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Foreword

Foreword by Editor-in-Chief

Prof. Nataliya Bhinder

Welcome to the second thrilling issue of the Annals of Innovation in Medicine—your essential guidebook to the frontier of modern healthcare! Are you an intrepid researcher navigating the intricate maze of medical science? An academic mulling over the next groundbreaking idea? Or a clinician at the crossroads of practice and discovery? Wherever you find yourself on the medical landscape, this issue promises to be your compass, steering you through the exciting yet complex terrains of innovation.

Why should you consider submitting to our journal? Here's the thing: this isn't just another medical journal that piles up on your desk or gets lost in your digital library. No, this is a revolution wrapped in pages, or pixels if you prefer the online version. We believe that science grows best when fertilized with diverse ideas. Whether it's a novel technique in telemedicine, a cutting-edge surgical robot, or a fresh look at managing pandemics, your research doesn't just get published—it gets celebrated.

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So, whether you're a seasoned author or a first-timer, we extend an open invitation: Submit your manuscripts, your ideas, your innovations. In the rapidly evolving saga of healthcare, your chapter is waiting to be written, and the Annals of Innovation in Medicine is the perfect place to share it.

Turn your research into action. Turn your ideas into impact. Join us in pushing the boundaries of what medicine can be, and let's pen the future together.

Warm Regards,

Editor-in-Chief

Prof. Nataliya Bhinder



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Literature review

Clinical decision-making theories

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Abstract: Clinical decision-making is a cornerstone of healthcare, influencing patient diagnosis, treatment, and ongoing care. This article explores the multifaceted nature of clinical decision-making, emphasizing its significance, challenges, and implications for modern healthcare. It delves into three primary decision-making theories: the rationalist approach, which prioritizes evidence-based decision-making; the phenomenological approach, focusing on intuition and experience; and the hypothetic-deductive approach, which seeks a balance between the previous two. These theories, while offering valuable perspectives, must be applied with consideration of the complex factors that influence decision-making, including competence, confidence, organizational support, and the clinical environment. Ultimately, clinical decision-making is both an art and a science, demanding a nuanced understanding to ensure patient-centered care and improved healthcare outcomes.

Keywords: Clinical Decision-Making, Healthcare Decision Theories, Evidence-Based Practice, Clinical Judgment, Patient-Centered Care

Introduction

Clinical decision-making forms the bedrock of healthcare, guiding the labyrinthine journey of patient diagnosis, treatment, and ongoing care. At the intersection of human cognition, medical expertise, and patient data lies the challenging endeavor of making decisions that are both informed and impactful. As the complexity of healthcare delivery continues to burgeon, due in part to technological advancements and evolving patient needs, there emerges an undeniable urgency to grasp the underpinnings of how clinicians arrive at their judgments.

Historically, the decision-making process in clinical settings was perceived as an intuitive art, deeply rooted in a clinician's reservoir of experience and knowledge. This enigmatic process, wherein the seasoned physician, armed with years of experience, made judgments that seemed almost second nature, has long been revered. However, as the landscape of healthcare has evolved, the allure of this intuitive process has been juxtaposed against the pressing need for structured, evidence-based decision-making models. The exigencies of modern healthcare—with its emphasis on evidence-based practices, patient safety, and a heightened awareness of medical errors—mandate a deeper understanding of the mechanisms that guide clinical decisions.

Understanding clinical decision-making is not merely an exercise in academic curiosity; it holds profound practical implications. Every day, healthcare professionals worldwide face a plethora of decisions, each with its own set of challenges and repercussions. These decisions range from the seemingly mundane to the critically pivotal, each one impacting the trajectory of a patient's care. By dissecting the mechanisms that underlie these decisions, there's potential to elevate the quality of care, reduce the incidence of errors, and better align clinical judgments with best practice guidelines and patient preferences.

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Furthermore, the decision-making process does not exist in a vacuum. It's intricately intertwined with the modern healthcare milieu. The advent of advanced diagnostics, the exponential growth of medical literature, and the ubiquity of electronic health records have collectively reshaped the contours of clinical decision-making. With a veritable deluge of information at their fingertips, clinicians face the double-edged sword of "infobesity" - the overwhelming nature of excessive information. This underscores the importance of robust decision-making models that can aid clinicians in distilling vast amounts of data into coherent, actionable insights.

Additionally, there's a growing emphasis on patient-centered care, which champions the integration of patients' values, beliefs, and preferences into the decision-making equation. This shift towards a more collaborative model challenges traditional hierarchies in healthcare and underscores the necessity for theories that encapsulate this evolving dynamic.

Beyond the tangible aspects of healthcare, clinical decisions are also deeply embedded in ethical terrains. They navigate the nuanced realms of patient autonomy, beneficence, and broader considerations of population health. Thus, any exploration of clinical decision-making theories must also be cognizant of these ethical dimensions, recognizing their indelible influence on clinical judgments.

In the forthcoming sections, we shall embark on a comprehensive exploration of the intricacies of clinical decision-making, examining its significance, challenges, and broader implications. Through this journey, we aspire to shed light on the myriad factors that shape clinical judgments, emphasizing their pivotal role in the overarching narrative of patient care.

Understanding Clinical Decision-making Theories

Clinical decision making is an essential part of clinical practice, and yet the term itself is a bit ambiguous. There are numerous definitions and approaches, and still, none seems to be complete. There is no single universal definition of clinical decision making, and there are many overlapping terms used to describe the same construct like clinical judgment, clinical reasoning, diagnostic reasoning, and so on [1].

Understanding of various decision-making theories may help improve clinical judgment and outcomes. There is always a need to justify professional decisions. Emergency nurses often face tough decisions, as they have to make conclusions based on the minimal available information, they are under the time pressure, and yet they need to justify and explain their decisions, demonstrate accountability [2].

Although there are many decisions making theories, this article looks at the approaches more commonly used in medical practice.

A rationalist approach to decision making

This approach is based on making informed decisions, an evidence-based approach. Decisions are made based on the highest degree of clinical evidence like data available from random controlled trials, systematic reviews, and meta-analysis. Such an approach removes the scope of uncertainties from the decisions taking. It is a step by step approach involving identification of the problem, exploring the options, and then making a choice. It breaks the complex task into smaller and manageable pieces of information [3,4]. In this kind of approach, the decision maker has a clearly defined problem, knows all the action alternatives and their consequences, and decision maker must choose the most optimum alternative. To a certain degree, it is an idealistic theory [1]. Supporters of this theory believe that it is the only way to move forward, despite its known limitations. Some specialists think that only such an approach can help medical science move forward [5].

However, this theory clearly has some drawback, as decision making with such an approach is time taking, and such a method may not suit for quick decision making like that in the A&E department. Further, in the chaotic world, data is often missing for various reasons. Not all clinical conditions can be supported by hard evidence, trends, information [5]. In the

real world, nurses or other medical staff is faced with complex situations where there is a lack of information, not enough cues to judge the condition rationally.

Phenomenological approach to decision making

This approach is also called intuitive approach and is known through the work of Benner. It is most commonly mentioned in the context of quick decision making in clinical practice. There is no single definition of intuitive or a phenomenological approach, and many describe it as an understanding without rationale. It is something that becomes better with professional experience as one learns to recognise specific patterns. It is said that a higher level of intuitive approach distinguishes expert from the novice [6]. There is poor understanding about how it occurs; it is a judgment or reasoning that just happens; even the decision makers are not able to explain the reason behind their choices. Novices can also have intuition, but they have higher chances of going wrong. Benner describes this approach as one of the significant characteristics of experienced medical professionals and nurses, as experienced professionals are not just dependent on analytical thinking.

Strength of this decision-making process lies in its speed, as decision maker is not dependent on the data analysis. It means that this method is well suited when quick decisions must be taken when the situation is uncertain and risky. It does not mean that there is no science behind the intuitive thinking, as it is based on the experience, pattern recognition, common sense, sense of salience, skills earned over the years, and use of rationality to a degree [7].

The supporters of the theory say that there is a limitation to relying on the data and rational thinking. In many cases, data is merely not available. Moreover, in certain clinical situations, there is an acute shortage of time. Additionally, even the evidence-based guidelines heavily rely on expert opinions [5].

However, not everyone agrees with intuitive theory, as there is no justification for decision making, and it has implications for accountability. Critics say that decision makers may use this approach to ease the cognitive work involved in rational or deductive approaches. One may base a decision on just one single piece of information. Or one may use it as a rationale to confirm one's perceptions. Moreover, this theory has a very narrow application, and one cannot use this theory of decision making out in areas of less experience. Many think that this theory contradicts the science, on which the whole medical field is based. While others argue that pure intuition does not exist as expertise is always based on extensive knowledge, and an experienced professional is a person with abundant knowledge of the subject. Thus the decision that may be seen intuitive is still based on knowledge and rationale [1].

Hypothetic-deductive approach to decision making

Also called information-processing theory is the most common theory used in medical research and clinical decision making. It has four major stages. The first stage is about gathering preliminary information about the patient by going through a patient's history, physical examination. There is a need for a systematic approach else one may miss the vital information; further, the accuracy of collected information also depends on the clinical skills of the specialist. It is essential that the thought process should follow a certain logic. The second step is the hypothesis generation when a specialist needs to make some initial conclusion regarding the disease condition based on the information gathered, experience, and knowledge/education. The third step is the clue interpretations. This step involves checking the validity of clues from step one against the generated hypothesis. It is about deciding which clue is relevant and which does not hold relevance. Finally, in the fourth stage, one must see if the hypothesis can be confirmed or not. This final stage also involves diagnostic reasoning. Studies show that this model is the most commonly used model by nurses and medical practitioners. Further, in this method, the nurse may frequently corroborate with colleagues to validate their knowledge and interpretations. However, sometimes need for verification is required as a person is not able to reach the decision. This model has its drawbacks too, as it is quite reliant on the decision trees, which are not perfect and may have inaccuracies resulting in false deductions. A person may have the wrong hypothesis. Further, most decisions trees assume that all the information is available at the time of deduction, which is not the case in

practice. Moreover, it is not an entirely rational approach; further, some nurses may start to use intuition in the process, though it may happen unconsciously [8].

Some of the factors influencing clinical decision making

There are many factors that may facilitate or inhibit decision making in nursing and medical practice. Feeling competent can improve decision making, which is highly dependent on the knowledge level and experience of the nursing staff. Self-confidence can also boost decision making in clinical situations. A confident person is self-reliant, independent, and proactive. Decision making is not only about knowledge or inherent qualities, and organisation structure may also influence the level of authority, organisational culture, tolerance to mistakes, degree of autonomy gives to various participants. Support provided by organisation and peers may also positively influence decision making. Like support from senior nursing staff, better financial and emotional support by the organisation. Finally, Continued education can help improve decision making [9,10]. A study by Gizaw shows that confident nurses are 3.4 times more probable to engage in decision making than less confident nurses. Nurses supported by senior staff are 2.8 times more probable to practice decision making. Nurses who do not get an opportunity for continued medical education are 79% less likely to make decisions. On the other hand, reduced patient-nurse ratio, poor organisational culture, lack of diagnostic facilities, poor communications between various stakeholders, lack of feedback, may inhibit decision making [11].

Discussion

Clinical decision-making, as described in the provided text, is not just a singular, straightforward process but rather a complex orchestration of various theories and influencing factors. Its profound importance in patient care necessitates a deep understanding and, when possible, a mastery of its nuances. In analyzing the body of the article, we are presented with a rich tapestry of perspectives, shedding light on the multifaceted nature of this essential aspect of medical practice.

The rationalist approach to decision-making seems to champion an era of evidence-based medicine, an era where every decision made in the clinic is underpinned by rigorous research and empirical data. This perspective underscores a methodical, step-by-step evaluation, where decisions evolve from a foundation built on systematic reviews, randomized controlled trials, and meta-analyses. However, while its systematic nature is undoubtedly a strength, especially in scenarios demanding meticulous assessment, its applicability might be constrained in high-pressure, time-sensitive situations, like those in emergency departments. Real-world scenarios are often fraught with information gaps, necessitating a more adaptive approach than a purely rationalist one.

Contrastingly, the phenomenological approach dives into the more elusive realm of intuition. Grounded in experience and pattern recognition, this theory suggests that seasoned professionals often have an innate understanding, an intuitive 'knowing,' which enables them to make decisions swiftly. Benner's work highlights how this intuition differentiates novices from experts. While the speed and efficiency of intuitive decision-making can be invaluable in certain clinical settings, especially when rapid judgments are crucial, its potential for subjectivity can't be overlooked. Sole reliance on intuition, absent empirical checks and balances, might introduce biases, with implications for patient care and professional accountability.

Attempting to harmonize the strengths of both the previous theories is the hypothetico-deductive approach. By championing a systematic process of gathering patient data, forming hypotheses, interpreting clues, and validating these assumptions, this method endeavors to combine the methodical nature of the rationalist approach with the adaptability of the phenomenological perspective. Yet, while it's a balanced method on paper, its real-world implementation can sometimes be hindered. Dependencies on decision trees, which might not fully encapsulate the complexity of certain clinical situations, and potential inaccuracies arising from this reliance, are pertinent considerations.

Beyond the theories themselves, the text brings to the forefront the myriad external and internal factors influencing clinical decision-making. Competence, confidence, and experience

emerge as cornerstones, serving as both drivers and reflections of sound clinical judgment. An environment that fosters learning, offers robust support mechanisms, and encourages continuous professional development further augments decision-making prowess. On the flip side, challenges like reduced patient-nurse ratios, poor organizational culture, and gaps in communication can potentially impede the process. Thus, while the theories offer the framework, it's these influencing factors that modulate the practical application of decision-making in clinical settings.

Conclusion

The act of clinical decision-making, as painted by the article, is both an art and a science. It demands a seamless integration of empirical data, intuition, experience, and a deep understanding of the unique circumstances surrounding each patient. While the three presented theories offer valuable insights into the potential pathways of decision-making, real-world scenarios often necessitate a blended approach. As healthcare professionals navigate this intricate maze, recognizing the strengths and limitations of each theory and the influencing factors becomes paramount. Such an understanding ensures that patient care remains holistic, informed, and, above all, patient-centric.

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Narrative Review

Environmental factors in the development of Alzheimer's disease

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Abstract: This article delves into the profound significance of the early diagnosis of Alzheimer's disease (AD), the leading cause of dementia worldwide. With no current cure for AD, early detection stands as a cornerstone in managing the disease. Early diagnosis not only enables symptomatic treatment to enhance the quality of life but also facilitates proactive planning, addressing health care and living arrangements for the future. Additionally, early diagnosis can promote participation in clinical trials, granting patients access to emerging treatments. An essential component to this early detection is a robust understanding of the disease's causes. The paper examines the pathological indicators, such as beta-amyloid plaques and neurofibrillary tangles, while highlighting the multifaceted origins of AD encompassing genetics, environmental factors, inflammation, and potential links with other diseases. An in-depth discussion on the influence of the environment further illustrates the complex interplay between genetics and external factors. Toxic chemicals, lifestyle choices in western societies, and other environmental determinants are scrutinized for their potential role in AD onset. In summary, the piece underscores the importance of a holistic understanding of Alzheimer's etiology, emphasizing that only through comprehensive knowledge can we aspire to identify, manage, and ultimately find a cure for this debilitating condition.

Keywords: AD, Alzheimer's disease, dementia, environment, environmental factors, Alzheimer's causes

Introduction

Alzheimer's disease (AD), the most common cause of dementia, presents a major global health challenge. With the rapid aging of the world's population, the prevalence of AD is anticipated to grow exponentially. As of now, no cure exists for Alzheimer's, making its early diagnosis even more critical. This essay elucidates the significance of early identification of AD and underscores the role of understanding its causes in achieving this early detection.

A timely diagnosis of Alzheimer's offers a multitude of advantages. Firstly, it provides patients and their families the opportunity to seek symptomatic treatments that can improve quality of life, at least temporarily. While current treatments do not halt the progression of the disease, they can mitigate symptoms such as memory loss, confusion, and behavioral changes. The earlier these treatments are initiated, the more effective they tend to be in ameliorating symptoms.

Secondly, an early diagnosis empowers individuals and families to plan for the future. They can make decisions related to health care, living arrangements, financial planning, and care responsibilities while the patient is still in a position to contribute to these discussions. This proactive approach can alleviate potential crises in later stages of the disease.

Lastly, early diagnosis can facilitate the inclusion of patients in clinical trials. Researchers continually seek participants for studies to test novel treatments and interventions. Those

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diagnosed early are more likely to meet the criteria for participation, providing them access to potentially beneficial treatments not yet available to the broader public.

The advantages of early detection are evident. However, achieving this necessitates an understanding of the causes of AD, as the pathophysiological events leading to Alzheimer's often commence years, if not decades, before clinical symptoms manifest.

From a pathological standpoint, AD is characterized by two hallmark abnormalities in the brain: the accumulation of beta-amyloid plaques and the formation of neurofibrillary tangles consisting of hyperphosphorylated tau protein. But what leads to these abnormalities?

At the forefront of AD research is the role of genetics. Several genes have been implicated in the development and progression of Alzheimer's, with some variations directly increasing the risk. For example, mutations in the genes APP, PSEN1, and PSEN2 have been identified in families with early-onset Alzheimer's. Additionally, the APOE ε4 allele is a well-established genetic risk factor for late-onset AD. Understanding these genetic components can aid in identifying individuals at high risk long before they exhibit symptoms.

Environmental factors and lifestyle also play pivotal roles. Chronic conditions like hypertension, diabetes, and obesity in midlife have been linked to an increased risk of developing AD in later years. Additionally, traumatic brain injuries and exposure to environmental toxins have been implicated as potential risk factors. Therefore, monitoring and managing these factors early on can be instrumental in AD prevention and early detection.

Furthermore, the role of inflammation and the body's immune response is under extensive investigation. Chronic inflammation, whether in the brain or elsewhere in the body, has been associated with AD. This knowledge has propelled researchers to study the impacts of anti-inflammatory treatments and their potential in staving off the disease.

Finally, recent research has begun to explore the connection between Alzheimer's and other diseases. For instance, there's evidence to suggest that certain pathogens, such as herpes simplex virus type 1, may be involved in AD pathogenesis. Identifying such connections can lead to novel diagnostic methods and intervention strategies.

Role of Environmental Factors in Alzheimer's Development

Alzheimer's is among those diseases where genetics is known to play a profound role but is not the sole factor. Evidence that environment has lots to do with it is mounting. It is now known that right kind of nutrition and lifestyle may be preventive in many cases [1]. It is also the fact that not all identical twins develop similar genetic diseases, thus proving that quite often environment is more powerful force than genetics [2]. In this article, we do not intend to dismiss the role of genetics, but rather focus on the interplay between genetics and environment.

So does that mean that genetic diseases like Alzheimer's are preventable? Maybe not completely, but surely to a large extent, if we recognize the triggering environment factors. Changing the genetic sequence may be out of the realms of modern science, but as the studies of epigenetics show that it is not the only way to prevent genetic diseases. Environment factors can alter gene expression (how the genes functions), in fact, there is growing evidence that these newly acquired traits can also be passed to next generation. Thus if we learn more about these factors, we may able to decrease the prevalence of Alzheimer's in our and coming generations [3].

Interplay of Environment and Genetics

Certain environmental factors have long shown to increase the risk of Alzheimer's, dementia and Parkinsonism, like a toxic chemical and brain injury [4], but not all intricacies of this interaction between environment and genetics are understood. What we know for sure is that environment does play an important role in development, and genetics is a predisposing factor.

Thus for example, as per studies of genetics, a gene called ApoE4 is considered to be the major risk factor for developing Alzheimer's [5]. However, the studies have shown the much lower prevalence of Alzheimer's in sub-Saharan Africans as compared to Africans living in western societies, which shows that pollution, industrial food, stress, and sedentary lifestyle render people more susceptible to Alzheimer's [6]. There have been very few studies comparing the prevalence of Alzheimer's among the genetically similar populations, living in the completely different environment from each other. One such study compared the residents of small Nigerian town with African Americans and found the incidence of Alzheimer's much higher in those living in America [7]. Thus confirming the role of environment, further underlying the problems of environment and lifestyle in western societies. So let us look at the factors that have been strongly linked with the neurodegeneration, dementia and Alzheimer's.

Environmental Chemicals

Acute exposure and poisoning with heavy metals and pesticides have been well studied and documented. However, neurodegeneration occurs due to chronic low-level exposure to these toxic elements. Thus long term accumulative exposure to the lead has been shown to cause a decrease in memory, and progressive decline in mental functions [8]. In contrast to lead, the role of Aluminum has long been overlooked, it is present in many medications (like antacid suspensions), it is additive to various commercially available food products, food colorant, and even sometimes used to clarify water. Now there is increasing evidence that it may be playing a role in the development of Alzheimer's [9].

Air pollution is something to which we are exposed at very young age, and in most cases, we do not have much choice. It is a toxic cocktail of organic and non-organic compounds, metals, and gases. Evidence of a link between neurodegeneration and air pollution is growing [10].

Western lifestyle and disease cluster

In western societies unlike developing nations, non-infectious diseases are the main threat, and faulty life style is the main causing factor. As per some estimates, obesity and sedentary life style in western societies are now killing more people than other diseases. Research shows that the risk of developing Alzheimer's increase manifold in obese people, with high blood pressure and cholesterol (as much as 6.2 times), especially at midlife [11].

Social, Mental, and Physical Activity

Physical activities decrease the risk of practically any disease, thus having a direct and indirect effect on the development of Alzheimer's. Apart from physical exercise, it is also important to stay mentally active. Thus people who continue to participate in activities, like learning new things, or reading, or even listening to music have reduced chances of decline in brain function [12]. Further what may help to remain mentally active is social participation. Many people tend to become isolated as they grow, but if the person maintains a high level of social activity and participation, it not only decreases stress, uplifts mood but may also prevent or delay Alzheimer's [13].

Psychological stress

Psychological stress results in increased level of stress hormones, which has been found to be damaging for brain functionality. Emotional distress like depression and anxiety in young and midlife has been suggested to increase the risk of developing dementia and Alzheimer's later in life. Some in the scientific community think that emotional distress could be rather an early symptom of neurodegeneration. Nevertheless, there is now a wide consensus among the doctors and scientific community that emotional distress is a risk factor for dementia and mental decline [14].

Nutritional Factors

We may be discussing the nutritional factors in last, but no doubt that it is the single most important factor, that can either prevent or aggregate mental decline. A balanced diet rich in fruits and vegetables is preventive, due to the high content of vitamins, microelements, and antioxidants. While diet with high content of saturated fats and cholesterol is harmful,

these fats block blood vessels and are the reason for stroke and cardiac diseases. As the brain is mostly made of fats, therefore it is important to have a balanced diet. Omega-3 has been shown to be neuroprotective [15], and products like fish oil, soya oil, walnuts, are a rich source of it.

Thus it may be wise to conclude that familial genetic history of neurodegenerative diseases does not essentially mean that person will develop mental decline. Neurodegenerative diseases are still highly preventable. By avoiding the triggers in the environment and living healthy, active life, one may expect to live a life of a mentally alert person.

Conclusion

In conclusion, the early diagnosis of Alzheimer's disease holds undeniable importance, not only for enhancing the life quality of affected individuals but also for advancing research and potential treatments. Recognizing the causes of Alzheimer's is intrinsic to facilitating this early identification. By delving deeper into genetic predispositions, understanding environmental and lifestyle impacts, investigating inflammation pathways, and exploring connections with other diseases, we broaden our diagnostic capabilities. As we move forward in the fight against this devastating disease, a holistic understanding of its etiology remains paramount. Only through a comprehensive grasp can we hope to identify, intervene, and eventually find a cure for Alzheimer's disease.

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Literature review

Assessment of Bone Marrow Failure Syndrome Management Outcome in Pediatrics – Saudi Perspective

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Abstract: Bone Marrow Failure Syndrome (BMFS) is a rare yet severe condition affecting pediatric populations, characterized by a reduced production of hematopoietic lineages leading to pancytopenia. This article explores the multifaceted nature of BMFS in children, its diverse etiologies, treatment modalities, and outcomes, with a particular focus on the Saudi Arabian context. BMFS encompasses both inherited and acquired forms, often presenting diagnostic challenges due to its heterogeneity. Inherited BMFS accounts for 30% of cases and includes rare conditions like Fanconi Anemia and Schwachman-Diamond Syndrome, where treatment approaches vary depending on severity. Acquired BMFS, constituting 70% of cases, may exhibit complete recovery or require prolonged treatment with immunosuppressants. Hematopoietic Stem Cell Transplantation (HSCT) remains a primary treatment option, with outcomes influenced by factors such as donor type and graft success. Saudi Arabia, despite its high-income status, has faced limited data availability on BMFS outcomes, but the number of HSCT procedures performed in the country is steadily increasing. Survival rates in HSCT patients vary based on factors such as donor match and the underlying cause of BMFS. Additionally, the risk of secondary malignancies is relatively high in BMFS patients, adding complexity to long-term management. While Saudi studies indicate survival rates comparable to international standards, challenges in the assessment of BMFS outcomes persist, given the condition's rarity and diversity. This article underscores the importance of continued research and data collection to enhance our understanding and management of BMFS in the pediatric population, both in Saudi Arabia and globally.

Keywords: Bone Marrow Failure Syndrome, Pediatric Population, Hematopoietic Stem Cell Transplantation, Etiology and Treatment, Saudi Arabia

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Introduction

Bone marrow failure syndrome (BMFS) in the pediatric population is among the uncommon health issues, affecting only a small number of children each year. However, the condition is severe posing treatment challenges. Despite the best treatment, adverse outcomes are not rare in the condition. Moreover, it results in reduced life expectancy almost in all cases. Nonetheless, many children can expect close to normal life for a long.

BMF is a condition characterized by reduced production of one or more hematopoietic lineages, depending on the cause. This results in reduced production of one or another kind of blood cells or even leads to pancytopenia. Though not in all, BMFS leads to pancytopenia in many cases, especially if the condition is inherited. Hence, in the case of inherited bone marrow failure syndrome (IBMFS), the treatment of choice is almost always hematopoietic stem cell transplantation (HSCT). In the case of acquired BMF, many cases (up to 30%) may resolve either spontaneously or with the help of conservative treatment.[1] Nonetheless, those who develop severe aplastic anemia (SAA) require bone marrow transplantation. The optimal choice of the donor in most cases is matched sibling if possible.[2] However, in most

cases, this option is not present, and thus donor is usually HLA matched individual outside the family, which affects the treatment outcomes adversely.

As one can understand that assessing the outcomes of BMF poses significant challenges. The first challenge is the heterogeneity of the condition. It is a condition that occurs for many reasons, and in many cases, the cause remains unidentified. Additionally, outcomes also depend on the choice of treatment. Even in the case of bone marrow transplantation, outcomes depend on the donor's choice.[2] Another significant challenge in assessing BMFS outcomes in the pediatric population is the limited availability of global and Saudi studies data. Further, most studies have sample sizes as the conditions are among rare disorders. Despite numerous challenges in assessing outcomes of BMFS in the pediatric population, we look at the various aspects to develop a better understanding.

Etiology, Treatment, and Outcomes

BMFS is a heterogeneous disorder, and outcomes would significantly depend on the etiological factors. It is vital to understand that BMFS occurs due to a range of inherited and acquired health conditions. In many cases, the cause of BMFS even remains unidentified (idiopathic), causing much distress to the patient and parents. Studies suggest that about 30% of BMF cases in the pediatric population occur due to inherited disorders and another 70% due to acquired health conditions.[3]

Studies show that BMFS has a triphasic peak, with the first peak at 2 to 5 years, another 20 to 25 years, and then after 65 years of age.[3] In the pediatric population, about one-third of cases are due to inherited disorders. Most of these disorders are rare, and their prevalence does not seem to have much relation to geographies and ethnicities. Among the inherited causes are conditions like Congenital Amegakaryocytic Thrombocytopenia, Fanconi Anemia, Telomere Biology Disorder, Diamond Blackfan Anemia, Schachman Diamond Syndrome, and Severe Congenital Neutropenia.[2] Among them, the most common is Fanconi anemia affecting 1 to 5 children out of a million. It appears that in about 75% of cases of inherited BMFS, the cause remains unidentified.[3] When it comes to the Saudi experience, a Saudi study by AlMozain et al. analyzed 183 (155 adults and 28 pediatric) patients with myelodysplastic syndrome (MDS) and found that the cause of BMFS could not be identified in half of the pediatric cases.[4] Hence, it is pretty evident that the cause of BMFS remains unidentified in most cases in Saudi.

In the pediatric population, 70% of BMFS are due to inherited disorders like Idiopathic Aplastic Anemia, Infections (hepatitis A, B, C, CMV, HIV, EBV, Fungal, Tuberculosis), radiation, drugs and toxins, autoimmune disorders (SLE and RA). However, the most relevant cause is bone marrow infiltration due to conditions like leukemia, myelodysplastic syndrome, and metaplastic malignancy.[2] Among cancers, leukemia is the most common but still among rare disorders. In 15 years period from 1999-2013, 8712 cases were reported, and thus estimated burden in the pediatric population was less than 2 in 100,000.[5] BMFS due to other causes like infections or aplastic anemia, or autoimmune disorders is also rare.[6] It means that if we consider that inherited and acquired BMFS are rare events, there are only a few hundred cases of BMFS occurring in Saudi Arabia every year.

When considering outcomes of BMFS, much would depend on whether the condition was inherited or acquired and the kind of treatment used. When it comes to inherited, which makes up 30% of cases of BMFS in the pediatric population, many with severe cytopenia are treated with bone marrow transplant or hematopoietic stem cell transplantation (HSCT). However, it depends on the condition's severity and if the inherited disorder was identified.

Among inherited conditions, Fanconi Anemia (FA) is most common, often diagnosed between 5 to 10 years, with varied clinical presentation. The risk of bone marrow (BM) failure in the conditions is 50-90%. It means that most would need HSCT. In the Schwachman-Diamond Syndrome (SDS) case, only about 20-33% develop BM failure and thus have a much better prognosis and outcomes. Thus, as one can see, not all patients living with inherited BMFS require HSCT, and many have good outcomes with conservative treatment and can

even expect prolonged remission, or they may benefit from other treatments like blood transfusion, steroids, and so on.[7]

In the case of acquired BMFS, one-third can expect a complete recovery, and many others would require prolonged treatment with androgens, immunosuppressants, and other medications.[2], [8] It means that less than half of those living with acquired BMFS would require HSCT. This means that a few hundred children need HSCT in Saudi every year. Thus, when assessing BMFS management outcomes in pediatrics, it would be wise to focus on HSCT outcomes, as it remains the primary treatment in those who develop BMFS.

When it comes to hematopoietic stem cell transplantation (HSCT) outcomes in Saudi, there is a paucity of data. Moreover, it is worth understanding that Saudi is a high-income nation, which means that many cases of BMFS are treated abroad. Nonetheless, things are fast changing in Saudi, and the first HSCT was done in 1984 in the nation. Fortunately, now most HSCT procedures are done in the nation, and thus the number of HSCTs done in the nation has constantly been rising. Studies show that about four medical centers located in Riyadh, Jeddah, and Dammam are carrying out more than 90% of all HSCT in Saudi. Consequently, data shows that between 2008 and 2016, the total number of HSCT procedures done in Saudi in Pediatrics ranged from 120 to 160 cases.[9]

It would be correct to say that inherited BMFS outcomes in severe cases are significantly proportional to HSCT outcomes. The success of HSCT significantly depends on the underlying cause and graft source. Studies show that the 10-year survival rates of HSCT are moderately good at 83%, 73%, 68%, and 51% for each consecutive decade. Hence, one can see that despite the amazing results, the life expectancy of those living with BMFS is much less than that of healthy adults. Here, the survival rate would be much higher with sibling-matched donors. Studies show that survival for 40 years is extremely high and almost close to 100% in those who do not require ongoing steroid use. However, this rate declines to 50% if immunosuppressant therapy is needed.[3], [7] However, some studies show that in the case of unrelated donor transplantation, long-term survival is 30-40%.[7]

Thus, as one can see, outcomes depend on the underlying cause of BMFS, as some conditions may resurge, and in others, one may experience prolonged remission. Furthermore, much depends on the graft's success. Thus, for example, a study in HSCT patients demonstrated that a 5-year survival rate was 83% or higher in graft failure-free patients. Graft rejection rates increase considerably in the case of HLA-mismatched HSCT. Even in the case of a graft match, one-third of the patients may expect some graft-versus-host disease.[10] Similarly, a study using data from 563 Aplastic Anaemia (AA) children showed that long-term survivability was as high as 91% in the case of HLA-matched family donors.[11] Studies also suggest that outcomes are worst in patients with unidentified BMFS causes.[12]

Though there are few Saudi studies reporting outcomes in patients diagnosed with BMFS, nonetheless, most data suggest that short-term and long-term survivability rates in Saudi are quite similar to that reported in the US and Europe. A study by Lujain Talib et al. from Jeddah, SA, reported that two-year survivability in HSCT patients was 96.6%. However, outcomes are much worse in those who require Paediatric Intensive Care Unit (PICU) admissions. They found that about one-fourth of all patients who have undergone HSCT do need PICU admission, and in such patients, 2-year survivability is reduced to 58%.[13]

Apart from survivability in individual conditions causing BMFS, or considering the outcomes of HSCT, another critical factor to consider is the risk of malignancies. It appears that the risk of secondary malignancies in those affected by various disorders causing BMFS or those who have undergone HSCT is relatively high. For example, studies suggest that those living with FA have a risk of developing solid tumors between 28% to 40% in the long run, that is, in 15-20 years, which may also affect the disease or treatment outcomes.[7]

Conclusion

To sum up, BMFS is a condition that occurs due to numerous reasons, and thus predicting outcomes is quite challenging. Generally, outcomes would depend on the etiology of the

condition. For example, FA has a worse outcome among inherited conditions than SDS. Additionally, for those with unidentified inherited BMFS, the prognosis is worse. But, regretfully, studies show that in the case of inherited BMFS, the cause remains unidentified in the majority of the cases. It means that most of those living with BMFS would ultimately need HSCT.

Studies suggest that 70% of the BMFS cases are acquired even in the pediatric population, with many conditions benefiting from conservative treatment. Among acquired conditions, malignancies are challenging to treat. Many patients with secondary BMFS, would also need HSCT.

It means that perhaps half of all cases of BMFS would ultimately need HSCT. Therefore, outcomes in those living with BMFS significantly depend on the outcomes of HSCT. In the case of HLA-matched family donors, long-term outcomes of HSCT are pretty good, with long-term survivability of greater than 80%. However, in the case of the non-family donor or unmatched donor, the outcomes are much worse, with long-term survivability of about 30-40%. Additionally, early PICU admissions post-HSCT could be regarded as predictive factors.

Finally, it is worth understanding that even with excellent conservative treatment outcomes or with good HSCT outcomes, those living with BMFS are at significant risk of developing secondary malignancies. In the long run, almost every second long-term survivor may be affected by malignancies.

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Narrative review

A Comprehensive Review of Acute Coronary Syndrome

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Abstract: A significant sign of coronary artery disease is the acute coronary syndrome (ACS). Angina pectoris, ST-elevation myocardial infarction, and non-ST-elevation myocardial infarction (NSTEMI) are just a few of the conditions that are grouped together under the general term “ACS.” The main cause of death worldwide is cardiovascular disease, which puts ACS under a heavy financial strain. Reduced blood flow to the heart, primarily as a result of plaque rupture and thrombus development, is a pathogenesis of ACS. Numerous risk factors, both modifiable (such as smoking, hypertension, diabetes, hypercholesterolemia, obesity, and inactivity) and non-modifiable (like age, gender, and inheritance), can lead to the development of ACS. Electrocardiography (ECG), clinical evaluation, history-taking, and cardiac biomarkers are all used in the diagnosis process. For the best management, prompt diagnosis and risk classification are essential. Reperfusion therapy, anti-anginal therapy, and renin-angiotensin blocking are a few of the suggested procedures in treatment techniques that aim to minimise myocardial ischemia and restore coronary blood flow. Long-term management also strongly depends on modifying one’s lifestyle, including giving up smoking, eating a healthy diet, getting regular exercise, and obtaining rehabilitation. Acute cardiac failure, ventricular septum or papillary muscle rupture, arrhythmias, recurrent angina, and other consequences of ACS are also highlighted in the paper. The prognosis varies depending on variables, including persistent myocardial injury and the existence of ventricular arrhythmias; an unfavourable prognosis is frequently related to arrhythmias and is associated with poor left ventricular function. . This article offers a thorough review of ACS and gives readers important information about its pathophysiology, risk factors, diagnosis, therapy, and prognosis.

Keywords: Acute Coronary Syndrome, Myocardial Infarction, Angina, Cardiovascular Disease.

INTRODUCTION:

Acute coronary syndrome (ACS), a particularly risky form of coronary artery disease, is common, which has a large cost and health impact. ACS is primarily responsible for CAD-related deaths, which are currently the world’s leading cause of mortality.¹ Acute coronary syndromes (ACS) can appear in a variety of clinical ways and are a major cause of mortality. Electrocardiographic signs, particularly ST-segment elevation, are used to make the diagnosis. In emergency care, adherence to scientific recommendations is essential for ensuring optimal treatment based on the likelihood of ACS. In order to select the best treatments and time for revascularization, it is critical to assess ischemia and hemorrhagic risks. Key elements of emergency treatment, such as ACS diagnosis and risk stratification, are summarised in this article.² With regard to morbidity and death, acute coronary syndrome (ACS) imposes a heavy burden. In this review, the pathophysiology, diagnosis, treatment, and management of complications of ACS are discussed. It seeks to enhance information in order to improve ACS patients’ results.³ STEMI, NSTEMI, and unstable angina are all included in ACS. Because it encapsulates the similarities in presentation and management across these conditions, the phrase is useful.⁴ The three classic forms of acute coronary syndrome (ACS) are unstable angina, NSTEMI, and STEMI. Due to high-sensitivity troponin tests, which can identify myocardial cell death brought on by ischemia even in the absence of a STEMI pattern on the ECG, the diagnosis now favours NSTEMI. With this modification, myocardial ischemia patients are

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accurately identified, allowing for proper management and treatment techniques.⁵ The 2018 joint task force of the European Society of Cardiology (ESC), American College of Cardiology Foundation (ACCF), American Heart Association (AHA), and World Health Federation (WHF) defined acute myocardial injury, whether STEMI or NSTEMI, as the existence of abnormal cardiac biomarkers in the presence of evidence of acute myocardial ischemia.⁶ Acute coronary syndrome, which includes unstable angina and myocardial infarction, is a group of illnesses brought on by an abrupt stoppage of the blood supply to the heart. It causes serious issues for young adults and is quickly rising to the top of the global list of killers, with high rates of morbidity and mortality being reported in Western European hospitals. The prevalence of cardiovascular disease is rising in South Asian nations as well, and this burden is expected to grow significantly in the coming years.²⁰

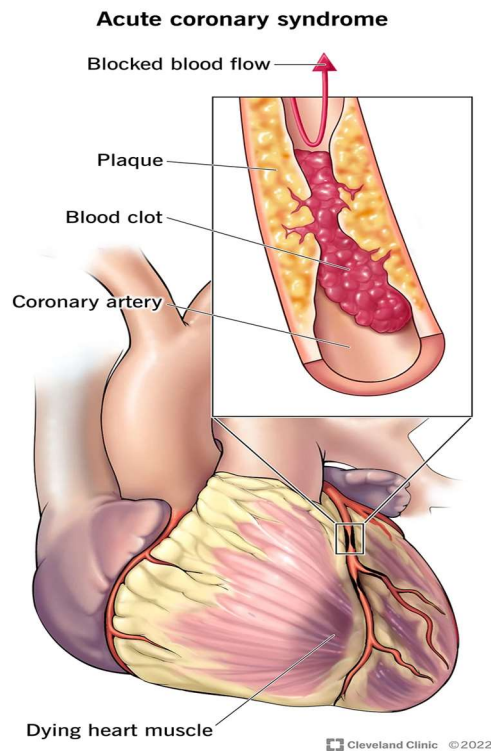


Figure 1: An obstruction causes blood flow to be sluggish or cease in acute coronary syndrome.¹⁷

PATHOPHYSIOLOGY:

Reduced blood flow to a section of the heart muscle is a pathogenesis of acute coronary syndrome (ACS). Vasospasm, plaque rupture, thrombus development, and in some situations, vasospasm can all contribute to this. As a result, infarction and ischemia occur. The location, size, and length of the obstruction are among the variables that affect the severity and outcomes of ACS. There may be some degree of cell necrosis even in milder episodes of ACS, which can vary from transitory ischemia to infarction. Numerous factors, including coronary vasospasm, calcified nodules, plaque rupture, plaque erosion, and myocardial bridging, can cause ACS. For an accurate ACS diagnosis and successful therapy, it is crucial to comprehend the intricate pathophysiology.^{7, 8, 13, 15}

Atherosclerosis and Plaque Rupture:

Nearly all acute myocardial infarctions have thrombosis on a responsible coronary atherosclerotic plaque as their underlying cause. An increased risk of future thrombosis is indicated by vulnerable plaques, which include a big lipid core, a high macrophage density, a low smooth muscle cell density in the plaque cap, a high tissue factor content, and a thin,

disorganised collagen structure in the cap.¹¹The likelihood of upcoming acute episodes in people with coronary artery disease depends on the quantity of susceptible plaques. Individual disparities in recurrent occurrences are explained by differences in the quantity of these plaques.¹²

Thrombus formation and coronary artery occlusion:

A plaque rupture causes thrombus to develop, limiting blood flow and resulting in ischemic consequences. Platelets, red blood cells, vasoconstrictors, and fibrin fibres make up the thrombus; the fibrin fibres' properties determine the thrombus' stability and susceptibility to dissolution.¹⁴Plaque cap disruption or endothelial denudation may lead to thrombosis on a plaque's surface. Major thrombi are more frequently associated with disruption of the plaque than with superficial endothelial denudation.¹² Acute coronary syndromes can result from coronary artery thrombus, which is brought on by plaque rupture or erosion. The patient's prognosis and the results of percutaneous coronary intervention are affected by the existence and length of the thrombus.¹⁶

Myocardial Dysfunction:

Ischemic tissue has poor relaxation and contractility, which results in hypokinetic or akinetic segments. During systole, these segments could exhibit paradoxical motion. Depending on how much of the affected area is damaged, the implications might range from minor effects to heart failure or cardiogenic shock. Ischemic cardiomyopathy can be brought on by persistent heart failure and poor cardiac output. Mitral valve regurgitation may result from ischemia in the papillary muscle, and mural thrombus development may be facilitated by abnormal wall motion.⁸

Myocardial Infarction (MI):

Reduced coronary blood flow results in myocardial necrosis and myocardial infarction (MI). Although the right ventricle and atria may also be affected, the left ventricle may be the primary site. Transmural and nontransmural MI are distinguished by whether they affect the entire myocardial thickness and produce aberrant Q waves on the ECG. ST-segment and T-wave abnormalities result from nontransmural infarctions. The distinction between ST-segment elevation MI (STEMI) and non-ST-segment elevation MI (NSTEMI) is based on the presence or absence of Q waves or ST-segment elevation. Large-scale ventricular wall necrosis can result in rupture, ventricular aneurysm, or the development of a pseudoaneurysm.⁸

Electrical dysfunction

Electrical dysfunction is a key factor in acute coronary syndrome. The inability of ischemic and necrotic cells to produce regular electrical activity results in a variety of ECG abnormalities, arrhythmias, and conduction issues. The ST-T abnormalities associated with ischemia include peaked T waves, T-wave inversion, ST-segment elevation, and ST-segment depression. Disturbances in conduction may be a sign of injury to the AV node, sinus node, or specific conduction tissues. While some alterations are transient, others might be long-lasting.⁸

RISK FACTORS:

Diabetes, diet, hypercholesterolemia, hypertension, lack of exercise, obesity, smoking, alcohol use, and stress are all modifiable risk factors for cardiovascular disease. Age, ethnicity, gender, and genetics are all non-modifiable risk factors. People can lower their risk of cardiovascular disease by adopting healthy lifestyle changes like stopping smoking, improving their nutrition, and engaging in more physical activity.^{18, 19}

MODIFIABLE RISK FACTORS:

Smoking:

Smoking is a significant contributor to atherosclerosis and myocardial infarction risk. Particularly among women who smoke while using birth control pills, it raises the risk of cardiac

mortality and is a major cause of death in the US. Nicotine has an impact on the cardiovascular system by raising blood pressure, heart rate, and the risk of arrhythmias, as well as vasoconstriction. Additionally, it promotes the growth of smooth muscle cells and platelets in coronary arteries. Peripheral artery disease, which increases the risk of heart attacks and strokes, is associated with smoking. The risk of dying from coronary heart disease is also increased by exposure to secondhand smoke. Health is improved by quitting smoking, and help and medication can increase success. The risk of coronary heart disease is 50% lower after a year of quitting.^{21, 22, 23, 24, 25}

Alcohol:

Regularly consuming a small amount of alcohol is frequently viewed as advantageous. However, excessive alcohol use can raise the risk of atherosclerosis progression and be a role in conditions including high triglycerides, high blood pressure, weight gain, and irregular heartbeats. Due to the short epidemiological follow-up in this area, the association between alcohol use and cardiovascular illnesses, particularly their atherogenic and antiatherogenic qualities, is still up for debate..^{26, 27, 28}

Hypertension:

Systolic blood pressure, which is particularly harmful to the coronary arteries and raises the risk of myocardial infarction, is an important predictor of cardiovascular disease risk. Over time, it also puts more strain on the heart, which causes the left ventricle to expand and weaken. The chance of serious cardiovascular events grows as blood pressure raises. Comorbidities raise the risk of heart disease even more. Maintaining a healthy weight, controlling stress, abstaining from smoking, and abstaining from excessive alcohol intake are all necessary to reduce this risk. To control high blood pressure and lower the risk of coronary heart disease, doctors may prescribe medications.^{29, 30, 31}

Diabetes Mellitus:

Diabetes ups the risk of CHD. The most common cause of death for those with diabetes, CVD is a serious consequence of the disease. 65% of diabetic deaths are caused by heart disease and stroke. Diabetes patients have a 2-4 times greater incidence of CHD.³² Obesity, cholesterol issues, and higher blood pressure rates are all linked to type 2 diabetes and raise the risk of CVD. People with diabetes who smoke have a twofold increased risk of CVD. When cholesterol levels are the same, those with diabetes are more prone to heart disease than people without diabetes.³³

Blood Cholesterol:

The risk of coronary heart disease (CHD) grows as blood cholesterol levels rise, especially when other risk factors are present. Myocardial ischemia is caused by cholesterol buildup in the coronary arteries, which results in arterial damage and occlusion. Elevated LDL levels contribute to atherosclerosis, whereas elevated HDL levels assist in reducing inflammation and thwarting LDL oxidation. Heart disease is thought to be predicted by low HDL levels. To control and lower the risk of CHD, managing cholesterol levels by diet and medicine is crucial.^{34, 35, 36}

Obesity:

In addition to raising the risk of cardiometabolic disorders due to the visceral and subcutaneous fat buildup, obesity is directly linked to myocardial infarction (MI). It has been associated with diabetes, elevated blood lipid levels, and hypertension. Reduced risk of MI can be attained through weight loss brought on by dietary adjustments, improved physical activity, stress reduction, and moderate alcohol consumption.^{37,38,39}

Physical Inactivity:

High cardiovascular risk is linked to physical inactivity.⁴⁰ Although exercise has a cardioprotective impact, it is not well understood how it helps people with ACS. Resistance training can improve myocardial function, but due to exercise-induced myocardial ischemia, it may hinder the heart's ability to prepare for an ischemic event.⁴¹ The American Heart Association suggests engaging in moderate physical activity for at least 2 ½ hours a week, or 30 to 60 minutes, on most days. The best options include cycling, dancing, swimming, walking, and jogging.⁴²

NON MODIFIABLE RISK FACTORS:

Age:

For cardiovascular disease (CVD), age is a well-known, unchangeable risk factor. Progressively, more CVD risk factors are added to an individual as they age.⁴³ People over 65 account for over 80% of heart disease deaths in humans.⁴⁴

Gender:

Men are more likely to have CHD, although women are more at risk as they age. Cardiovascular risk factors can play different roles depending on a person's gender. Men get heart attacks earlier in life, while women's risk rises after menopause but is still lower than that of men. However, heart disease is the number one killer of both sexes. Men and women both have fair or bad health rates as they age, but women could have more difficulties participating in social and physical activities. Heart disease is a major health problem for both men and women despite the fact that gender influences CVD risk factors.^{45,46,47}

Heredity/Family history:

According to epidemiological research, a major risk factor for coronary heart disease (CHD) is a familial or parental history of myocardial infarction.⁴⁸ A first-degree blood relative who experienced a coronary heart disease or stroke before the ages of 55 for men and 65 for women is linked to an increased chance of developing heart disease.⁴⁹

Ethnicity:

People with ancestry from South Asia, Africa, or the Caribbean are more likely to develop cardiovascular disease, possibly as a result of greater prevalence of type 2 diabetes. To prevent heart and circulation disorders, people of all backgrounds are advised to lead healthy lifestyles.⁵⁰

CLINICAL PRESENTATION OF ACUTE CORONARY SYNDROME:

Three types of ACS exist: unstable angina (UA), non-ST-Elevation myocardial infarction (NSTEMI), and ST-Elevation myocardial infarction (STEMI). Risk categorization and prompt diagnosis are crucial. Restoring blood flow and lessening myocardial ischemia are the main goals of treatment. A increased risk of cardiac mortality and myocardial damage is associated with ACS.⁹ Significant ST segment increases on the ECG and increased troponin levels are indicators of STEMI. According to troponin levels, NSTEMI-ACS refers to situations lacking ST elevations on the ECG and can also be classified as NSTEMI or UA. On the ECG, ST segment depressions and T-wave inversions are frequently seen in NSTEMI-ACS.⁵³ This classification of acute coronary syndromes is illustrated in Figure 3.

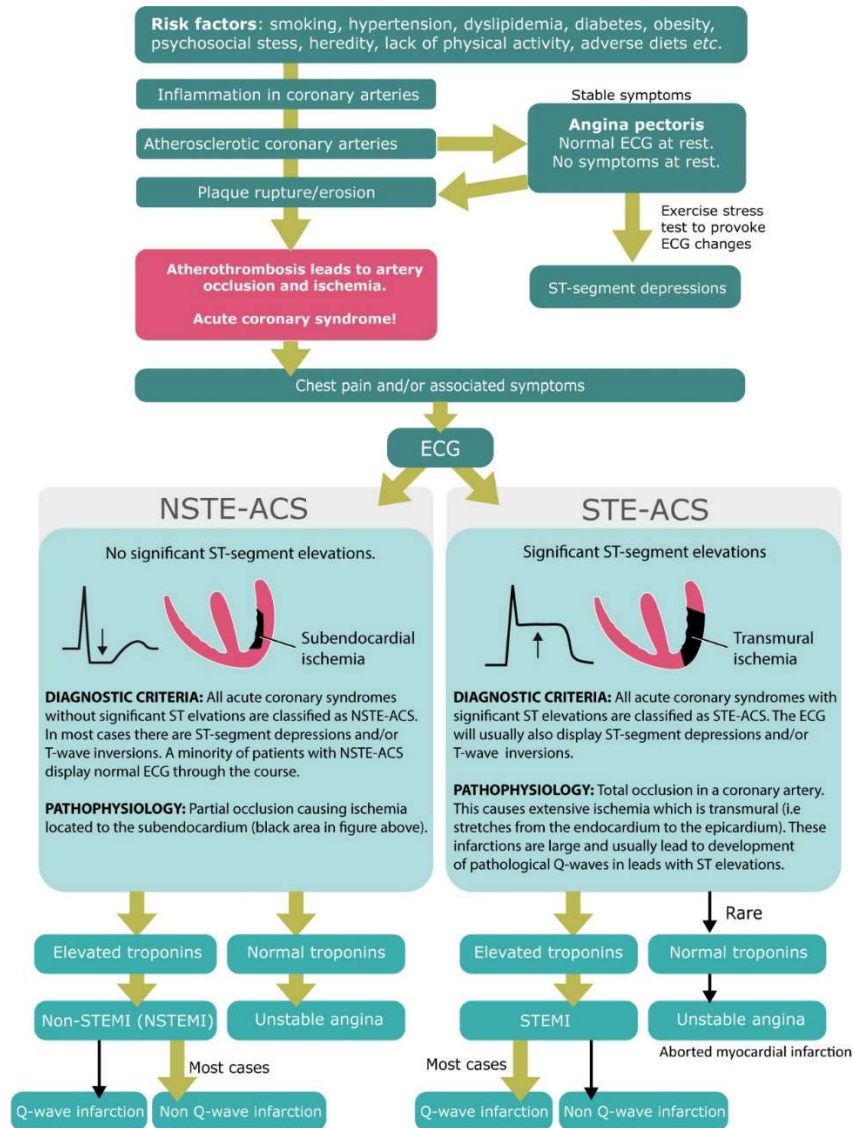


Figure 3: Classification of Acute Coronary Syndromes in STE-ACS (STEMI- ST Elevation Myocardial Infarction) and NSTEMI-ACS (Non-STEMI and Unstable Angina).⁵³

DIAGNOSTIC APPROACHES FOR ACUTE CORONARY SYNDROME:

Clinical Assessment and History Taking

Chest discomfort, breathlessness, sweating, motion sickness, exhaustion, dizziness, and palpitations are classic ACS symptoms. However, in other patient populations, symptoms may be abnormal or even nonexistent. For the best results, early diagnosis and proper management are essential.⁵¹

The pain associated with acute myocardial infarction (MI) is strong, persistent, and frequently described as a tightness or weight in the chest. There may also be nausea and shortness of breath. It is possible for MI to be silent or painless, especially in the elderly or in people with diabetes. It's critical to get medical attention right once when symptoms appear.⁵²

To distinguish between STEMI and NSTEMI/unstable angina, an ECG is performed within 10 minutes after the initial assessment of suspected ACS. The diagnosis is aided by cardiac enzymes, chest X-rays, and blood tests. Considerations should be made for additional problems, such as aortic dissection and pulmonary embolism.¹⁵

Electrocardiography (ECG)

A bundle branch block or a previous MI block may make it challenging to interpret the normal 12-lead ECG, which is crucial for diagnosing ACS. In roughly one-third of instances, the initial ECG results may be normal or equivocal. Repeated ECGs are essential, especially when there is ambiguity or symptoms that continue.⁵²

Cardiac biomarkers

Serial troponin readings are crucial in making an ACS diagnosis. Troponin levels are not significantly elevated in unstable angina, although they are elevated in MI. Troponin levels start to climb in 3 to 6 hours, reach their peak in 36 hours, and then continue to rise for up to 2 weeks. There may be an increase in other cardiac enzymes. Leukocytosis may be seen on a full blood count, and high levels of ESR and CRP are also present. Following presentation, lipid measurements must be done within 24 hours.⁵²

Radiography

To determine the size of the heart and detect pulmonary edema, a chest X-ray is performed. Cardiomegaly may exist as a result of previous cardiac injury.⁵²

Echocardiography

Prior to hospital discharge, echocardiography is conducted to evaluate ventricular function and identify any problems, such as mural thrombus, cardiac rupture, ventricular septal defect, mitral regurgitation, and pericardial effusion.⁵²

Coronary angiography

In high-risk patients who do not react to pharmacological therapy, have significant ECG abnormalities, elevated troponin levels, or have severe stable angina, coronary arteriography is taken into consideration for revascularization. It assists in identifying candidates who would benefit from immediate coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI).⁵²

MANAGEMENT STRATEGIES OF ACUTE CORONARY SYNDROME:

Due to the significant risk of death or repeated myocardial ischemia, all suspected ACS patients should be admitted to hospitals immediately. Early medical intervention can at least 60% lessen problems. The in-hospital management should take place in a cardiac unit with the necessary training and resources. Clinical risk factor analysis, such as the GRACE score, aids in the identification of patients needing early inpatient coronary angiography and intense therapy. Patients with low risk and no issues may be mobilised on day two and released in two to three days. Low-risk patients without spontaneous angina are advised to do exercise tolerance tests around 4 weeks after an ACS to assess whether further testing is necessary. The principles of long-term management are summarized in Figure 05.⁵²

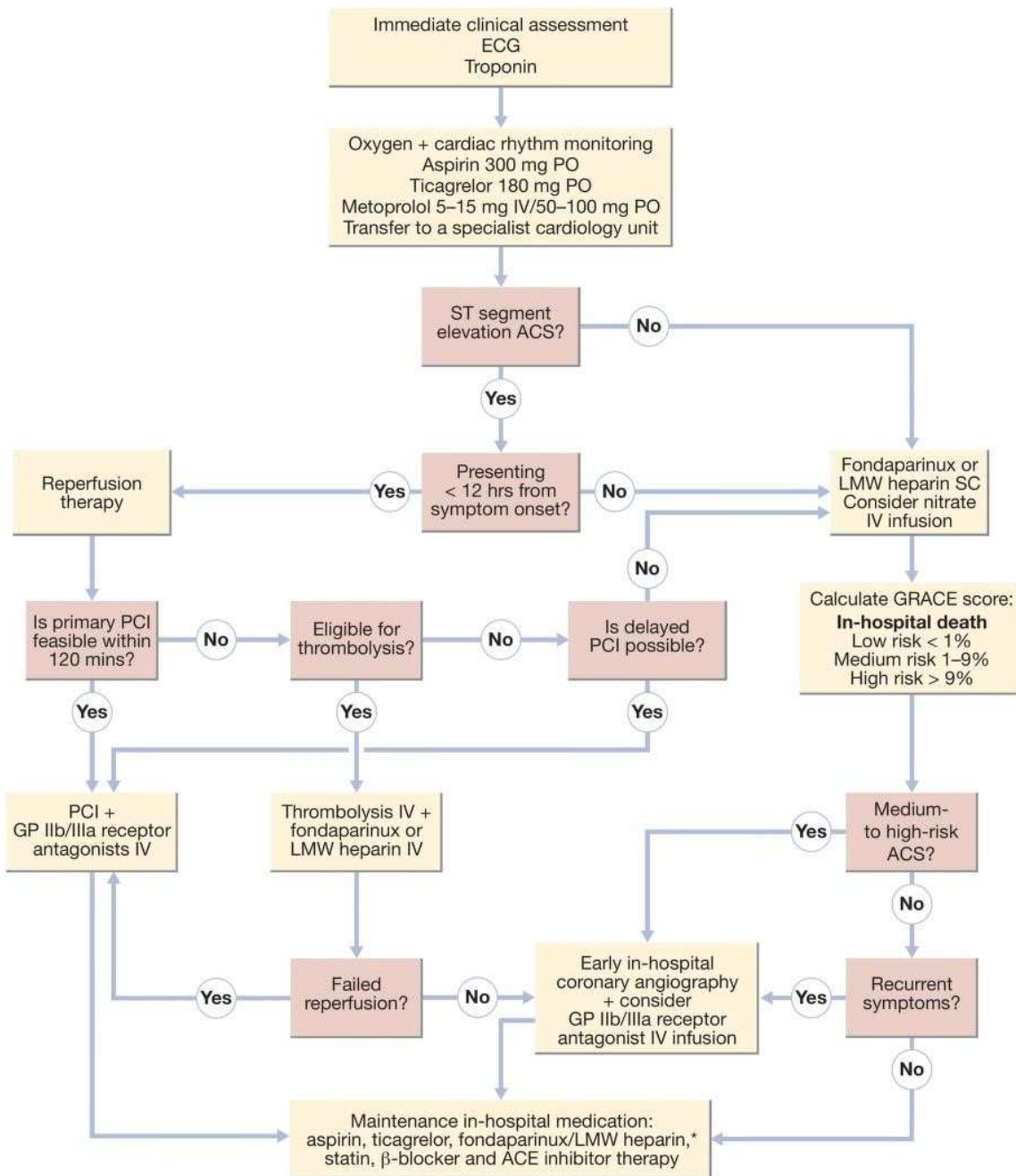


Figure 05. Summary of treatment for acute coronary syndrome (ACS). [52]

Analgesia

To minimise vascular resistance and adrenergic drive, enough analgesia is essential. Intravenous opiates should be administered first, such as morphine sulphate (5–10 mg) or diamorphine (2.5–5 mg). When necessary, take antiemetics such metoclopramide 10 mg.⁵²

Reperfusion therapy:

For particular ECG abnormalities in ACS, immediate reperfusion therapy with PCI (percutaneous coronary intervention) is advised. The best time to do PCI is within 12 hours after the onset of symptoms. PCI should still be completed as soon as possible even if timely completion is not achievable within 120 minutes. PCI within the first 24 hours may be taken into consideration, even if spontaneous reperfusion or thrombolytic treatment has already place. Rapid pain alleviation, ST elevation resolution, and decreased mortality are all associated with PCI, which has a high success rate in restoring coronary artery patency. For patients at a medium- to high-risk, coronary angiography and revascularization may be explored.⁵²

Thrombolytic therapy:

PCI can be replaced with intravenous thrombolytic treatment (TNK, rPA). It has a risk of cerebral haemorrhage but is most effective in the first 12 hours. If there is a significant danger of major bleeding, thrombolytic therapy should be avoided.⁵²

Anti-anginal therapy

In addition to beta-blockers, anti-anginal therapy for ACS also uses sublingual and injectable nitrates. For unstable angina, glyceryl trinitrate is administered sublingually. Nitrates administered intravenously reduce ischemia pain and left ventricular failure. Intravenous beta-blockers decrease arrhythmias, lessen discomfort, and increase short-term mortality.⁵²

Renin-angiotensin blockade:

Enalapril, ramipril, valsartan, and candesartan are examples of ACE inhibitors or ARBs that can block the renin-angiotensin system and benefit survival and the prevention of heart failure. These drugs lessen recurrent myocardial infarction, stop heart failure, and avoid ventricular remodelling. Patients with overt heart failure, asymptomatic left ventricular dysfunction, and retained left ventricular function benefit the most from them.⁵²

Mineralocorticoid receptor antagonists

For particular patients with acute MI and left ventricular failure (ejection fraction 35%), mineralocorticoid receptor antagonists such as eplerenone or spironolactone, notably those with pulmonary edema or diabetes mellitus, provide further benefits.⁵²

Lipid-lowering therapy

Regardless of their cholesterol levels, patients should receive statin medication after acute coronary syndrome. Patients who need more intense therapy with atorvastatin (80 mg daily) had LDL cholesterol levels above 3.2 mmol/L (about 120 mg/dL). Other lipid-lowering medications such as ezetimibe, fibrates, anion exchange resins, and injectable PCSK9 inhibitors may be tried if statins alone are insufficient.⁵²

Smoking cessation

The improvement of long-term results depends on quitting smoking. The 5-year death rate is much lower for patients who stop smoking at the time of developing acute coronary syndrome compared to those who don't. The success of smoking cessation can be increased by supportive advice and medication therapy.⁵²

Diet and exercise

Patients with acute coronary syndrome may benefit in the long run by adopting a healthy diet and regularly exercising.

It is advised to keep your weight in check, eat like the Mediterranean Diet, and control your blood pressure and diabetes well.⁵²

Rehabilitation

Recovery from ACS depends greatly on rehabilitation. For the first 4-6 weeks, limit physical activity to promote healing. On the second day, get the patient moving and progressively ramp up the activities. A four-week return to work target has been set. Long-term results are improved by emotional support, counselling, and formal rehabilitation programmes with graded exercise and counselling.⁵²

Implantable defibrillators

In patients with significant left ventricular dysfunction (ejection fraction 30%) following myocardial infarction, implantable defibrillators (ICDs) are helpful in averting sudden cardiac death. ICDs shock the heart to treat potentially fatal arrhythmias. Patients who are at a high risk of sudden cardiac death should use them.⁵²

COMPLICATIONS OF ACUTE CORONARY SYNDROME:

Arrhythmias: Arrhythmias are common in ACS, but they're frequently brief and have no real clinical impact. Arrhythmia risk can be reduced by providing appropriate pain management, getting enough rest, and treating hypokalemia. Vulnerable ventricular function and a higher

risk of sudden death, however, may be indicated by the occurrence of ventricular arrhythmias during the recovery period.⁵²

Recurrent Angina: Patients who experience recurrent angina following an acute coronary syndrome should get immediate coronary angiography to see if they can get revascularized. Treatment options include emergency coronary revascularization, intra-aortic balloon counter-pulsation, and intravenous glycoprotein IIb/IIIa receptor antagonists.⁵²

Acute Heart Failure: It is characterised by severe myocardial injury as well as a dismal prognosis. When acute heart failure is present, managing additional consequences is crucial.⁵²

Pericarditis: Develops after an infarction and is characterised by positional pain and audible pericardial rub. While NSAIDs and steroidal anti-inflammatory medications should be avoided, opiate-based analgesia is advised.⁵²

Dressler's Syndrome: Usually develops weeks or months after a myocardial infarction and is characterised by a lingering fever, pericarditis, and pleurisy. High-dose aspirin, NSAIDs, or glucocorticoids may be used as a form of treatment.⁵²

Papillary Muscle Rupture: Presents with severe mitral regurgitation, acute pulmonary edoema, and shock. Echocardiography confirms the diagnosis, and it could be required to replace the valve immediately.⁵²

Ventricular Septum Rupture: Causes abrupt right heart failure by causing left-to-right shunting through a ventricular septal defect. There needs to be an urgent surgical correction.⁵²

Ventricular Rupture: Typically, deadly condition that causes cardiac tamponade. Some situations might require emergency surgery.⁵²

Embolism: The development of thrombus on the endocardial surface might result in systemic embolism, which can result in consequences like strokes or ischemic limbs. Early mobilisation and preventative anticoagulants help lower the danger.⁵²

Ventricular Remodeling: Acute transmural myocardial infarction may have the side effect of thinned and stretched ventricular walls. Heart failure can be avoided with the aid of ACE inhibitors and mineralocorticoid receptor antagonists.⁵²

Ventricular Aneurysm: Develops in around 10% of myocardial infarction patients, especially when the infarct-related artery is persistently blocked.⁵²

PROGNOSIS:

Following acute coronary syndrome survival, the prognosis is influenced by variables such as persistent ischemia, the degree of damage, and the existence of arrhythmias. Given that a major portion of fatalities happen within minutes or during the first 24 hours, immediate medical attention is essential. Compared to myocardial infarction, unstable angina normally has a lower fatality rate. Poor left ventricular performance, an AV block, and persistent arrhythmias are a few factors that have an impact on long-term outcomes. In comparison to inferior infarcts, the prognosis for anterior infarcts is typically worse. Death rates are higher when a person is older, depressed, and socially isolated. After surviving an attack, about 80% of patients live for at least one year, with survival statistics eroding over time. Mortality and recurrent cardiovascular events are rather common in young patients with ACS, and poor prognostic indicators include hypertension, LAD disease, and coronary intervention without stenting. Early risk factor-targeting and compliance-improving therapies, especially in hypertensive patients, may improve prognosis.^{52, 54}

CONCLUSION:

In conclusion, acute coronary syndrome (ACS) is a serious symptom of coronary artery disease (CAD) and a major global health concern. This article has given a thorough review of ACS, including information on its categorization, risk factors, diagnosis, and management techniques. It emphasises the significance of lifestyle changes including quitting smoking,

adopting a nutritious diet, exercising frequently, and managing risk factors like high blood pressure and high cholesterol. For rapid risk stratification and effective care, an early and accurate diagnosis using a combination of clinical assessment, electrocardiography (ECG), and cardiac biomarkers is essential. Reperfusion therapy, anti-anginal drugs, and dietary changes are available as forms of treatment. To further enhance results and lessen the burden of ACS, further research and innovations are required. For early diagnosis and prevention of this potentially fatal disorder, increasing awareness of ACS among medical professionals and the general public is crucial. With perseverance, we can enhance care, lessen the effects of ACS, and save lives.

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Lion's Mane Mushroom- From Culinary to Medicine

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Abstract: Lion's Mane, a distinctive mushroom found across the Northern Hemisphere, has captivated the world with its unique appearance and potential health benefits. This article explores the diverse facets of Lion's Mane, from its taxonomy and habitat to its rich nutritional composition, including proteins, carbohydrates, fats, vitamins, minerals, and an array of biologically active compounds, notably polysaccharides and phenolic compounds. Lion's Mane is emerging as a potent dietary supplement, with research highlighting its positive impact on brain health, nerve recovery, mood stabilization, gastric health, heart health, blood sugar regulation, cancer prevention, and immunity enhancement. While Lion's Mane offers promising health benefits, it is essential to recognize its role as a complementary dietary addition rather than a substitute for medical treatments. Fortunately, Lion's Mane is generally considered safe for prolonged consumption, with minimal reported side effects. As research continues to unveil the multifaceted potential of Lion's Mane, it stands as a fascinating and versatile natural resource with the promise of contributing to improved well-being and longevity.

Keywords: lion's mane, polyphenols, polysaccharides, medicine uses, nutraceuticals

Introduction

Mushrooms are delicate, beautiful and provided humans with one of the first antibiotics, penicillin. Some are toxic, and most are consumable. Yet, they are wonderful in the way that they have their kingdom. They are neither plant nor animal – they are entirely different beings. The whole body of the mushroom, together with fruit (mushroom) and root (mycelium), is called **fungi**. So, yes, all mushrooms are essentially fungi residing in their distinct class. Fungi emerged as separate unicellular organisms in the Precambrian period (from 4.6 billion to 541 million years ago)[1]. So, mushrooms are distant relatives of humans in some ways. However, they continued their distinct journey of evolution in the Cambrian period.

Humans have consumed mushrooms since they were hunters and gatherers. They learned about their nourishing properties, realized their medicinal value. People also knew that some could be used for recreation, while other mushrooms are toxic. Despite such an old relationship with mushrooms, we are just starting to explore their health benefits fully. In fact, the situation is so absurd that experts are even unsure of how many species of fungi are there in the world. Though estimates vary, but researchers think that there are few million species of fungi. It also means that there are few thousand types of edible and medicinal mushrooms that are widely used[2]. This article explores one such mushroom that is both edible and has many health effects. It is nutritious, and can be source of remedies.

Lion's Mane, a mushroom of many names

Lion's Mane (also called “bearded tooth”) grows in most parts of the Northern Hemisphere, except in tropical or arctic regions. Thus, it has a different name in each language. It is commonly called Lion's Mane due to its appearance. It is called *Hericium Erinaceus* in Latin. “Shishigashira” or “Houtou” in China, and the Japanese call it “Yamabushitake”[3].

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Although it is present in most of Europe, it is among the rare mushrooms in the wilderness. It is more common in North America, China, and Japan. It has a long history of use in traditional medicine in China. China is also among the leading growers of mushrooms globally[4].

Those looking to find these fungi in a natural environment should be careful. It has a protected status in many European nations. Its picking is prohibited in England and Wales[5].

Fungi can be big and small

All fungi are made up of a thread-like filament called hyphae. However, these hyphae combine in different ways to produce so many different fungi. Fungi are further divided into lower fungi (smaller in size) and higher fungi (larger in size). Higher fungi can grow in large as their filament or hyphae are divided into multiple compartments with the help of a wall-like structure called septa[1].

Lion's Mane is a higher fungus or macro-fungi. There are known 14000 species of higher fungi, and out of them, 350 are consumed by humans[6].

Lion's Mane grows mainly on dead and decaying trees

Experts would call it a saprophyte, a kind of mushroom that grows on dead and decaying trees. However, in rare cases, it may be parasitic and grow on living trees[7]. It mostly grows on dying deciduous trees. In some countries like China, people also cultivate it.

It propagates in nature through spores. Its spores are pretty resistant to various climatic conditions and can survive for up to 7 years.

It appears to love warmth, but not heat. It **grows pretty well in temperatures of 25 to 30°C**. It may also grow well in lower temperatures like 20°C, but not in freezing conditions. Its sporulation stops at temperatures between 31-33°C. It explains why it is mainly found in Europe in later summer or Autumn. But, it cannot grow in tropical or sub-tropical regions. Moreover, it does not appear to like very high humidity[7].

Lion's mane constituents

Mushrooms are the best example of food as a medicine. Various varieties of mushrooms are consumed as a food, including Lion's Mane. However, people are significantly more interested in its various biologically active compounds as they are responsible for its numerous health benefits[7-9].

Composition of Lion's Mane:

- 20-22% proteins
- 57-67% carbohydrates
- 2.8-3.5% fats
- Numerous vitamins (like tocopherols) and minerals (trace elements)
- Biologically active compounds

Lion's Mane is definitely quite nutritious and can be an excellent source of proteins for vegans. However, people are more interested in the content of biologically active compounds that confer health benefits.

Most of the compounds responsible for health benefits are polysaccharides (complex carbs) and phenolic compounds. Researchers are particularly interested in polysaccharides other than glucose: ribose, arabinose, xylose, galactose, and mannose. Polysaccharides like

xylans, galactoxyloglucans, heteroxyloglucans, glucoxylans, erinacines, and hericenones have numerous health benefits. However, it is vital to understand that this list is not comprehensive, as researchers have identified hundreds of bio-active compounds[7,9,10].

Some bioactive compounds and their action[7]:

Bioactive compounds	Some known health effects
Polysaccharides	Anti-inflammatory, immunomodulatory, anticancer, antimicrobial, gastroprotective, hepatoprotective, glucose-lowering, cholesterol-lowering
Hericenones A-B	Anticancer or cytotoxic, reduces platelet aggregation
Hericenones C-H, erinacines A-I	Neuroprotection, prevention of neurodegenerative disorders
Hericirine	Anti-inflammatory
Polyphenols	Antioxidants

Lion's mane health benefits

Lion's mane extract is often used as a health supplement. Researchers are studying its numerous health benefits. It is especially regarded to be good for nerve health. However, it is worth understanding that health supplements cannot claim to diagnose or treat disease conditions.

Brain health/Nootropic/Memory support

Neurodegenerative disorders like dementia are now a significant health threat in the UK. A healthy lifestyle may lower dementia's risk[11]. Adding Lion's Mane to the diet may have certain benefits. Experimental studies suggest synergistic interaction between Lion's mane extract and nerve growth factor (NGF). Lion's mane also appear to help with memory. One of the systemic reviews found that mushroom extracts like that of Lion's Mane have a positive impact on cognition[12–15].

In practice, it means that Lion's Mane is good for brain health. Its regular consumption may be one of the ways of lowering cognitive decline. However, it is not a treatment for brain diseases.

Accelerate recovery from nerve injury

Lion's Mane is also proposed to be good for nerve health. Peripheral nerves may get damaged due to physical injury, toxins, anticancer treatment, or more commonly, diabetes. In experimental studies, Lion's mane extract appears to promote nerve recovery and growth. Thus, it may have a role as a health supplement in preventing neuropathies[13,16,17].

It helps counter mild anxiety and depression

Chronic ingestion of Lion's mane extract promotes nerve growth and modulates the activity of certain neurohormones. Thus, it may exert a mood-stabilizing effect, help prevent anxiety, lower the risk of depression. It may help on regular use for 4 weeks or more. Thus, it may be used as one of the ways of preventing mood disorders. However, it should not be used as a monotherapy for the treatment of severe mood disorders[18–20].

Gastric health

Traditional Chinese medicine regards Lion's Mane as good for gastric health. Modern experimental studies show that it may help prevent damage to gastric cells caused by ethanol. It also suppresses the activity of H. Pylori, a bacteria frequently responsible for gastric ulcers. Thus, regular use of Lion's Mane may help prevent gastric issues[21–23].

Heart health and cholesterol control

Mushrooms are naturally low in fats and do not contribute to hypercholesteremia. Additionally, certain mushrooms like Lion's Mane have compounds that suppress lipid oxidation and exert an antihyperlipidemic effect. Thus, Lion's Mane is regarded as good for cardiovascular health[24,25].

Lower blood sugar levels

Mushrooms can be safely consumed by those living with diabetes, as they are low in glycemic index. Additionally, some mushrooms like Lion's Mane contain compounds that may help lower the risk of metabolic disorders. For example, lion's Mane appears to exert an inhibitory effect on α -amylase and α -glucosidase, thus helping keep blood glucose levels in check[26,27].

Cancer prevention

A balanced diet and the right lifestyle choices may lower cancer risk. Polysaccharides and aromatic compounds in Lion's Mane show anticancer properties in lab studies. Researchers have identified numerous mechanisms of action. Lion's mane extract may suppress the growth of various cancer cells like lung cancer, breast cancer. Researchers are exploring its role as an adjuvant in cancer management[28–30].

Potential Immunity enhancer

Polysaccharides, hericirine, polyphenols, and other compounds in Lion's Mane help suppress inflammation, exert an antioxidant effect, and modulate immune responses. Thus, its prolonged use may help support the immune system[31–33].

Safety and toxicity

Lion's Mane is relatively safe for prolonged use. Quite like other herbal extracts, it may sporadically cause gastrointestinal issues or allergies. Toxicological studies could not identify any severe side effects of the mushroom and concluded it safe for prolonged use[34]. However, there is still a need for more studies regarding its safety. Like most mushrooms, data is limited. Nevertheless, most preliminary data is highly encouraging.

Conclusion

In conclusion, Lion's Mane, a mushroom known by many names across different regions, holds a special place in the world of fungi. Its unique appearance and widespread distribution, especially in North America, China, and Japan, have earned it recognition not only for its culinary uses but also for its potential health benefits. As a member of the higher fungi category, Lion's Mane is just one among thousands of fungal species. Yet, it stands out due to its remarkable constituents, including proteins, carbohydrates, fats, vitamins, minerals, and a plethora of biologically active compounds. These compounds, notably polysaccharides and phenolic compounds, have garnered significant attention for their potential health-promoting effects.

Lion's Mane offers a range of health benefits, from supporting brain health and memory to aiding in nerve recovery and growth. It may also contribute to mood stabilization, gastric health, heart health, cholesterol control, and blood sugar regulation. Moreover, ongoing research suggests its potential role in cancer prevention and immunity enhancement. While Lion's Mane extract is commonly used as a health supplement, it's important to emphasize that it cannot replace medical treatments for diseases. It should be seen as a complementary dietary addition to promote overall well-being.

Fortunately, Lion's Mane is generally considered safe for extended consumption, with few reported side effects. Like any dietary supplement, some individuals may experience mild gastrointestinal issues or allergies, but toxicological studies have not revealed any significant concerns. Intriguing and versatile, Lion's Mane continues to captivate researchers and health enthusiasts alike, offering a promising avenue for natural health support. As our understanding of this remarkable mushroom deepens, it may become an even more valuable addition to our quest for improved well-being and longevity.

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