11] A serious complication that can develop in older patients with type 2 DM is hyperosmolar hyperglycemic nonketotic syndrome. In this condition, the body attempts to remove excess sugar by excreting it through urine, often triggered by illness, infection, or other factors.[12]

Diabetes mellitus can cause serious complications. A study found that about 127 (38.5%) had one or more chronic complications.[13] In Indonesia, the most common complication among all patients is cardiovascular disease (24%). Followed by neuropathy (14%), nephropathy (7%), cerebrovascular disease (6%), retinopathy (5%), and peripheral vascular disease (2%).[14] One concerning complication is erectile dysfunction (ED). This condition, characterized by difficulty achieving or maintaining an erection, is significantly more prevalent in men with diabetes, particularly those with type 2 DM. Chronically high blood sugar levels that present in diabetes mellitus patients damage nerves and blood vessels throughout the body, including those critical for erectile function.[15] This damage disrupts the delicate interplay between nerves, blood flow, and muscles required for an erection, leading to ED. The association between diabetes and ED underscores the importance of managing blood sugar levels effectively to prevent complications and maintain overall health.

ERECTILE DYSFUNCTION

Pathophysiology

Erectile dysfunction (ED) is a condition that is characterized by the consistent or recurrent inability to attain and/or maintain a rigid penile erection that is sufficient for satisfactory sexual performance.[16] In physiological conditions, the main process in penile erection is the relaxation of the intracavernosal smooth muscle. This process would allow blood flow to enter the corpora cavernosa and fill it with blood while compressing the emissary veins to prevent venous outflow. The paraventricular and medial preoptic nuclei of the hypothalamus regulate the erectile process. Signals travel through the parasympathetic nervous system to the parasympathetic nerves of the S2-S4 sacral plexus, which then reach the penis via the cavernosal nerves. Nitric oxide released by the cavernous nerve terminals initiates the erectile process, while nitric oxide from endothelial cells helps maintain it by promoting penile vasodilation. Nitric Oxide promotes penile vasodilation by diffusing across the smooth muscle membrane and activating sGC to produce cGMP, resulting in an enzymatic cascade that inhibits calcium influx, lowers cytosolic calcium concentrations, and thus induces relaxation of cavernosal smooth muscle. The pathophysiology of penile erection stems from any disruption or dysfunction within the aspects mentioned. So far, the pathophysiology of erectile

dysfunction has been classified into 4 organic causes: Vasculogenic, Neurogenic, and Endocrinologic.[17]

Vasculogenic pathophysiology is closely linked to the obstruction or traumatic effect on the arterial and venous system, which can decrease the pressure and blood flow to the penis. For example, atherosclerotic of the hypogastric-cavernous-helicine arterial system can reduce the pressure and blood flow towards the sinusoidal spaces, resulting in a longer time to achieve maximum erection and a decrease in the firmness of the erect penis. In other conditions, Inadequate venous occlusion has been suggested as a primary reason for vasculogenic impotence. Veno-occlusive dysfunction, which might have been caused by the degeneration of the tunica albuginea or structural alterations in the fibroelastic components of the trabeculae, cavernous smooth muscle, and endothelium, may hinder the closing and compression of the emissary veins, resulting in venous leak.

In the neurogenic pathophysiology of erectile dysfunction, the root cause stems from the pivotal structure responsible for the mechanism of penile erection, namely the paraventricular and medial preoptic nuclei of the hypothalamus. Pathological processes in these regions, such as Parkinson's disease, stroke, encephalitis, or temporal lobe epilepsy, are frequently linked to erectile dysfunction. Another potential pathophysiology that emerges from neurological conditions is the injury of the spinal cord and the nervous systems that innervate the penis, particularly the cavernosal nerves.

In endocrinologic pathophysiology of erectile dysfunction, hormonal alterations are the primary cause of erectile dysfunction. Conditions such as hypogonadism, hyperprolactinemia, and hyperthyroidism, might fluctuate or decrease hormones that interfere with sexual function such as androgen, testosterone, and prolactin. Low levels of androgen and testosterone may contribute to erectile dysfunction through the development of metabolic conditions. On the other hand, elevated levels of prolactin can interfere with the release of gonadotropin-releasing hormone, resulting in reduced testosterone levels and subsequent erectile dysfunction.

In accordance with Type 2 Diabetes Mellitus (T2DM), the occurrence of Erectile dysfunction has been found to have a strong correlation with it. Erectile dysfunction The incidence of ED in diabetic males is high, with studies reporting rates ranging from 35% to 90%.[18] A scientific review of several studies has shown that a duration of diabetes for more than 10 years is statistically associated with erectile dysfunction (ED) in patients with diabetes.[19] Poor blood sugar and blood pressure control also contribute to an increased risk of ED in diabetic men. Several factors contribute to the correlation between T2DM and ED, including vascular, hormonal, and neural complications. Diabetic neuropathy can cause autonomic and somatic neural disorders, which are crucial for erection. Additionally, diabetes can lead to disorders in the relaxation of cavernous smooth muscles, which may be a side effect of glycated products.[20] Men with diabetes may also experience hypogonadism, which can indirectly reduce levels of pituitary hormones responsible for stimulating testosterone production in the testicles. Low testosterone levels can lead to a loss of sex drive or ED. The prevalence of ED in men with T2DM is significantly higher than in the general population, with estimates suggesting that diabetic men are three times more likely to experience ED. Regular assessment of sexual function by nurses is vital for identifying the effects of ED in men with T2DM. Another study Investigated the relationship between remnant cholesterol (RC) and erectile dysfunction (ED) in individuals with diabetes. The study found that higher RC levels are associated with an increased likelihood of ED through T2DM, which may be due to dietary and lifestyle factors, insulin resistance, and high blood glucose levels.[21]

Erectile Dysfunction Pharmacotherapies

Initial treatments for erectile dysfunction (ED) include couples therapy and oral medications like phosphodiesterase type-5 (PDE5) inhibitors, as well as local treatments such as intra-urethral suppositories and intracavernosal injections. While effective for many with mild to moderate ED, some individuals cannot tolerate these drugs or have contraindications, especially those with post-prostatectomy ED, diabetes, or severe ED related to vascular disease or smoking. For those resistant to medication, penile implants are an option, offering high patient satisfaction despite associated risks. However, most patients and their partners prefer restoring spontaneous erections over pharmacological or surgical interventions, emphasizing the importance of treatments that support natural physiological function.[22]

Phosphodiesterase 5 Inhibitors (PDE5I) are commonly used for erectile dysfunction treatment, but they're not always effective and can cause side effects. About 40% of patients don't respond to PDE5I, and many discontinue use due to ineffectiveness, adverse events, or anxiety. Some experience mild side effects like headache and nasal congestion. Despite its efficacy for some, PDE5I shouldn't overshadow simpler, cheaper, and equally effective treatments with fewer side effects. Intracavernosal Self-Injection Therapy (ICI) and Medicated Urethral System for Erection (MUSE) are second-line therapies when PDE5I fails. ICI, using vasoactive substances directly, is more effective than MUSE, but both can help in rehabilitation after procedures like prostatectomy.[23] However, ICI therapy has its complications. Priapism is a significant concern, as are pain, ecchymosis, and hematoma formation. Discontinuation rates are not insignificant, with rates of > 50% over 5 years reported in some series.[24]

An alternative for PDE5 has been sought out from plant-based medicine. A thorough literature review on medicinal plants used for treating erectile dysfunction (ED) has identified 718 plants traditionally used as aphrodisiacs or sexual stimulants. While some plants have been scientifically validated, there is ample opportunity for further research to support traditional claims and develop active compounds into safe and effective drugs for ED treatment. Safety evaluations are crucial to prevent adverse events associated with plant usage. Developing a cost-effective method for screening PDE5 inhibitory activity would aid in comparing experimental results and accelerating the development of medicinal plants into therapeutics.[25]

Platelet-rich plasma (PRP) has recently gained attention as a promising treatment for erectile dysfunction (ED) through intracavernosal injections, attributed to its angiogenic, vasculogenic, and regenerative properties, rendering it a promising therapeutic avenue for ED. PRP has shown effectiveness in numerous animal studies and is currently undergoing evaluation in human trials. Despite its potential, published studies on PRP for ED treatment remain scarce.[26] PRP, derived from platelets, contains various growth factors such as fibroblast growth factor (FGF), platelet-derived growth factor (PDGF), and vascular endothelial growth factor (VEGF), known for their roles in wound healing and tissue repair. These factors suggest PRP's potential to repair damaged penile tissue and restore erectile function. However, the evidence regarding the efficacy of PRP in treating ED in humans remains unclear.[27]

MEDITERRANEAN DIET

Definition and Mechanism of Mediterranean Diet

The Mediterranean Diet is a nutritional approach that prioritizes plant-based foods, beneficial fats, and reasonable portions of fish, poultry, and dairy items. This diet is comprised of a daily abundance of vegetables, a variety of minimally processed whole grain bread, along with cereals and legumes as the mainstay; nuts and seeds, along with fresh fruit, serve as the typical daily dessert, while sweets containing nuts, olive oil, and honey are reserved for celebratory occasions; cold pressed extra-virgin olive oil (EVOO), nuts, and seeds are the primary sources of fat; dairy products, mainly local cheese and yogurt, are consumed sparingly; fish, poultry, and eggs are moderately included in the diet, while red meat is consumed infrequently, typically once a week; wine is moderately consumed, usually accompanying meals.[28]

Research indicates that the mediterranean diet can positively impact erectile dysfunction among individuals with type 2 diabetes. This dietary regimen may help prevent the deterioration of sexual function over time in both sexes who have recently been diagnosed with type 2 diabetes.[29] This study compared the mediterranean diet with a low fat diet and found that changes in erectile function (IIEF) and female sexual function (FSFI) were significantly lower in the mediterranean diet group. In addition, several studies have proven that the consumption of nuts and vegetables, which are the main components of the Mediterranean diet, is inversely related to erectile dysfunction.[30,31] This indicates that dietary components associated with the mediterranean diet may have a direct impact on reducing the risk of ED in diabetic patients.

The Applicability of Mediterranean Diet

Numerous studies have confirmed the beneficial impact of the Mediterranean diet in managing various diseases, including diabetes and reproductive issues.[32–34] However, even in Mediterranean regions, traditional dietary practices have gradually shifted towards Westernized eating habits, characterized by reduced intake of fruits, vegetables, and legumes, and increased

consumption of red meat, refined carbohydrates, and processed and fast foods.[35,36] This transition is particularly evident in developed nations, where time constraints lead consumers to prioritize convenience over health, opting for cheaper and faster meals that often lack nutritional quality and are highly processed.[33]

The primary challenges associated with implementing the Mediterranean diet in contemporary society revolve around a decline in home cooking due to increased workloads, leading to reduced home-prepared meals.[37] Time constraints further compel individuals to opt for ultra-processed foods, prioritizing convenience and cost-saving. To combat these challenges, comprehensive nutrition education and promotion of healthy lifestyles are essential for every household.[38] Emphasizing the value of home cooking is crucial, not only for improving family health but also for reinforcing the significance of home and family bonds.[39] Additionally, government efforts should focus on ensuring that fresh foods and groceries are readily available in all neighborhoods, not just urban centers.[33]

3. Summary

This review underscores the need for further scientific inquiry into the effects of the Mediterranean diet on male fertility, especially within diabetic populations. Elucidating the mechanistic pathways through which this dietary pattern influences fertility can provide valuable insights for developing targeted interventions and optimizing management strategies for male infertility associated with diabetes. Moreover, promoting the adoption of the Mediterranean diet and encouraging healthier dietary practices hold significant promise in mitigating the escalating prevalence of diabetes and its related complications, including male infertility. Future research endeavors should aim to elucidate the precise mechanisms underlying the beneficial effects of the Mediterranean diet on male fertility and explore its potential as an adjunctive therapy for individuals with diabetes-related male infertility.

Author's Contribution

All authors played a role in shaping the final manuscript. The first author gathered and processed data, analyzed and interpreted data, drafted the manuscript, and created figures. The second and third authors contributed to outlining the main conceptual ideas of the research and providing critical revisions to the article.

Conflict of Interest

The authors assert that there are no conflicts of interest concerning this research.

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References

1. Leslie SW, Soon-Sutton TL, Khan MA. Male Infertility. StatPearls Publishing; 2023.
2. Aulia SN, Lestari SW, Pratama G, Harzief AK, Sumapraja K, Hestiantoro A, et al. The pattern of abnormalities on sperm analysis: A study of 1186 infertile male in Yasmin IVF clinic Jakarta. J Phys Conf Ser. 2017 Aug;884:012138.
3. Babakhanzadeh E, Nazari M, Ghasemifar S, Khodadadian A. Some of the Factors Involved in Male Infertility: A Prospective Review. Int J Gen Med. 2020 Feb;Volume 13:29–41.
4. Piera-Jordan CÁ, Prieto Huecas L, Serrano De La Cruz Delgado V, Zaragoza Martí A, García Velert MB, Tordera Terrades C, et al. Influence of the Mediterranean diet on seminal quality—a systematic review. Front Nutr. 2024 Feb 15;11.
5. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. Diabetes Res Clin Pract. 2019 Nov;157:107843.
6. Kementerian Kesehatan Republik Indonesia. Laporan Nasional RISKESDAS 2018. Lembaga Penerbit Badan Penelitian dan Pengembangan Kesehatan; 2019.
7. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Diabetes Care. 1997 Jul 1;20(7):1183–97.
8. Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB, et al.

Pathophysiology of Type 2 Diabetes Mellitus. Int J Mol Sci. 2020 Aug 30;21(17):6275.
9. Maria Z, Campolo AR, Lacombe VA. Diabetes Alters the Expression and Translocation of the Insulin-Sensitive Glucose Transporters 4 and 8 in the Atria. PLoS One. 2015 Dec 31;10(12):e0146033.
10. JM L, A G, V G. Adult Diabetic Ketoacidosis. StatPearls Publishing; 2023.
11. Moini J. Pathophysiology of Diabetes. In: Epidemiology of Diabetes. Elsevier; 2019. p. 25–43.
12. Levine SN, Sanson TH. Treatment of Hyperglycaemic Hyperosmolar Non-Ketotic Syndrome. Drugs. 1989 Sep;38(3):462–72.
13. Sheleme T, Mamo G, Melaku T, Sahilu T. Prevalence, Patterns and Predictors of Chronic Complications of Diabetes Mellitus at a Large Referral Hospital in Ethiopia: A Prospective Observational Study. Diabetes Metab Syndr Obes. 2020 Dec;Volume 13:4909–18.
14. Hidayat B, Ramadani RV, Rudijanto A, Soewondo P, Suastika K, Siu Ng JY. Direct Medical Cost of Type 2 Diabetes Mellitus and Its Associated Complications in Indonesia. Value Health Reg Issues. 2022 Mar;28:82–9.
15. Defeudis G, Mazzilli R, Tenuta M, Rossini G, Zamponi V, Olana S, et al. Erectile dysfunction and diabetes: A melting pot of circumstances and treatments. Diabetes Metab Res Rev. 2022 Feb 21;38(2).
16. SW L, T S. Erectile Dysfunction. StatPearls Publishing; 2024.
17. Sangiorgi G, Cereda A, Benedetto D, Bonanni M, Chiricolo G, Cota L, et al. Anatomy, Pathophysiology, Molecular Mechanisms, and Clinical Management of Erectile Dysfunction in Patients Affected by Coronary Artery Disease: A Review. Biomedicines. 2021 Apr 16;9(4):432.
18. Parmar R, Verma S, Neelkamal, Pathak V, Bhadoria A. Prevalence of erectile dysfunction in Type 2 diabetes mellitus (T2DM) and its predictors among diabetic men. J Family Med Prim Care. 2022;11(7):3875.
19. Shiferaw WS, Akalu TY, Petrucka PM, Areri HA, Aynalem YA. Risk factors of erectile dysfunction among diabetes patients in Africa: A systematic review and meta-analysis. J Clin Transl Endocrinol. 2020 Sep;21:100232.
20. Bahar A, Elyasi F, Moosazadeh M, Afradi G. Sexual Dysfunction in Men with Type II Diabetes. Caspian J Intern Med [Internet]. 2020 [cited 2024 Apr 23];11(3):295–303. Available from: https://caspjim.com/article-1-2003-en.html
21. Huang K, Yin S, Xiao Y, Wang J, Cui J, Wang J, et al. Sexual dysfunction in patients with diabetes: association between remnant cholesterol and erectile dysfunction. Lipids Health Dis. 2024 Feb 22;23(1):55.
22. Liu JL, Chu KY, Gabrielson AT, Wang R, Trost L, Broderick G, et al. Restorative Therapies for Erectile Dysfunction: Position Statement From the Sexual Medicine Society of North America (SMSNA). Sex Med. 2021 Jun 1;9(3):100343–100343.
23. Beecken WD, Kersting M, Kunert W, Blume G, Bacharidis N, Cohen DS, et al. Thinking About Pathomechanisms and Current Treatment of Erectile Dysfunction—"The Stanley Beamish Problem." Review, Recommendations, and Proposals. Sex Med Rev. 2021 Jul;9(3):445–63.
24. Chakra MA, Bailly H, Klampke F, Boaz J, Jida M, Yassine AA, et al. An update on the use of stem cell therapy for erectile dysfunction. Asian J Urol. 2024 Mar;
25. Sin VJE, Anand GS, Koh HL. Botanical Medicine and Natural Products Used for Erectile Dysfunction. Sex Med Rev. 2021 Oct;9(4):568–92.
26. Shaher H, Fathi A, Elbashir S, Abdelbaki SA, Soliman T. Is Platelet Rich Plasma Safe and Effective in Treatment of Erectile Dysfunction? Randomized Controlled Study. Urology. 2023 May;175:114–9.
27. Suharyani S, Leonardo M, Oentoeng HH, Pardamean Lumban Tobing ER, Tansol C, Hariyanto TI. Efficacy and safety of platelet-rich plasma intracavernosal injection for patients with erectile dysfunction: A systematic review, meta-analysis, and meta-regression. Asian J Urol. 2024 Jan;
28. Tosti V, Bertozzi B, Fontana L. Health Benefits of the Mediterranean Diet: Metabolic and Molecular Mechanisms. The Journals of Gerontology: Series A. 2018 Mar 2;73(3):318–26.
29. Maiorino MI, Bellastella G, Caputo M, Castaldo F, Improta MR, Giugliano D, et al. Effects of Mediterranean diet on sexual function in people with newly diagnosed type

2 diabetes: The MÈDITA trial. J Diabetes Complications. 2016 Nov;30(8):1519–24.
30. Ramírez R, Pedro-Botet J, García M, Corbella E, Merino J, Zambón D, et al. Erectile dysfunction and cardiovascular risk factors in a Mediterranean diet cohort. Intern Med J. 2016 Jan 27;46(1):52–6.
31. Wang F, Dai S, Wang M, Morrison H. Erectile Dysfunction and Fruit/Vegetable Consumption Among Diabetic Canadian Men. Urology. 2013 Dec;82(6):1330–5.
32. Guasch-Ferré M, Willett WC. The Mediterranean diet and health: a comprehensive overview. J Intern Med. 2021 Sep 23;290(3):549–66.
33. Sotos-Prieto M, Del Rio D, Drescher G, Estruch R, Hanson C, Harlan T, et al. Mediterranean diet – promotion and dissemination of healthy eating: proceedings of an exploratory seminar at the Radcliffe institute for advanced study. Int J Food Sci Nutr. 2022 Feb 17;73(2):158–71.
34. Sofi F, Macchi C, Abbate R, Gensini GF, Casini A. Mediterranean diet and health status: an updated meta-analysis and a proposal for a literature-based adherence score. Public Health Nutr. 2014 Dec 29;17(12):2769–82.
35. Colozza D, Avendano M. Urbanisation, dietary change and traditional food practices in Indonesia: A longitudinal analysis. Soc Sci Med. 2019 Jul;233:103–12.
36. Baker P, Friel S. Food systems transformations, ultra-processed food markets and the nutrition transition in Asia. Global Health. 2016 Dec 3;12(1):80.
37. Watanabe JA, Nieto JA, Suarez-Diéguez T, Silva M. Influence of culinary skills on ultraprocessed food consumption and Mediterranean diet adherence: An integrative review. Nutrition. 2024 May;121:112354.
38. Lăcătușu CM, Grigorescu ED, Floria M, Onofriescu A, Mihai BM. The Mediterranean Diet: From an Environment-Driven Food Culture to an Emerging Medical Prescription. Int J Environ Res Public Health. 2019 Mar 15;16(6):942.
39. Pfeifer D, Rešetar J, Gajdoš Kljusurić J, Panjkota Krbavčić I, Vranešić Bender D, Rodríguez-Pérez C, et al. Cooking at Home and Adherence to the Mediterranean Diet During the COVID-19 Confinement: The Experience From the Croatian COVIDiet Study. Front Nutr. 2021 Mar 31;8.