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PREFACE

Clinical laboratories have long been at the core of medical decision-making, supporting diagnosis, prognosis, and treatment monitoring. However, in recent years, the nature of laboratory data has changed significantly. It is no longer limited to a few routine parameters; instead, clinicians are now faced with increasingly large and complex datasets, ranging from standard hemogram results to advanced molecular and omics-based analyses. Overall, the integration of artificial intelligence into laboratory medicine does not simply represent a technological shift; it reflects a broader transformation in how clinical data are interpreted. In this book chapter, the contribution of artificial intelligence to the analysis of laboratory data and biomarker discovery has been examined from both clinical and molecular perspectives.

Workplace accidents are a crucial issue, both for the individual and their families, as well as for the national economy and industries in general. Because health is a fundamental constitutional right of individuals and is also classified as a global public good, the problems, injuries, and deaths resulting from workplace accidents are a public matter, affecting not only the workplace and its employees but also society as a whole. In this context, this book chapter discusses how artificial intelligence systems can be utilized in the field of occupational health and safety and addresses the impact of sectoral differences on their implementation.

Pernicious anemia is a relatively rare autoimmune disorder characterized by impaired absorption of dietary vitamin B12, leading to vitamin B12 deficiency and, subsequently, megaloblastic anemia.

This book chapter provides a comprehensive overview of the etiology, epidemiology, pathophysiology, clinical manifestations, diagnosis, and treatment of pernicious anemia.

Prof. Dr. ALİ BİLGİLİ

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CONTENTS

CHAPTER 1

THE USE OF ARTIFICIAL INTELLIGENCE APPLICATIONS ON WORK ACCIDENTS AND THE IMPACT OF SECTOR DIFFERENCES

1. AHMET TAŞDELEN [1], MELEK HATİBOĞLU[2]

1. Introduction

Workplace accidents are a crucial issue, both for the individual and their families, as well as for the national economy and industries in general. Because health is a fundamental constitutional right of individuals and is also classified as a global public good, the problems, injuries, and deaths resulting from workplace accidents are a public matter, affecting not only the workplace and its employees but also society as a whole.

Occupational health and safety is defined as systematic work carried out to eliminate hazards that may arise when performing work in the workplace and to ensure more favorable

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working conditions in the workplace by eliminating conditions that may cause harm to health (Olcay, 2019).

In recent years, the importance of occupational health and safety has increased, as it aims to reduce human and financial losses caused by unsafe behavior in enterprises, leading to industrial accidents. In this regard, enterprises have begun to prioritize the development of occupational health and safety management systems to enhance the level of occupational safety (Tüzüner and Özarslan, 2011).

While occupational health and safety are crucial for employees, employers, the economy, production, and all systems, it can be argued that there are still significant shortcomings today. While potentially preventable, accidents involving injuries and deaths remain unprevented, resulting in serious problems. This is due to inadequate precautions, lack of inspections, and lack of emergency response. In this regard, artificial intelligence systems can yield significant and effective results by facilitating faster and more effective interventions, implementing emergency measures, and enhancing inspections. Therefore, this section aims to demonstrate how artificial intelligence systems are used in the field of occupational health and safety and to demonstrate the impact of sectoral differences.

2. Occupational safety

Occupational safety is defined as the protection, improvement, and maintenance of the physical, mental, and social well-being of workers in all professions at the highest level, as well as ensuring harmony between work and the individual and the worker. Occupational safety, in turn, refers to a set of measures necessary to create a safe working environment and prevent accidents in production related to activities aimed at ensuring livelihoods (Solmaz and Solmaz, 2017).

The purpose of occupational health and safety measures is to protect employees from accidents and illnesses at work and to create a healthier working environment. However, two other factors must be taken into account: increasing productivity through production safety and ensuring operational safety (Özkılıç, 2005).

The first legal studies and regulations concerning the principle of protecting workers from industrial accidents and occupational diseases appeared at the end of the 19th century. The adoption of separate regulations concerning industrial accidents and occupational diseases, before and independently of the adoption of laws on social insurance, was due to the seriousness and scale of the social significance of this problem. The working class that emerged as a result of the industrial revolution began to pay for the social prosperity that arose and developed along with it. Realizing the incompatibility of this situation with social justice, legal acts regulating industrial accidents and occupational diseases were adopted (Çiçek and Öçal, 2016).

Ensuring safety in the workplace is especially important from an economic point of view, as it contributes to increased productivity. Protecting workers in the workplace will reduce the loss of labor and working days due to occupational diseases and accidents, thereby protecting production and increasing productivity due to the safety and security that a healthier and safer work environment provides (Horozoğlu, 2017).

The concept of occupational health and safety encompasses not only hazard prevention but also risk prediction, assessment, and efforts to eliminate or minimize risks. Occupational health and safety is a broad concept that covers the prediction of potential hazards and risks in a company before a hazard or malfunction occurs, as well as determining their acceptability (Tozkoparan and Taşoğlu, 2011).

3. Artificial Intelligence

The concept of artificial intelligence was first formulated in a proposal presented by John McCarthy, Marvin L. Minsky, Nathaniel Rochester, and Claude E. Shannon at the Dortmund Conference in 1956. However, John McCarthy is considered the inventor of the concept. It is the computational component of the ability to achieve goals in the world. Intelligence of varying types and degrees is observed in humans, many animals, and some machines (Arslan, 2020).

Ardent opponents of artificial intelligence argue that machines are inherently different from humans, claiming that they are incapable of experiencing love, unable to distinguish between right and wrong using common sense, and unable to think like humans. However, proponents of artificial intelligence argue that the same phenomenon can be applied to machines, arguing that the human brain is made up of unconscious components that are incapable of independent thought, but when combined, become thoughtful and conscious (Pirim, 2006).

Artificial intelligence is defined as the science and engineering of creating human-like intelligent machines, brilliant computer programs. This definition can be expanded as follows: Accordingly, artificial intelligence can be defined as a computer that exhibits human-like behavior such as reasoning, problem solving, inference, and generalization, i.e., using higher-order cognitive skills (Arslan, 2020).

Artificial intelligence has become a field of science and technology that creates intelligent machines, particularly intelligent computer programs. The main goal is to develop algorithms that will give computers the characteristics of human intelligence and to create systems that can solve problems by demonstrating intelligent behavior similar to humans. From a realistic and scientific point of view, artificial intelligence is an approach that can learn from experience, draw conclusions based on the acquired knowledge, recognize shapes, images, and patterns, generate solutions to complex problems, understand language and operate with words, and offer a new perspective on the world of computing (Öztemel, 2020).

While definitions of artificial intelligence vary, a common thread is that AI is a meta-evaluation model that combines information and digital systems. This structure allows for complex operations involving big data to be performed much more quickly with computer systems.

4. The Use of Artificial Intelligence in Workplace Accidents and the Effect of Sector Differences

Technological advances and changes have increased the need for skilled labor. As a result, the value of humans has increased, and labor protection, an interdisciplinary science, has now become an independent branch of science. The goal of labor protection is to identify and implement methods necessary for their prevention, the causes and consequences of accidents and occupational diseases, as well as strategies for their prevention (Ceylan, 2012).

Recently, the need to take preventive measures to prevent industrial accidents and occupational diseases has been recognized, and regulations have been adopted in the field of labor protection and safety. The need to adapt workers' working conditions to changes in society caused by industrialization and technological progress has become obvious. It should be emphasized that to ensure a safer and more reliable working environment, it is necessary to establish specific safety regulations and train workers to comply with them (Ateş 2020).

Labor protection refers to the work required to identify existing or external hazards in the workplace, analyse and rank the factors that convert these hazards into risks, as well as the risks arising from these hazards, and determine control measures. Risk assessment involves assessing the risks arising from hazards, considering the adequacy of existing measures, and determining whether these risks are at an acceptable level (Akpınar and Çakmakkaya, 2014).

The main goal of labor protection is to create a healthier and safer working environment for employees based on scientific data. Since labor protection is directly dependent on technical progress, it requires dynamic innovations that accompany new technological advances (Ceylan, 2012).

Occupational health and safety conditions vary significantly across social groups, economic sectors, and countries. In developing countries, where a large proportion of the population is engaged in hazardous work such as agriculture, mining, and fishing, deaths and injuries are more common. Moreover, women, children, and migrant workers, the poorest and most vulnerable members of the global workforce, are among the social groups most affected by occupational accidents and diseases (Kılkış and Demir, 2012).

Although the development of AI applications in the world is still relatively new, it is already leading to the emergence of new products in many areas. This indicates that computers and machines capable of achieving human intelligence levels may become a significant part of people's daily lives in the coming years. It can be said that AI technologies are already being used today not only in many areas but are also beginning to have an impact on education (İşler and Kılıç, 2021).

In the healthcare services sector, all modern healthcare areas, including medical healthcare, digital healthcare, and mobile healthcare, intersect with artificial intelligence. AI-based solutions are evident in mobile healthcare, such as voice control systems, and in the medical field, in applications such as diagnostics and prognosis. AI-based applications form the basis of almost all digital healthcare services (Akalın and Veranyurt, 2020).

Developments show that AI systems are making significant progress in diagnosing and treating human diseases. This can help healthcare workers in monitoring diseases and save time for early diagnosis and treatment of many diseases. Although the use of AI-based monitoring tools for surveillance and monitoring of enterprises to detect abnormal situations in the workplace has not been widely adopted, the number of users and capabilities of these tools are growing daily. Tracking and monitoring systems integrated with AI into existing enterprise cameras will play a crucial role in emergency response and early intervention by providing instant data (Ayan et al, 2024).

Artificial intelligence technologies and expert systems, which currently have a global transformative and diversifying impact on economic, social, and life-threatening aspects, will continue to evolve in the future. These changes and transformations will also affect the field of occupational health and safety (Akduman and Yılmaz, 2024).

The socio-economic consequences of the use of artificial intelligence technologies and expert systems in the field of occupational health and safety for our society can be explained by the increase in unemployment, the transfer of skilled employees to other companies, internal migration and, from an economic point of view, sectoral shifts in income levels and employment opportunities in our country. It is expected that such negative situations may arise and affect the production, cost price, sales, and other indicators of various professions and their divisions at the institutional or corporate level (Şenöz and Bozkurt, 2025).

Overall, the results demonstrate that AI applications can address many gaps and address serious issues, particularly in the field of occupational health and safety. Therefore, AI may be able to effectively address the challenges faced in occupational health and safety practices across various sectors.

Conclusion

Accidents at work are a serious problem for the worker and their family, as well as for the economy and businesses as a whole. The issues, injuries, and fatalities brought on by workplace accidents are public matters that impact not only the workplace and its employees but also society at large, since health is a fundamental constitutional right of individuals and is also categorized as a global public benefit.

It may be argued that there are still serious issues with occupational health and safety, despite its essential nature for workers, employers, the economy, production, and all systems. Even when incidents that cause injuries and fatalities can be avoided, they still occur, leading to major issues. This is largely due to insufficient emergency response, inspections, and measures. By enabling quicker and more efficient interventions, implementing emergency plans, and improving inspections, artificial intelligence systems can produce noteworthy and useful outcomes in this area.

The current literature and developments show that AI applications, especially in the area of occupational health and safety, can fill a lot of gaps and deal with essential problems. Consequently, AI might be able to successfully handle the difficulties encountered in occupational health and safety procedures in a variety of industries. To achieve more effective results in occupational health and safety and ensure individuals' rights to both life and health, it is necessary to support research in this area. Artificial intelligence applications, in a sense, allow for statistical and contextual analysis and inferences from the concept of big data. Therefore, this issue should be addressed in future studies.

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CHAPTER 2

ARTIFICIAL INTELLIGENCE IN LABORATORY MEDICINE AND BIOCHEMISTRY

MERVE KILIÇ[1]

Introduction

Clinical laboratories have long been at the core of medical decision-making, supporting diagnosis, prognosis, and treatment monitoring. However, in recent years, the nature of laboratory data has changed significantly. It is no longer limited to a few routine parameters; instead, clinicians are now faced with increasingly large and complex datasets, ranging from standard hemogram results to advanced molecular and omics-based analyses.

This rapid expansion in both the volume and diversity of data has made traditional interpretation approaches less sufficient in certain contexts. While classical statistical methods remain valuable, they often fall short when it comes to capturing complex, multidimensional relationships. In this regard, artificial intelligence (AI), particularly machine learning techniques, has emerged as a powerful complementary approach for handling large-scale biomedical data (Topol, 2019:44).

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One of the most important contributions of AI lies in its ability to reveal patterns that may not be immediately apparent through conventional evaluation. Routine laboratory parameters—such as hemogram indices or biochemical markers—may contain subtle relationships that are difficult to recognize when assessed individually. When analyzed collectively through AI-based models, however, these parameters can provide deeper clinical insights, particularly in conditions such as anemia, infections, and metabolic disorders (Rajkomar et al., 2019:1347).

At the same time, the increasing use of high-throughput technologies has introduced new challenges. Omics data, including genomics, proteomics, and metabolomics, offer valuable information at the molecular level but are inherently complex and difficult to interpret using traditional approaches alone. AI provides a framework that allows these multilayered datasets to be analyzed in a more integrated manner, facilitating the identification of novel biomarkers. In this context, molecules such as microRNAs (miRNAs) and zinc protoporphyrin (ZnPP) have attracted attention due to their potential clinical relevance (Libbrecht & Noble, 2015:321).

Overall, the integration of AI into laboratory medicine does not simply represent a technological shift; it reflects a broader transformation in how clinical data are interpreted. The following sections explore how AI contributes to laboratory data analysis and biomarker discovery from both clinical and molecular perspectives.

Analysis of Clinical Laboratory Data

The evaluation of clinical laboratory data has traditionally relied on the interpretation of individual test results. However, this approach may not fully reflect the complexity of biological systems, where multiple parameters interact simultaneously. For this reason, there has been a growing shift toward multivariate analysis strategies that consider laboratory findings as part of an interconnected system rather than isolated values.

AI-based approaches are particularly useful in this context. Instead of focusing on linear relationships, machine learning algorithms are capable of modeling more complex interactions within the data. Supervised learning methods—such as logistic regression, support vector machines, and random forest models—are frequently used to establish associations between laboratory parameters and disease outcomes. These models can assist in classification and prediction tasks, often with a level of accuracy that exceeds traditional methods (Beam & Kohane, 2018:1317).

In addition to supervised methods, unsupervised techniques also play an important role. Clustering algorithms, for example, can identify patient subgroups that may not be obvious through routine clinical assessment. This can be particularly valuable in heterogeneous conditions where patients with similar laboratory values may have different underlying pathophysiological processes.

Another area where AI has shown promise is the analysis of temporal data. In clinical practice, laboratory parameters are rarely static; they change over time, especially in critically ill patients or those with chronic diseases. By analyzing these temporal patterns, AI models—particularly those based on deep learning—can contribute to the development of early warning systems and help anticipate clinical deterioration (Esteva et al., 2019:24).

It is also important to note that laboratory data are not always ideal. Missing values, measurement variability, and outliers are common challenges. AI-based preprocessing techniques, including data imputation and normalization, can help address these issues and improve the reliability of predictive models.

Taken together, these approaches suggest that AI is not merely a tool for analyzing laboratory data but also a means of enhancing how such data are understood and utilized in clinical practice.

Interpretation of Hemogram and Biochemical Parameters

Hemogram and biochemical parameters remain among the most frequently used tools in everyday clinical practice. Despite their routine nature, their interpretation is not always straightforward. While reference ranges provide a useful framework, they do not fully account for inter-individual variability or the complex interplay between different physiological processes.

In this respect, AI introduces a more integrative perspective. Rather than evaluating parameters in isolation, AI-based models consider them collectively, allowing for a more nuanced interpretation. For example, hematological indices such as hemoglobin, hematocrit, mean corpuscular volume, and red cell distribution width can be analyzed alongside biochemical markers like ferritin, transferrin saturation, C-reactive protein, and albumin. When interpreted together, these parameters can provide a clearer picture of conditions such as anemia and inflammation (Johnson et al., 2018:2668).

One of the key advantages of AI is its ability to detect subtle differences that may not be easily recognized through conventional methods. This is particularly relevant in cases where clinical findings overlap, such as distinguishing iron deficiency anemia from anemia of chronic disease. Machine learning algorithms can identify patterns across multiple variables, improving diagnostic accuracy.

Similarly, certain parameters may have broader clinical implications than traditionally assumed. For instance, red cell distribution width has been associated not only with anemia but also with systemic inflammation and cardiovascular risk (Patel et al., 2009:515). AI-based models can help uncover such extended relationships.

In the context of biochemical parameters, AI also offers potential for early disease detection. Routine markers—such as glucose levels, lipid profiles, liver enzymes, and renal function indicators—can be used to develop predictive models for metabolic and systemic diseases.

Despite these advantages, it is important to approach AI-based interpretations with caution. Data quality, model transparency, and clinical context all play a critical role. AI should therefore be viewed as a supportive tool that complements, rather than replaces, clinical judgment.

AI-Based Evaluation of Anemia, Infectious, and Metabolic Diseases

The application of AI in disease evaluation has expanded rapidly, particularly for conditions characterized by complex and multifactorial mechanisms. Anemia, infectious diseases, and metabolic disorders are among the areas where AI has shown considerable potential.

In anemia, one of the main challenges lies in distinguishing between subtypes that present with similar laboratory findings. Traditional markers may be influenced by inflammation or comorbid conditions, making interpretation more difficult. AI models can integrate multiple parameters—including hematological indices and iron metabolism markers—to improve classification accuracy (Kourou et al., 2015:8).

Recent attention has also focused on the role of molecular biomarkers. Among these, miRNA-210 has emerged as a particularly interesting candidate. In the study conducted by Kılıç et al. in hemodialysis patients, miRNA-210 expression was found to be significantly higher in individuals with iron deficiency anemia and showed a negative correlation with hemoglobin levels. Furthermore, ROC analysis suggested that this molecule may help differentiate between anemia subtypes. These findings indicate that combining molecular data with AI-based models could enhance diagnostic precision (Kılıç et al., 2026:1).

In infectious diseases, AI has been widely explored for early detection, especially in critical conditions such as sepsis. By integrating laboratory markers—including procalcitonin, CRP, and leukocyte counts—AI models can identify early inflammatory responses and support timely clinical interventions (Shashikumar et al., 2017:739).

For metabolic diseases, AI contributes to risk prediction and early diagnosis. By analyzing parameters related to glucose metabolism, lipid profiles, and inflammation, predictive models can identify individuals at risk even before clinical symptoms develop. Studies using deep learning approaches have demonstrated promising results, particularly when longitudinal data are available (Choi et al., 2017:361).

Overall, AI provides a framework that allows complex clinical data to be interpreted in a more comprehensive and clinically meaningful way.

Omics Data and Biomarker Discovery: AI-Based Approaches

The growing availability of omics data has significantly expanded the scope of biomedical research. Genomic, proteomic, and metabolomic datasets offer detailed insights into disease mechanisms but also introduce considerable analytical challenges due to their size and complexity.

AI has become an essential tool in addressing these challenges. By enabling the integration of multiple data layers, AI facilitates a more holistic understanding of biological systems. Instead of focusing on a single biomarker, researchers can now evaluate networks of interactions across different molecular levels (Hasin et al., 2017:83).

This approach is particularly valuable in biomarker discovery. AI techniques—such as feature selection and dimensionality reduction—allow researchers to identify relevant signals within high-dimensional datasets. This is especially important for regulatory molecules like microRNAs.

Among these, miRNA-210 stands out due to its role in hypoxia and iron metabolism. As demonstrated by Kılıç et al. (2026), its expression patterns may provide clinically meaningful information in anemia. When combined with biochemical parameters and analyzed through AI-based models, such markers may contribute to the development of more robust diagnostic tools.

In addition, integrating parameters such as ZnPP and erythrocyte membrane fatty acids further enhances the potential for multidimensional biomarker panels. These combined approaches may ultimately lead to more precise disease classification and improved clinical outcomes.

Conclusion and Future Perspectives

The integration of artificial intelligence into laboratory medicine and biochemistry represents more than just the adoption of a new technological tool. In recent years, the increasing volume and diversity of clinical data have made it clear that traditional interpretation methods may not always be sufficient. Within this context, AI offers a more comprehensive perspective, allowing clinicians to evaluate data in a multidimensional manner.

The examples discussed in this section illustrate that AI is not limited to analyzing existing laboratory results; it also has the capacity to uncover hidden relationships and generate clinically meaningful insights. The inclusion of molecular-level data, alongside conventional laboratory parameters, has opened new possibilities for improving diagnostic accuracy. In particular, miRNA-210, due to its involvement in hypoxia and iron metabolism, appears to be a promising biomarker that complements rather than replaces traditional indicators in anemia evaluation.

Looking ahead, it is highly likely that AI-based systems will become more widely integrated into clinical practice. However, the key challenge lies not only in improving algorithmic performance but also in ensuring that these systems are reliable and applicable in real-world clinical settings. Issues such as data standardization, cross-population validity, and model interpretability will play a critical role in this process.

At the same time, the idea that artificial intelligence will replace physicians does not fully reflect the current scientific perspective. A more realistic approach is to consider AI as a supportive tool within clinical decision-making processes. The combination of clinical expertise and data-driven insights has the potential to enhance patient care in a balanced and effective way.

In conclusion, the convergence of artificial intelligence and omics technologies marks the beginning of a new era in laboratory medicine. The integration of molecular biomarkers—particularly miRNA-210—into AI-based frameworks is expected to contribute significantly to the development of more sensitive and personalized diagnostic strategies in the future.

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CHAPTER 3

PERNİSİYÖZ ANEMİ

Ayşegül ŞAHİN[1]

Giriş

Pernisiyöz anemi (PA), besinlerle alınan vitamin B12 (kobalamin) emiliminin azalmasına, sonuç olarak B12 eksikliğine ve ardından megaloblastik anemiye neden olan, nispeten nadir görülen otoimmün bir hastalıktır (Vaqar ve Shackelford, 2023). Ağırlıklı olarak mide fundusunu tutan otoimmün atrofik gastrit ile ilişkilidir (Andres ve Serraj, 2012a). Özellikle otoimmün atrofik gastrit' in ileri aşamalarında gastrik intrinsik faktör (IF) eksikliği ve buna bağlı B12 vitamini eksikliği ortaya çıkabilir ve PA meydana gelebilmektedir (Esposito ve ark., 2022).

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Etiyoloji

PA’ da görülen anemi megaloblastik olup, IF eksikliğine bağlı B12 vitamin eksikliğinden kaynaklanır (Htut, Thein ve Oo, 2021). IF mide de parietal hücreler tarafından üretilir ve salgılanır. Bununla beraber IF, vit B12' ye bağlanarak emilim için terminal ileuma taşınmasını kolaylaştıran bir glikoproteindir. Pernisiyöz anemi, otoimmün atrofik gastrit hastalarının %25' inde görülmektedir (Vaqar ve Shackelford, 2023). Ek olarak Tip 1 diyabet, otoimmün tiroid hastalığı ve vitiligo gibi otoimmün bozuklukların PA ile birlikte görülme sıklığı da daha yüksektir (Vaqar ve Shackelford, 2023).

Epidemiyoloji

Otoimmün atrofik gastrit; mide antrumunun korunduğu, korpusu ve fundusu etkileyen, IF ve hidroklorik asit üreten parietal hücreleri yok eden antiparietal hücre antikorlarıyla karakterize bir hastalıktır. Bu nedenle otoimmün atrofik gastrik hastalarında hem IF hem de gastrik asit üretiminde bir düşme meydana gelir. Bu ortam diyet proteinlerinden B12 vitamini salınımını bozar ve ileumda IF aracılı vitamin emilimini azaltır (Kim, Punzalan ve Carlson, 2025).

PA, dünya genelinde her yaştan insanı etkileyebilmekte olup, özellikle 60 yaş üstü bireylerde görülmektedir (Vaqar ve Shackelford, 2023). Yetişkin bireylerde B12 vitamini eksikliğinin nedenlerinin %20-50' sinin PA’ nın oluşturduğu bilinmektedir (Andres ve Serraj, 2012a).

Yapılan çalışmalar PA' nın genel nüfusun % 0,1' ini ve >65 yaş grubundaki kişilerin %2-3' ünü etkilediğini göstermiştir (kadın:erkek oranı ~2:1) (Esposito ve ark., 2022). PA genel olarak Kuzey Avrupa kökenli yaşlı kadınlarla ilişkilendirilmesine rağmen, yapılan daha yeni çalışmalar Afrika, Beyaz ve Amerikan grupları dahil olmak üzere çeşitli etnik popülasyonlarda da mevcut olduğunu göstermektedir (Esposito ve ark., 2022).

Patofizyoloji

Pernisiyöz anemide ki birincil patofizyolojik mekanizma, interferon eksikliğine bağlı olarak diyetle alınan B12 emiliminin azalmasıdır. B12 vitamini et, yumurta, süt ürünlerinde bulunur ve eritropoez ve sinir miyelinizasyonu için gereklidir (Vaqar ve Shackelford, 2023). Bu nedenle B12 eksikliği, bozulmuş DNA sentezi ve demiyelinizan sinirler nedeniyle megaloblastik anemiye yol açabilir. B12 eksikliği oluşan tüm kan elemanlarında megaloblastik değişikliklere neden olur, ancak eritrositler en önemli değişiklikleri gösterir (Green, 2017).

Yapılan çalışmalarda; immünoglobulinler A, G ve M' nin yanı sıra otoreaktif T lenfositlerinin mide mukozasına siyanokobalamin bağlanma bölgelerini bloke ederek emilimini azalttığını ve bunun sonucunda peptik hücre yıkımına ve IF kaybına neden olduğunu destekleyen kanıtlar mevcuttur (García-Carrasco, Jiménez-Hernández, Rojas-Villarraga ve Ruiz-Argüelles, 2024).

Klinik Bulgular

Pernisiyöz aneminin klinik pratikte teşhisi zordur. Semptomların spesifik olmaması ve sinsi seyretmesi sebebi ile tanı geç konulabilmektedir. Hastalarda görülen en sık semptomlar devamlı yorgunluk hali, hafıza kaybı ve konsantrasyon bozukluğudur (Seage ve ve ark., 2024). Bununla beraber yapılan çalışmalar PA' nın gastrointestinal belirtiler, nörolojik ve bilişsel bozukluklar gibi geniş bir semptom yelpazisine sahip olduğunu göstermiştir

(Wolffenbuttel, Wouters, Heiner-Fokkema ve van der Klauw, 2019).

B12 vitamini eksikliğinin en yaygın ilk belirtisi, nörolojik semptomları olan hastaların %70' inde görülen parestezidir (Healton, Savage, Brust, Garrett ve Lindenbaum, 1991). Paresteziler ellerde veya her iki distal ekstremitede başlayan karıncalanma ve uyuşma şeklinde görülür. Diğer nörolojik belirtiler otonomik disfonksiyon (erektil ve mesane disfonksiyonu), görme kaybına kadar ilerleyen optik nöropati ve bunamaya kadar ilerleyen hafıza ve ruh hali tutulumudur (Esposito ve ark., 2022) . Ek olarak depresyon, mani ve psikoz gibi nöropsikiyatrik bulgularda görülebilmektedir (Dommisse, 1991).

Gastrointestinal belirtiler, PA' nın kaynaklandığı otoimmün atrofik gastrit ile ilişkili semptomları içerir. En sık görülen semptomlar, epigastrik ağrı, erken doyma, yemek sonrası şişkinlik ve dolgunluk gibi dispeptik yakınmalardır (Esposito ve ark., 2022).

PA’ nın başlıca belirtilerinden bir diğeri B12 eksikliği anemisinin neden olduğu makrositer anemi ile ilişkili hematolojik sonuçlardır. Hastalarda halsizlik, zihinsel konsantrasyonda azalma, baş ağrısı ve çarpıntı gibi anemi ile ilişkili semptomlar gösterebilir (Htut ve ark., 2021).

B12 vitamini eksikliğiyle ilişkili daha az görülen belirtiler arasında glossit, malabsorpsiyon, kısırlık ve tromboz bulunur (Kim ve ark., 2025).

Tanı

Pernisiyöz anemide makrositer ve normokrom bir anemi mevcuttur ve retikülositlerin mutlak sayısında azalma vardır. Ek olarak hipersegmente nötrofillerin olması megaloblastik anemiyi destekleyici olsa da spesifik değildir. Pansitopeni ise hastaların %5 ila %37 arasında değişen oranlarda görülür (Andrès ve ark., 2006).

Pernisiyöz anemi de iki tipte antikor tanımlanmıştır. B12 vitamininin IF' ye bağlanmasını engelleyen ve böylece B12 vitamini/IF kompleksinin oluşumunu önleyen bloke edici otoantikorlar (tip I); ve IF-vitamin B12 komplekslerine bağlanarak bağırsak mukozası tarafından emilimini engelleyen bağlayıcı otoantikorlar (tip II) (Andres ve Serraj, 2012b).

Bloke edici tipteki antikor ölçülebilen bir parametre olup, PA için oldukça spesifiktir (%100'e yakın özgüllükle) ve PA hastalarının %70'inde bulunur (Kim ve ark., 2025). Parietal hücrelere karşı antikorlar, pernisiyöz anemisi olan hastaların %90'ında bulunur, ancak basit atrofik gastrit, otoimmün tiroid hastalığı olan bireylerde ve normal popülasyonun %3-10' unda da görülebildikleri için daha az spesifiktirler (Kim ve ark., 2025).

Serum kobalamin seviyesi düşük olan bir hastada serum IF antikorlarının bulunmaması durumunda, IF çıktısının incelenmesi için gastrik tüp kullanımı bilimsel amaçlar için zorunludur. PA tanısı için "altın standart" IF salgılanmasındaki eksikliktir ve bu, sonunda yeni PCA da dahil olmak üzere serolojik belirteçler arasındaki ilişkilerin değerini değerlendirmek için kullanılmalıdır (Cattan, 2011).

Sonuç olarak PA tanısı, megaloblastik anemi, düşük serum B12 vitamini düzeyleri, gastrik atrofi ve gastrik parietal hücre veya IF' ye karşı antikorların varlığına dayanır (Ammouri ve ark., 2020). Kobalamin düzeyi açısından düşük seviyeler (<100 pg/mL) genellikle klinik eksiklikle ilişkilidir, ancak hem yanlış negatif hem de yanlış pozitif değerler yaygın olarak görülmektedir. Bunun nedeni, ölçülen toplam B12 vitamininin yalnızca %20'sinin hücresel taşıyıcı protein de bulunması; geri kalanının ise işlevi bilinmeyen bir protein olan haptokorrine bağlı olmasıdır (Ammouri ve ark., 2020). IF antikorları testte kullanılan IF reaktifiyle bağlanırsa ve IF-bloklayan antikorları denatüre etmek için yapılan denatürasyon aşamasında bir başarısızlık olursa, gerçekte normal olmayan fakat normal ya da yüksek görünen B12 düzeyleri ölçülebilir. Bu durumda, tedavi almamış hastalarda ve yalnızca nörolojik belirtileri olanlar da vitamin B12 eksikliği tanısında serum metilmalonik asit ve total homosistein ölçümü yararlıdır ve bu durumda her ikisi de belirgin şekilde yükselir (Ammouri ve ark., 2020).

Yapılan biyokimyasal değerlendirmeden sonra PA tanısı alan hastalara, otoimmun gastropati varlığını doğrulamak için gastroskopi ve biyopsi yapılması gerekmektedir (Esposito ve ark., 2022). Batı ülkelerinde, gastrik atrofi ve dolayısıyla PA tanısı için biyopsiler ve atrofinin varlığının histolojik olarak doğrulanması zorunlu kabul edilmekte iken; Doğu ülkelerinde, atrofik gastrit tanısı endoskopik bazı sınıflandırmalara dayanmaktadır (Esposito ve ark., 2022).

Tedavi

Pernisiyöz anemi hastaları için ömür boyu B12 vitamini tedavisi endikedir. Terminal ileumda emilen B12 vitaminin emilimi neredeyse tamamen intrinsik faktöre bağlanmasına bağlıdır (Chan, Low ve Lee, 2016).

Pernisiyöz anemisi doğrulanmış hastalar için ömür boyu tedavi, 1-2 hafta boyunca günlük veya gün aşırı uygulanan 1000 mikrogram B12'nin (Avrupa'da hidroksokobalamin veya Amerika Birleşik Devletleri' nde siyanokobalamin) intramüsküler (IM) enjeksiyonuyla başlayıp, ardından 1- 2 ay boyunca haftalık enjeksiyonlar yapılır, ardından aylık enjeksiyon (siyanokobalamin) veya 2 ila 3 ayda bir enjeksiyon (hidroksokobalamin) yapılır (Vaqar ve Shackelford, 2023).

İlk yoğun tedavi aşamasının ardından hastalar intramüsküler enjeksiyonlara devam edebilir veya yaşam boyu idame aşaması için yüksek doz oral B12 takviyesi önerilebilir. Yapılan bazı çalışmalar oral B12 vitaminin IM tedavilere alternatif olarak kullanılabileceğini ortaya koymuştur.

Sonuç

Pernisiyöz anemi, otoimmun bir hastalık olarak başlayıp sonrasında gastrik atrofi ve kobalamin yetmezliği ile sonuçlanmaktadır. Diğer otoimmun endokrin hastalıklarla olan birlikteliği nedeni ile bu tip hastalar da pernisiyöz anemi de araştırılmalı ve tedavi edilmelidir. Hematolojik belirti ve bulgular kobalamin tedavisi ile düzelme gösterse de nörolojik bulgular geri dönüşümsüz olabilmektedir(Aslaner, 2019). Bu nedenle erken tanı ve tedavi önemlidir. Tedavinin ömür boyu sürmesi ve ilk dönem takiplerinin tam düzelme sağlanıncaya kadar yakın takip edilmesi, sonrasında özellikle gastrik neoplazi gelişim açısından, kontrollerin 3-5 yılda bir yapılması önerilmektedir (Aslaner, 2019).

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