MOLECULAR PERSPECTIVES IN GASTROINTESTINAL HEALTH

ISBN:
978-625-92098-7-6

MOLECULAR PERSPECTIVES IN GASTROINTESTINAL HEALTH- 2026

ISBN: 978-625-92098-7-6

DOI: 10.5281/zenodo.20633854

June / 2026

Ankara / Türkiye

(The Licence Number of Publicator: 2014/31220)

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ISPEC Publishing House – 2026©

ISBN: 978-625-92098-7-6

June / 2026

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AUTHORS

Dr. Leylakhanym Arastun MELIKOVA

Abubakar Muhammad SANI

Murtala SA'ADU

Shamsuddeen Muhammad MUHAMMAD

G. DAVID

S. DEEPAK

A. PALANISAMY

C. RAVI

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PREFACE

Gastrointestinal diseases and cancer-related conditions continue to represent major challenges in contemporary medical and biomedical research. Advances in molecular diagnostics, infection-related disease studies, and cancer biology have significantly contributed to a deeper understanding of disease mechanisms, early detection strategies, and therapeutic possibilities. In this context, interdisciplinary approaches are essential for addressing the complex relationship between molecular markers, microbial factors, gastrointestinal disorders, and cancer progression.

The chapters in this volume examine selected topics in gastrointestinal health, oncology, and molecular medicine. The first chapter focuses on circulating cell-free DNA and circulating tumor DNA in tumor biology and liquid biopsy, highlighting their growing importance as biomarkers in cancer diagnosis, monitoring, and personalized medicine. The second chapter investigates the prevalence of *Helicobacter pylori* among patients attending Sir Yahaya Memorial Hospital in Birnin Kebbi, Nigeria, contributing to clinical and epidemiological discussions on gastrointestinal infections. The third chapter presents a comprehensive review of gastric disorders and colon cancer, with emphasis on pathophysiology, risk factors, diagnosis, and therapeutic advances.

By bringing together molecular, clinical, and epidemiological perspectives, this volume reflects the multidimensional nature of gastrointestinal disease research. The studies included here demonstrate how biomarker-based diagnostics, microbial investigations, and cancer-focused clinical reviews can contribute to improved understanding, prevention, and management of gastrointestinal conditions.

It is hoped that this book will serve as a valuable academic resource for researchers, healthcare professionals, students, and scholars interested in gastroenterology, oncology, molecular diagnostics, infectious diseases, and related biomedical fields. We extend our sincere appreciation to all contributing authors for their valuable scholarly efforts.

Editorial Team
April 5, 2026
Türkiye

CHAPTER 1
CIRCULATING CELL-FREE DNA (CFDNA) AND CIRCULATING TUMOR DNA (CTDNA) IN TUMOR BIOLOGY AND LIQUID BIOPSY

[1]Dr. Leylakhanym Arastun MELIKOVA

[1]Head of the Molecular Oncology Laboratory, National Oncology Center, Azerbaijan, Lmelikova20027@gmail.com, ORCID ID: 0000-0002-5934-2481

INTRODUCTION

Cancer is characterized by the progressive accumulation of genetic and epigenetic alterations that disrupt normal cellular regulatory mechanisms and drive malignant transformation, tumor progression, and metastasis (Wan et al., 2017). Traditional tumor characterization relies primarily on tissue biopsy, which remains the gold standard for histopathological diagnosis and molecular profiling. However, tissue biopsies are invasive procedures, may not fully represent tumor heterogeneity, and are often unsuitable for repeated sampling during disease monitoring. These limitations have stimulated growing interest in minimally invasive diagnostic strategies capable of dynamically reflecting tumor biology over time (Wan et al., 2017; Ma et al., 2024).

Circulating nucleic acids detected in body fluids have emerged as promising biomarkers for cancer diagnosis and monitoring. Among these, circulating cell-free DNA (cfDNA) and circulating tumor DNA (ctDNA) have gained particular attention due to their potential to provide real-time molecular information through a simple blood sample (Ge et al., 2024). Cell-free DNA refers to short DNA fragments that circulate freely in the bloodstream and originate primarily from apoptotic and necrotic cells. In patients with cancer, a fraction of cfDNA originates from tumor cells and is referred to as circulating tumor DNA. ctDNA carries tumor-specific molecular alterations, including point mutations, copy number variations, structural rearrangements, and epigenetic modifications that reflect the genomic landscape of the primary tumor (Cisneros-Villanueva et al., 2022; Ge et al., 2024). The biological origin of cfDNA is associated with several physiological and pathological processes, including apoptosis, necrosis, and active secretion mechanisms. Under normal physiological conditions, cfDNA is mainly derived from hematopoietic cells undergoing programmed cell death (Stejskal et al., 2023; Parums, 2025). However, in malignant diseases, increased tumor cell turnover and cell death result in the release of tumor-derived DNA fragments into the circulation, thereby increasing the ctDNA fraction within total circulating DNA. The proportion of ctDNA within cfDNA varies significantly depending on tumor type, stage, tumor burden, vascularization, and treatment response (Parums, 2025).

The identification of tumor-derived nucleic acids in the circulation has contributed to the emergence of the liquid biopsy concept, a diagnostic approach that enables non-invasive molecular characterization of cancer. Liquid biopsy involves the analysis of tumor-derived components present in body fluids, including circulating tumor cells, extracellular vesicles, and circulating tumor DNA (ctDNA). Compared with conventional tissue biopsy, this approach offers several important advantages, such as minimal invasiveness, the possibility of repeated sampling, and the ability to capture spatial and temporal tumor heterogeneity (Ge et al., 2024; Pessoa et al., 2020). Among these biomarkers, ctDNA has attracted considerable attention due to its ability to reflect the genomic landscape of the tumor. ctDNA represents a fraction of cell-free DNA released into the bloodstream from tumor cells through biological processes such as apoptosis and necrosis. As a result, ctDNA fragments may contain tumor-specific genetic alterations, including somatic mutations and indicators of genomic instability. Advances in high-throughput sequencing technologies have significantly improved the sensitivity of ctDNA detection and analysis. Several studies have demonstrated that ctDNA profiling can provide valuable information regarding tumor mutational burden, clonal evolution, and therapeutic response, thereby enabling minimally invasive molecular profiling and longitudinal disease monitoring (Wan et al., 2017; Mouliere et al., 2018). Furthermore, recent clinical investigations have emphasized the growing role of ctDNA analysis in cancer detection and monitoring, highlighting its increasing relevance in the context of precision oncology (Leylakhanim et al., 2025; Clemente et al., 2025).

Technological advances have significantly enhanced the sensitivity and accuracy of ctDNA detection. Techniques such as digital polymerase chain reaction (dPCR), BEAMing, and next-generation sequencing (NGS) now allow the identification of rare tumor-derived mutations at very low allele frequencies. These technological developments have expanded the clinical applications of ctDNA, including early cancer detection, minimal residual disease monitoring, assessment of treatment response, and identification of resistance mutations during targeted therapy (de Abreu et al., 2025; Bartolomucci et al., 2025). Beyond its diagnostic utility, the analysis of cfDNA and ctDNA provides important insights into tumor biology.

The fragmentation patterns, nucleosomal organization, and epigenetic signatures of circulating DNA fragments reflect underlying biological processes occurring within tumor cells and their microenvironment. These molecular characteristics have opened new avenues for early cancer detection, prognostic evaluation, and personalized therapeutic strategies (Kuligina et al., 2025).This chapter provides a comprehensive overview of the biological mechanisms underlying cfDNA release and the characteristics of ctDNA in cancer. In addition, the chapter reviews current technologies for ctDNA detection and discusses their clinical applications in oncology, including early diagnosis, disease monitoring, and precision medicine approaches.

1. BIOLOGY OF CELL-FREE DNA RELEASE

The presence of extracellular DNA fragments in the bloodstream was first described in 1948 by Mandel and Métais, who reported circulating nucleic acids in human plasma (Mandel & Métais,1948). Since that discovery, numerous studies have demonstrated that circulating cell-free DNA (cfDNA) originates from multiple physiological and pathological processes associated with cellular turnover and tissue injury (Wan et al., 2017; Thierry et al., 2016). In healthy individuals, cfDNA is primarily derived from hematopoietic cells undergoing normal apoptosis. However, in pathological conditions such as cancer, inflammation, trauma, and autoimmune diseases, the concentration and composition of cfDNA in circulation can increase significantly (Thierry et al., 2016).

In cancer patients, a proportion of cfDNA originates from tumor cells and is referred to as circulating tumor DNA (ctDNA). The release of cfDNA into the circulation occurs through several biological mechanisms, most notably apoptosis, necrosis, and active secretion by living cells. These processes produce circulating DNA fragments with distinct molecular characteristics, including differences in fragment size, nucleosomal patterns, and genomic content. Understanding the biological mechanisms underlying cfDNA release is essential for interpreting liquid biopsy results and improving the sensitivity and specificity of ctDNA detection technologies (Mouliere et al., 2018).

Apoptosis

Apoptosis is considered the primary physiological mechanism responsible for the release of cfDNA into the bloodstream. Apoptosis, or programmed cell death, is a tightly regulated cellular process that maintains tissue homeostasis by eliminating damaged or unnecessary cells. During apoptosis, chromatin is cleaved by endogenous nucleases into fragments that are typically multiples of nucleosomal units, resulting in DNA fragments approximately 160–180 base pairs in length. These fragments correspond to DNA wrapped around nucleosomes and represent a characteristic feature of apoptosis-derived cfDNA (Jahr et al., 2001). Following apoptotic cell death, DNA fragments are packaged into apoptotic bodies and subsequently cleared by phagocytic cells such as macrophages. However, incomplete clearance of apoptotic bodies can result in the release of nucleosomal DNA fragments into the extracellular environment and eventually into the bloodstream. In healthy individuals, apoptosis of hematopoietic cells in the bone marrow and peripheral blood represents the major source of circulating cfDNA (Snyder et al., 2016).

In cancer, apoptosis occurs at increased rates due to rapid tumor cell turnover, hypoxia, immune-mediated cytotoxicity, and the effects of anticancer therapies such as chemotherapy and radiotherapy. As a result, apoptotic tumor cells contribute significantly to the ctDNA pool. Importantly, the fragmentation pattern of apoptosis-derived DNA forms the basis for emerging diagnostic approaches such as fragmentomics, which analyze cfDNA fragment size distribution and nucleosomal positioning to improve cancer detection sensitivity (Mouliere et al., 2018).

Necrosis

Necrosis represents another important mechanism contributing to cfDNA release, particularly in pathological conditions associated with tissue injury and tumor progression. Unlike apoptosis, necrosis is an uncontrolled form of cell death that typically occurs in response to severe cellular stress, including hypoxia, inflammation, ischemia, or metabolic disruption. Necrotic cell death results in the breakdown of cellular membranes and the release of intracellular contents, including large fragments of genomic DNA, into the extracellular environment (Thierry et al., 2016).

In solid tumors, regions of hypoxia and insufficient vascularization often lead to extensive necrosis within the tumor microenvironment. Tumor necrosis is especially common in rapidly proliferating cancers, where inadequate blood supply leads to metabolic stress and cell death. DNA released during necrosis is typically less fragmented than apoptosis-derived DNA and can include longer fragments exceeding several kilobases. Consequently, necrosis-derived cfDNA may contribute to a broader size distribution of circulating DNA fragments observed in cancer patients (Wan et al., 2017). Furthermore, necrotic cell death can stimulate inflammatory responses, which may indirectly increase cfDNA levels through immune cell activation and secondary tissue damage. In advanced malignancies, necrosis may therefore represent a major source of circulating tumor DNA. The relative contributions of apoptotic and necrotic processes to ctDNA release depend on tumor type, tumor burden, vascularization, and treatment effects.

Active Secretion. In addition to passive release during cell death, increasing evidence suggests that living cells may actively release DNA fragments into the extracellular environment through regulated secretion mechanisms. Active secretion of DNA has been observed in association with extracellular vesicles, including exosomes and microvesicles, which are membrane-bound particles released by many cell types (Kahlert et al., 2014). Extracellular vesicles can contain various molecular components, including proteins, RNA, and DNA fragments derived from the nucleus or mitochondria. Tumor-derived exosomes have been shown to carry double-stranded DNA reflecting the mutational profile of the parental tumor cells. This mechanism provides an additional pathway through which tumor-derived genetic material can enter the circulation and potentially contribute to the ctDNA pool (Kahlert et al., 2014). Another mechanism of active DNA release involves neutrophil extracellular traps (NETs), which consist of DNA fibers released by activated neutrophils during immune responses. NET formation has been associated with inflammatory conditions and cancer progression and may contribute to circulating DNA levels in certain pathological states (Wan et al., 2017).

Although the relative contribution of active secretion to total cfDNA levels remains under investigation, this mechanism may play an important role in tumor–host interactions and intercellular communication within the tumor microenvironment. Tumor-derived extracellular DNA may influence immune responses, metastasis, and tumor progression, highlighting the complex biological roles of circulating DNA beyond its use as a diagnostic biomarker.

Collectively, apoptosis, necrosis, and active secretion represent the principal biological mechanisms responsible for the release of cfDNA into the bloodstream. These processes generate circulating DNA fragments with distinct molecular features that can be exploited for diagnostic and prognostic purposes in oncology. A detailed understanding of cfDNA release mechanisms is therefore essential for interpreting liquid biopsy data and for optimizing ctDNA

2. CHARACTERISTICS OF CIRCULATING TUMOR DNA

Circulating tumor DNA (ctDNA) represents the tumor-derived fraction of circulating cell-free DNA (cfDNA) found in plasma or other body fluids. Unlike cfDNA released from normal cells, ctDNA carries genetic and epigenetic alterations that reflect the molecular characteristics of the tumor from which it originates. Because ctDNA fragments retain tumor-specific molecular signatures, their analysis has become an important tool in cancer diagnostics, tumor monitoring, and precision oncology. Several molecular features distinguish ctDNA from non-tumor cfDNA, including differences in fragment size distribution, mutational landscape, and genomic alterations. Among these, fragment size patterns and mutation profiles represent key characteristics that enable the identification and quantification of ctDNA within the complex mixture of circulating DNA fragments (Wan et al., 2017; Mouliere et al., 2018).

Fragment Size Distribution

Fragment size is one of the most informative physical characteristics distinguishing ctDNA from background cfDNA. In healthy individuals, the majority of circulating cfDNA fragments originate from apoptotic hematopoietic cells and therefore exhibit a characteristic nucleosomal fragmentation pattern.

These fragments typically measure approximately 160–180 base pairs (bp), corresponding to the length of DNA wrapped around a nucleosome plus linker DNA (Jahr et al., 2001; Snyder et al., 2016). In contrast, ctDNA fragments tend to be shorter than the dominant cfDNA population. Multiple studies have demonstrated that tumor-derived DNA fragments are often enriched in shorter size ranges, typically between 90 and 150 base pairs. This size shift is thought to reflect differences in chromatin organization, nuclease activity, and DNA degradation processes occurring in tumor cells compared with normal cells (Mouliere et al., 2018). In particular, tumor cells undergoing apoptosis may generate distinct fragmentation patterns due to altered nucleosomal spacing and increased chromatin accessibility.

Recent advances in cfDNA fragmentomics the study of fragmentation patterns of circulating DNA have revealed additional structural features of ctDNA. For example, tumor-derived DNA fragments may display altered nucleosome positioning patterns that reflect gene expression activity in the tissue of origin. Analysis of fragment size distribution and nucleosome footprints can therefore provide information about the cellular origin of circulating DNA fragments and may enhance early cancer detection strategies (Snyder et al., 2016). Shorter ctDNA fragments have been shown to carry a higher proportion of tumor-specific mutations compared with longer fragments. This observation has led to the development of size-selection strategies in liquid biopsy workflows, where enrichment of shorter cfDNA fragments can improve the sensitivity of ctDNA detection in samples with low tumor fraction. Fragment size analysis has therefore become an important component of modern liquid biopsy approaches, particularly in early cancer detection where ctDNA concentrations may be extremely low (Mouliere et al., 2018).

Mutation Patterns

Another defining feature of ctDNA is the presence of tumor-specific genetic alterations that mirror the mutational landscape of the primary tumor. These alterations may include single nucleotide variants (SNVs), insertions and deletions (indels), copy number variations (CNVs), and chromosomal rearrangements.

Because ctDNA fragments originate directly from tumor cells, they contain the same somatic mutations present in the tumor genome and therefore provide a non-invasive window into tumor molecular biology (Wan et al., 2017). One of the most clinically relevant aspects of ctDNA analysis is the detection of driver mutations that contribute to tumor development and progression. Mutations in genes such as TP53, KRAS, EGFR, PIK3CA, and BRAF are frequently identified in ctDNA and may serve as biomarkers for targeted therapy selection and treatment monitoring. For example, detection of EGFR activating mutations and resistance mutations such as EGFR T790M in plasma ctDNA has become an established tool for guiding targeted therapy in non-small cell lung cancer (NSCLC) (Wan et al., 2017). ctDNA analysis can also reveal tumor heterogeneity and clonal evolution during cancer progression. Tumors often consist of multiple subclonal populations with distinct mutational profiles. As treatment exerts selective pressure on tumor cells, resistant clones may expand and release mutated DNA fragments into the circulation. Monitoring ctDNA over time therefore allows the detection of emerging resistance mutations before they become clinically apparent through radiological imaging (Thierry et al., 2016).

Another key feature of ctDNA mutation patterns is the low allele frequency at which tumor-derived variants may be present. In early-stage cancers or during minimal residual disease (MRD), ctDNA may constitute less than 0.1% of total circulating DNA. Detecting such rare mutations requires highly sensitive analytical technologies such as digital PCR, BEAMing, and ultra-deep next-generation sequencing. These technologies enable the identification of rare tumor-derived variants with high specificity, allowing ctDNA analysis to be used for early detection, treatment monitoring, and relapse prediction (Wan et al., 2017).

In addition to identifying known driver mutations, comprehensive sequencing of ctDNA can reveal broader mutational signatures associated with specific carcinogenic processes, such as ultraviolet radiation, tobacco exposure, or defective DNA repair mechanisms. These mutational signatures provide further insights into tumor biology and may have diagnostic or prognostic significance (Thierry et al., 2016).

Overall, the fragment size characteristics and mutation patterns of ctDNA represent critical molecular features that distinguish tumor-derived DNA fragments from background cfDNA. Advances in sequencing technologies and computational analysis have enabled increasingly precise characterization of these features, thereby enhancing the clinical utility of ctDNA as a biomarker for cancer detection, disease monitoring, and precision oncology.

3. DETECTION TECHNOLOGIES FOR CIRCULATING TUMOR DNA

The clinical utility of circulating tumor DNA (ctDNA) depends largely on the ability to detect extremely low concentrations of tumor-derived DNA fragments within a large background of normal circulating cell-free DNA (cfDNA). In many clinical contexts, particularly in early-stage cancers or minimal residual disease (MRD), ctDNA may represent less than 0.1% of total circulating DNA. Consequently, highly sensitive analytical methods are required to accurately identify and quantify tumor-specific genetic alterations. Over the past decade, significant technological advances have enabled the development of highly sensitive platforms capable of detecting rare ctDNA variants with high specificity. Among the most widely used approaches are digital polymerase chain reaction (dPCR), BEAMing (Beads, Emulsion, Amplification, and Magnetics), and next-generation sequencing (NGS) technologies (Wan et al., 2017; Heitzer et al., 2019).

Digital PCR

Digital polymerase chain reaction (dPCR) is one of the most sensitive techniques for detecting specific mutations in circulating tumor DNA. Unlike conventional PCR methods, which measure amplified DNA collectively, digital PCR partitions DNA samples into thousands to millions of individual reactions. Each partition contains either zero or one DNA template molecule, allowing absolute quantification of mutant and wild-type alleles through binary amplification signals (Hindson et al., 2013).

One of the most widely implemented forms of digital PCR is droplet digital PCR (ddPCR), in which DNA samples are emulsified into thousands of nanoliter-sized droplets. Each droplet acts as an independent PCR microreaction. Following amplification, fluorescence-based detection determines the presence or absence of the target mutation within each droplet. The proportion of mutation-positive droplets allows precise quantification of mutant allele frequency.

Digital PCR offers several advantages for ctDNA analysis, including high analytical sensitivity, rapid turnaround time, and relatively low cost compared with sequencing-based approaches. Detection limits as low as 0.01% variant allele frequency have been reported using optimized ddPCR assays. As a result, dPCR is widely used for targeted mutation detection in clinical oncology, particularly for monitoring known driver mutations such as EGFR, KRAS, or BRAF during targeted therapy (Wan et al., 2017; Heitzer et al., 2019). Digital PCR assays are limited by their targeted nature, as they require prior knowledge of specific mutations. Consequently, dPCR is most suitable for monitoring previously identified tumor mutations rather than for broad genomic profiling.

BEAMing

BEAMing (Beads, Emulsion, Amplification, and Magnetics) represents another highly sensitive digital PCR–based method used for ctDNA analysis. This technique combines emulsion PCR with flow cytometry-based detection to identify rare mutant DNA molecules in plasma samples (Diehl et al., 2008).

In BEAMing, DNA fragments are amplified within emulsion droplets containing magnetic beads. Each bead captures amplified DNA derived from a single template molecule. Following PCR amplification, beads are hybridized with fluorescent probes specific for mutant or wild-type sequences and subsequently analyzed using flow cytometry. This process allows highly sensitive detection of mutant alleles among large numbers of wild-type DNA fragments. BEAMing has demonstrated sensitivity comparable to digital PCR, with the ability to detect mutations at variant allele frequencies as low as 0.01%.

This method has been successfully applied to detect clinically relevant mutations in several cancers, including colorectal cancer, lung cancer, and breast cancer. For example, BEAMing-based ctDNA analysis has been used to identify KRAS mutations in metastatic colorectal cancer patients and to monitor the emergence of resistance mutations during anti-EGFR therapy (Wan et al., 2017; Siravegna et al., 2017).

Despite its high sensitivity, BEAMing requires specialized equipment and complex workflows, which may limit its widespread adoption in routine clinical laboratories. Nonetheless, the technique remains an important reference method for highly sensitive mutation detection in circulating DNA.

Next-Generation Sequencing

Next-generation sequencing (NGS) technologies have revolutionized ctDNA analysis by enabling comprehensive genomic profiling of tumor-derived DNA fragments in plasma. Unlike targeted PCR-based methods, NGS allows simultaneous analysis of large numbers of genomic regions, enabling the detection of multiple mutations, copy number alterations, and structural variants in a single assay (Heitzer et al., 2019). Several NGS-based approaches have been developed for ctDNA detection. Targeted sequencing panels focus on predefined sets of cancer-related genes and provide deep sequencing coverage, often exceeding 10,000×. This high sequencing depth improves the sensitivity of mutation detection in samples with low ctDNA fraction. Techniques such as CAPP-Seq (Cancer Personalized Profiling by Deep Sequencing) and Safe-SeqS (Safe Sequencing System) incorporate molecular barcoding strategies to reduce sequencing errors and improve detection of rare variants (Newman et al., 2016).

Another emerging strategy involves whole-genome sequencing (WGS) or whole-exome sequencing (WES) of circulating DNA. Although these approaches typically have lower sequencing depth compared with targeted panels, they enable global analysis of tumor-derived genomic alterations, including copy number changes and mutational signatures. Advances in bioinformatics and error-correction algorithms have further enhanced the accuracy of NGS-based ctDNA detection (Heitzer et al., 2019).

NGS-based ctDNA assays have now been integrated into clinical oncology practice. Several plasma-based genomic profiling tests have received regulatory approval for identifying actionable mutations in advanced cancers. For example, NGS-based liquid biopsy assays are routinely used to detect EGFR, ALK, and BRAF alterations in non-small cell lung cancer patients when tissue biopsy is unavailable or insufficient (Wan et al., 2017). Despite its advantages, NGS-based ctDNA analysis faces several challenges. These include the need for complex bioinformatics pipelines, potential sequencing artifacts, and the requirement for high sequencing depth to detect extremely rare variants. Nevertheless, continuous improvements in sequencing technology and error-suppression strategies are rapidly expanding the clinical applications of ctDNA analysis.

Collectively, digital PCR, BEAMing, and next-generation sequencing represent the principal technological platforms used for ctDNA detection. Each method offers distinct advantages and limitations in terms of sensitivity, throughput, and genomic coverage. The selection of an appropriate detection strategy depends on the specific clinical application, including mutation monitoring, minimal residual disease detection, or comprehensive tumor genomic profiling. As sequencing technologies continue to advance, ctDNA analysis is expected to play an increasingly central role in cancer diagnostics and precision medicine.

4. CLINICAL APPLICATIONS OF CIRCULATING TUMOR DNA

The analysis of circulating tumor DNA (ctDNA) has emerged as a powerful tool in modern oncology, providing a minimally invasive approach for cancer detection, disease monitoring, and treatment guidance. Because ctDNA carries tumor-specific genomic alterations, its analysis enables dynamic assessment of tumor burden and molecular evolution over time. In recent years, major advances in sequencing technologies and analytical sensitivity have significantly expanded the clinical applications of ctDNA. Current clinical uses include early cancer detection, identification of minimal residual disease (MRD), and monitoring of therapeutic response during systemic treatment (Heitzer et al., 2019; Wan et al., 2017).

Early Cancer Detection

Early detection of cancer remains one of the most promising applications of ctDNA analysis. Detecting cancer at an early stage significantly improves patient survival, yet many malignancies are diagnosed only after symptoms appear and the disease has progressed. Liquid biopsy approaches based on ctDNA offer a non-invasive strategy for identifying tumor-derived genetic alterations before clinical manifestation of advanced disease. However, early-stage tumors release only very small amounts of ctDNA into circulation, often representing less than 0.01% of total cfDNA. This extremely low tumor fraction presents major analytical challenges and requires highly sensitive detection methods. Recent technological developments, including ultra-deep next-generation sequencing and advanced bioinformatic error-correction algorithms, have enabled the detection of rare ctDNA variants with increasing accuracy (Heitzer et al., 2019).

Large multicancer early detection (MCED) studies have demonstrated the feasibility of using cfDNA methylation patterns and mutation profiling to detect multiple cancer types simultaneously from a single blood sample. For example, cfDNA methylation-based assays have shown promising results in identifying the tissue of origin and detecting cancers such as lung, colorectal, pancreatic, and ovarian cancer in asymptomatic individuals (Liu et al., 2020). Similarly, genome-wide fragmentation analysis and methylation profiling of cfDNA have improved sensitivity for early-stage cancer detection in several recent studies (Klein et al., 2021). Despite these advances, challenges remain for the widespread implementation of ctDNA-based screening programs. Sensitivity for very early-stage tumors remains limited, and false-positive results may occur due to clonal hematopoiesis of indeterminate potential (CHIP), a phenomenon in which age-related mutations arise in hematopoietic stem cells and may be detected in plasma DNA. Nevertheless, continued improvements in assay sensitivity and bioinformatic interpretation are expected to enhance the role of ctDNA in population-level cancer screening in the future.

Minimal Residual Disease (MRD)

One of the most clinically impactful applications of ctDNA analysis is the detection of minimal residual disease (MRD) following curative-intent treatment. MRD refers to the presence of microscopic tumor cells that remain in the body after surgery, chemotherapy, or radiotherapy but are not detectable by conventional imaging methods. These residual tumor cells may eventually lead to disease recurrence.

ctDNA analysis provides a highly sensitive approach for detecting MRD by identifying tumor-specific mutations in plasma after treatment. Several studies have demonstrated that the presence of ctDNA following surgical resection of solid tumors strongly predicts disease relapse. In colorectal cancer, for example, postoperative ctDNA detection has been shown to identify patients at extremely high risk of recurrence months before radiologic evidence of relapse appears (Tie et al., 2019). Similarly, ctDNA-based MRD detection has demonstrated prognostic value in several malignancies, including breast cancer, lung cancer, and melanoma. Longitudinal monitoring of ctDNA levels after treatment allows early identification of molecular relapse, often preceding clinical recurrence by several months. This early detection of relapse may enable earlier therapeutic intervention and potentially improve patient outcomes (Reinert et al., 2019). MRD detection strategies typically rely on highly sensitive personalized sequencing approaches that track patient-specific tumor mutations identified from primary tumor tissue. Techniques such as personalized multiplex PCR and targeted deep sequencing can detect ctDNA at extremely low allele frequencies, sometimes below 0.01%. As a result, ctDNA-based MRD testing is increasingly being incorporated into clinical trials and is expected to play an important role in guiding adjuvant therapy decisions in the future (Abbosh et al., 2017).

Therapy Monitoring

Another major clinical application of ctDNA analysis is monitoring response to anticancer therapy. Because ctDNA levels reflect tumor burden, changes in ctDNA concentration during treatment may provide an early indicator of therapeutic response.

Decreases in ctDNA levels following initiation of therapy are often associated with tumor regression, whereas rising ctDNA levels may indicate treatment resistance or disease progression (Wan et al., 2017). Serial ctDNA measurements allow real-time monitoring of tumor dynamics and may detect molecular progression earlier than conventional imaging techniques. For example, in metastatic colorectal cancer and lung cancer, increasing ctDNA levels have been shown to precede radiological evidence of disease progression by several weeks to months (Siravegna et al., 2017). In addition to monitoring tumor burden, ctDNA analysis can also identify emerging resistance mutations during targeted therapy. Tumors frequently acquire secondary mutations that confer resistance to targeted agents. Detection of these resistance mutations in ctDNA allows clinicians to adjust treatment strategies accordingly. A well-known example is the detection of the EGFR T790M resistance mutation in non-small cell lung cancer patients treated with first-generation EGFR inhibitors, which guides the use of third-generation targeted therapies (Wan et al., 2017). Furthermore, ctDNA analysis is increasingly used in immunotherapy monitoring. Several studies have demonstrated that changes in ctDNA levels during immune checkpoint inhibitor therapy correlate with treatment response and may help distinguish true progression from pseudoprogression in certain patients.

Overall, ctDNA-based monitoring provides a dynamic and minimally invasive method for evaluating treatment response, detecting emerging resistance mechanisms, and guiding personalized treatment decisions. As liquid biopsy technologies continue to evolve, ctDNA analysis is expected to become an integral component of precision oncology and longitudinal cancer management.

5. CHALLENGES AND LIMITATIONS OF CIRCULATING TUMOR DNA ANALYSIS

Although circulating tumor DNA (ctDNA) analysis has become an important tool in precision oncology, several biological and technical challenges still limit its clinical implementation.

One of the major difficulties arises from the extremely low abundance of ctDNA fragments in plasma compared with the large background of circulating cell-free DNA (cfDNA) derived from normal cells. In addition, biological confounders such as clonal hematopoiesis of indeterminate potential (CHIP) may introduce non-tumor somatic mutations into plasma DNA, complicating interpretation of sequencing results. Understanding these limitations is essential for accurate analysis and clinical interpretation of ctDNA-based assays (Heitzer et al., 2019; Wan et al., 2017).

Low Allele Fraction

One of the most significant challenges in ctDNA analysis is the extremely low allele fraction of tumor-derived DNA fragments in circulation. The term variant allele fraction (VAF) refers to the proportion of DNA fragments carrying a specific mutation relative to the total number of DNA molecules present in the sample. In many clinical scenarios, particularly in early-stage cancer or minimal residual disease (MRD), ctDNA may represent less than 0.1% of total circulating cfDNA (Heitzer et al., 2019). This low abundance creates substantial analytical challenges, as rare mutant DNA molecules must be detected within a large background of wild-type DNA derived from normal cells. Conventional sequencing approaches often lack sufficient sensitivity to detect such rare variants. Therefore, specialized ultra-sensitive methods such as droplet digital PCR (ddPCR), BEAMing, and error-corrected next-generation sequencing have been developed to identify ctDNA variants at very low frequencies (Wan et al., 2017).

In addition to technological limitations, biological factors also influence ctDNA allele fraction. Tumor burden is one of the most important determinants of ctDNA levels. Patients with advanced metastatic disease generally exhibit higher ctDNA concentrations compared with patients with early-stage tumors. Similarly, tumor vascularization, cell turnover rate, and metastatic location may affect the release of ctDNA into the circulation (Corcoran & Chabner, 2018).

Another challenge associated with low allele fraction is the potential for sequencing artifacts and false-positive results. Polymerase errors, sequencing noise, and sample contamination may produce variants that mimic true tumor mutations.

To address this issue, modern ctDNA sequencing workflows often incorporate molecular barcoding strategies, also known as unique molecular identifiers (UMIs), which enable error suppression and improve detection accuracy for rare variants (Newman et al., 2016).

Despite these technological improvements, detecting ctDNA in early-stage cancer remains difficult due to the extremely low number of tumor-derived DNA fragments in circulation. Continued development of ultra-sensitive detection technologies and improved bioinformatic algorithms is therefore essential to expand the clinical applications of ctDNA-based diagnostics.

Clonal Hematopoiesis

Another important limitation in ctDNA analysis is the presence of clonal hematopoiesis of indeterminate potential (CHIP), a phenomenon characterized by the expansion of hematopoietic stem cell clones carrying somatic mutations. CHIP becomes increasingly common with aging and may be detected in up to 10–20% of individuals over the age of 70 (Genovese et al., 2014; Jaiswal et al., 2014). Mutations associated with clonal hematopoiesis frequently occur in genes that are also commonly mutated in cancer, including DNMT3A, TET2, ASXL1, TP53, and JAK2. Because cfDNA in plasma is largely derived from hematopoietic cells, these mutations may appear in circulating DNA and be mistakenly interpreted as tumor-derived mutations during ctDNA analysis (Razavi et al., 2019). The presence of CHIP mutations represents a major source of false-positive results in liquid biopsy assays. For example, plasma sequencing may detect mutations in TP53 or DNMT3A that originate from clonal hematopoietic cells rather than from tumor tissue. Without appropriate analytical controls, these mutations may lead to incorrect conclusions regarding tumor genotype or treatment response (Razavi et al., 2019).

Several strategies have been proposed to mitigate the effects of clonal hematopoiesis on ctDNA analysis. One commonly used approach involves parallel sequencing of matched white blood cell DNA obtained from the same patient. By comparing mutations identified in plasma with those present in leukocyte DNA, investigators can distinguish hematopoietic-derived mutations from true tumor-specific alterations (Heitzer et al., 2019).

Bioinformatic filtering strategies and improved mutation annotation databases have also helped reduce the impact of CHIP on ctDNA interpretation. Nevertheless, clonal hematopoiesis remains an important confounding factor in plasma-based genomic profiling and must be carefully considered in both research and clinical applications of ctDNA.

In summary, although ctDNA analysis offers substantial promise for non-invasive cancer detection and monitoring, several important challenges remain. Low allele fraction and clonal hematopoiesis represent major biological and technical obstacles that may affect the sensitivity and specificity of ctDNA assays. Continued technological innovation, improved analytical strategies, and careful clinical interpretation are required to overcome these limitations and fully realize the potential of ctDNA in precision oncology.

CONCLUSION

The rapid evolution of liquid biopsy technologies has significantly expanded the potential applications of circulating cell-free DNA (cfDNA) and circulating tumor DNA (ctDNA) in oncology. Although ctDNA analysis has already demonstrated considerable value in cancer detection, minimal residual disease monitoring, and therapy response assessment, ongoing technological and methodological developments are expected to further enhance its clinical utility. Future research in this field is likely to focus on improving analytical sensitivity, integrating multi-omic biomarkers, and applying advanced computational approaches to enable more precise and comprehensive cancer diagnostics.

One of the most promising directions in cfDNA research is the expansion of fragmentomics, which refers to the study of fragmentation patterns of circulating DNA molecules. Recent studies have demonstrated that cfDNA fragmentation profiles reflect nucleosome positioning, chromatin accessibility, and gene expression patterns in the tissue of origin. These fragmentation signatures can therefore provide information about the biological source of cfDNA fragments and may enhance early cancer detection strategies.

By integrating fragment size distribution, nucleosomal footprints, and end-motif patterns, researchers have developed novel fragmentomics-based approaches capable of distinguishing cancer patients from healthy individuals with improved diagnostic accuracy (Cristiano et al., 2019; Mouliere et al., 2018).

Another rapidly advancing area involves epigenetic profiling of cfDNA, particularly DNA methylation analysis. Methylation patterns are highly tissue-specific and often undergo characteristic alterations during tumorigenesis. Consequently, cfDNA methylation profiling has emerged as a powerful method for identifying both the presence of cancer and the tissue of origin of tumor-derived DNA. Large multicancer early detection (MCED) studies have demonstrated that genome-wide methylation analysis of cfDNA can detect multiple cancer types simultaneously from a single blood sample with relatively high specificity (Liu et al., 2020; Klein et al., 2021). Continued improvements in methylation-based assays may significantly enhance the sensitivity of ctDNA detection in early-stage cancers.

Future ctDNA research is also expected to benefit from the integration of multi-omic liquid biopsy approaches. In addition to DNA mutations and methylation patterns, circulating biomarkers such as circulating tumor cells (CTCs), extracellular vesicles, tumor-derived RNA, and circulating proteins may provide complementary information about tumor biology. Combining multiple biomarker types into integrated diagnostic platforms may increase the overall sensitivity and specificity of cancer detection compared with single-analyte assays (Wan et al., 2017; Heitzer et al., 2019). Such multi-omic strategies may be particularly useful in early cancer detection, where the concentration of tumor-derived DNA fragments is extremely low.

Advances in artificial intelligence (AI) and machine learning are also expected to play an important role in the future development of ctDNA-based diagnostics. Modern ctDNA assays generate large and complex datasets that include genomic mutations, fragmentation patterns, methylation profiles, and sequencing noise signals. Machine learning algorithms can analyze these multidimensional datasets to identify subtle patterns associated with cancer presence, tumor subtype, or treatment response.

Several recent studies have demonstrated that AI-driven analysis of cfDNA sequencing data can improve classification accuracy for early cancer detection and may assist in determining the tissue of origin of circulating tumor DNA (Cristiano et al., 2019).

Another important future direction involves the application of ctDNA technologies in pediatric oncology. Compared with adult malignancies, pediatric cancers often exhibit lower mutational burdens and distinct genomic landscapes. Nevertheless, ctDNA analysis has shown promising results in monitoring pediatric tumors such as neuroblastoma, medulloblastoma, Ewing sarcoma, and certain leukemias. Liquid biopsy approaches may provide a particularly valuable tool in pediatric oncology by reducing the need for invasive biopsy procedures and enabling longitudinal monitoring of tumor evolution during treatment (Wan et al., 2017). Furthermore, improvements in sequencing technologies and error-correction methods are expected to substantially increase the sensitivity of ctDNA detection. Emerging techniques such as ultra-deep sequencing, duplex sequencing, and personalized tumor-informed assays are capable of detecting ctDNA at extremely low variant allele frequencies, potentially enabling detection of minimal residual disease at earlier time points. These technological advances may allow ctDNA-based monitoring to guide treatment decisions more effectively and improve patient outcomes. Despite these promising developments, several challenges remain before ctDNA analysis can be fully integrated into routine clinical practice. Standardization of sample collection, sequencing protocols, and bioinformatic pipelines will be essential to ensure reproducibility across laboratories. In addition, large prospective clinical trials are required to validate the clinical utility of ctDNA-based biomarkers for screening, treatment monitoring, and therapeutic decision-making.

In conclusion, cfDNA and ctDNA research is rapidly transforming the field of cancer diagnostics and precision medicine. Advances in fragmentomics, epigenetic profiling, multi-omic liquid biopsy platforms, and artificial intelligence are expected to significantly enhance the sensitivity and clinical applicability of ctDNA-based assays. As these technologies continue to mature, liquid biopsy approaches may become an integral component of routine cancer screening, disease monitoring, and personalized treatment strategies.

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CHAPTER 2
PREVALENCE OF *HELICOBACTER PYLORI* AMONG PATIENTS ATTENDING SIR YAHAYA MEMORIAL HOSPITAL, BIRNIN KEBBI, KEBBI STATE, NIGERIA

[1]Abubakar Muhammad SANI
[2]Murtala SA'ADU
[3]Shamsuddeen Muhammad MUHAMMAD

[1]Department of Microbiology, Faculty of Life Science, Abdullahi Fodio University of Science and Technology Aliero, Kebbi State, Nigeria, abubakarsani464@gmail.com, ORCID ID: 0000-0001-6986-2408
[2]Department of Microbiology, Faculty of Life Science, Abdullahi Fodio University of Science and Technology Aliero, Kebbi State, Nigeria, murtalas123@gmail.com, ORCID ID: 0000-0001-8720-2403
[3]Department of Microbiology, Faculty of Life Science, Abdullahi Fodio University of Science and Technology Aliero, Kebbi State, Nigeria, deenshams2000@gmail.com, ORCID ID: 0000-0003-3328-6685

INTRODUCTION

Helicopter pylori (*H. pylori*) is a highly mobile, curved Gram-negative rod that colonizes the human gastroduodenal mucosa of approximately half the world's populatio\\n (Gravina *et al.,* 2018). Most people have no symptoms, but their presence is associated with an increased risk of peptic ulcer and gastric carcinoma (Chmiela and Kupcinskas, 2019).

H. pylori eradication therapy is one of the pillars of the strategy to eliminate gastric cancer and peptic ulcer, but in recent years an increase in antibiotic resistance has been observed, which has resulted in therapeutic failures. Hence the importance of detecting resistance before starting treatment thanks to the use of new diagnostic techniques (Pohl *et al.,* 2019).

H. pylori colonizes various regions of the upper digestive system, mainly the stomach and duodenum causing stomach and duodenal ulcers and certain stomach cancers. The infection is today surprisingly common, and the bacteria are believed to colonize more than half of the world's population (Aziz *et al.,* 2015).

Helicobacter pylori is a microaerophilic, Gram-negative spiral bacterium. Its helix shape is thought to have evolved to penetrate the mucoid lining of the stomach, where they are protected by the mucus and the body immune cells are not able to reach them. The bacteria can interfere with immune response and ensure that they are not destroyed. This can lead to stomach ulcers. *Helicobacter pylori (H. pylori*), is an important global infection with a worldwide prevalence of about 45%. This infection is mostly acquired during childhood through the fecal-oral and oral-oral route. *H. pylori* is contagious, although the exact route of transmission is not well known. Person-to-person transmission by either the oral-oral or fecal-oral route is most likely. Initial infection with this organism is usually asymptomatic but symptoms and pathologic changes occur later in life. The clinical conditions and pathologic changes associated with *H. pylori* infection include gastritis, gastric and duodenal ulcers, gastric cancers, iron deficiency anaemia and idiopathic thrombocytopenic purpura. *Helicobacter pylori* is a common type of bacteria that grows in the digestive tract and has a tendency to attack the stomach lining.

It infects the stomach of approximately 45 percent of the world's adult population. *H. pylori* infections are usually harmless, but they are responsible for the majority of ulcers in the stomach and small intestine. (Pounder *et al.,* 2015) *H. pylori* are adapted to live in the harsh, acidic environment of the stomach. These bacteria can change the environment around them and reduce its acidity so they can survive. The spiral shape of *H. pylori* allows them to penetrate the stomach lining, where they are protected by mucus membrane and the body's immune cells are not able to reach them. The bacterium can interfere with immune response and ensure that they are not destroyed**.** This can lead stomach problems (Holcombe *et al.,* 2014). It is still not known exactly how *H. pylori* infections spread. The bacterium have coexisted with humans for many thousands of years. *H. pylori* infection exhibits a varied geographic distribution on both local and global scales. A number of other symptoms may be associated with *H. pylori* infection, including: excessive burping, feeling bloated, nausea, heartburn, fever, lack of appetite, or anorexia, unexplained weight loss, trouble swallowing, anemia and blood in the stool. These are common symptoms that could be caused by other conditions. Some of the symptoms of *H. pylori* infection are also experienced by healthy people.

There has been gradually increasing evidence that duodenal and duodenitis are also associated with *H. pylori* infection. In 2005, Warren and Marshall received the Nobel prize in physiology or medicine for the discovery of *H. pylori* pathogenicity and rekindled interest in the study of this microorganism. Since then, the association of *H. pylori* with digestive diseases has been the subject of much research attention (Reshetnyak *et al.,* 2017).

1. *Helicobacter pylori (H.pylori)*

Helicobacter pylori (H. pylori) is a spiral-shaped bacterium linked to various gastrointestinal diseases, particularly peptic ulcers and chronic gastritis. Observations of spiral bacteria in the stomachs of animals date back to the late 19th century, but these findings did not initially lead to significant medical advancements. The real breakthrough came in the late 1970s and early 1980s when J. Robin Warren, a pathologist in Perth, Australia, observed spiral bacteria in stomach biopsies of patients with gastritis and peptic ulcers.

He was joined by Barry J. Marshall, who successfully cultured the bacterium in 1982, initially naming it *Campylobacter pyloridis* before it was renamed *Helicobacter pylori*. In 1984, Marshall ingested a culture of *H. pylori*, developed gastritis symptoms, and confirmed the presence of the bacterium in his stomach, providing strong evidence of its pathogenic role.

Helicobacter pylori has been the subject of intense investigation since its culture from a gastric biopsy in 1982 from the beginning, this gram negative bacterium has provoked interest of bacteriologist, gastroenterologist, infectious diseases specialist, cancer biologists, epidemiologist, pathologist, and pharmaceutical scientists, The possibility that a bacterium could cause gastritis, peptic ulcer, and over time, cancer was a concept that was difficult to put forward. To convince colleagues and the public, Barry Marshall drank a suspension of the bacterium and proved Koch's postulates for gastritis and made the idea that *H. pylori* is the etiological agent of many gastric maladies more easy to swallow (Baako *et al.,* 2016).

Understanding the epidemiological aspects of *H. pylori* infection is significant and helpful in illustrating the consequences and complications of the infection. It is also fundamental for the eradication, treatment, and the establishment of the pattern of antibiotic resistance. Several Countries in the World Health Organization, Eastern Mediterranean Regional Office(EMRO) including a group of developing countries in southwest and western Asia as well as North Africa and the ancient land of Iran, have no systematic reviews on the prevalence and epidemiology of *H. pylori* infections (Eshraghian, 2014).

In most regions, the main mechanism of spread is intra familial transmission. The prevalence remains high in most developing countries and it is generally related to socioeconomic status and levels of hygiene. Understanding the global epidemiologic patterns of *H. pylori* will aid us in prioritizing and customizing public health efforts to better manage the burden of this disease (Hooi *et al.,* 2017).

2. SOURCE OF INFECTION

A number of studies have proposed that an acquisition of *H. pylori* occurs via a common environmental source. In particular, animals and water have been implicated as potential source of infection (Castro *et al.,* 2018).

H. pylori infection occurs when *H. pylori* bacterium infect stomach (Molina-Castro *et al.,* 2022). *H. pylori* bacterium is usually passed from person to person through direct contact with saliva, vomit, or stool (Sugimoto *et al.,* 2020). *H. pylori* may also be spread through contaminated food or water (Cheung *et al.,* 2022). The exact way *H. pylori* bacterium causes gastritis or a peptic ulce,r in some people is still unknown (World Health Organization, 2020).

2.1 Animals as the Potential Source of *H. pylori*

While humans are the primary reservoir for *Helicobacter pylori*, there is ongoing research into whether animals might also contribute to the bacterium's prevalence (Molina-Castro *et al.,* 2022). Some studies suggest that domestic animals, such as cats and dogs, may harbor *H. pylori* or related species, although definitive evidence of zoonotic transmission (from animals to humans) remains limited and controversial (Sugimoto *et al.,* 2020). Reports of *H. pylori*-like organisms in livestock, including pigs and cows, suggest these animals could potentially serve as reservoirs, but the significance of this is not well understood (Cheung *et al.,* 2022). Wild animals, including non-human primates, have also been found to carry *H. pylori* or similar bacteria, indicating that the bacterium might have a broader host range than previously thought (World Health Organization, 2020). Additionally, other *Helicobacter* species, such as *Helicobacter suis* and *Helicobacter heilmannii,* which infect animals, can occasionally infect humans and cause similar gastrointestinal issues (Molina-Castro *et al.,* 2022). Despite these findings, human-to-human transmission remains the primary source of *H. pylori* infection in humans (Sugimoto *et al.,* 2020). The potential role of animals in the transmission cycle of *H. pylori* is still an area of ongoing research, with current evidence not conclusively supporting animals as a significant source of human infection (Cheung *et al.,* 2022).

2.2 Water as a Potential Source of *H. pylori*

Water is considered a potential source of *Helicobacter pylori (H. pylori)* transmission, particularly in areas with inadequate sanitation and poor water quality (Molina-Castro *et al.,* 2022).

Studies have indicated that *H. pylori* can survive in water under certain conditions, suggesting that contaminated water could play a role in spreading the bacterium (Sugimoto *et al.,* 2020). *H. pylori* can persist in water for extended periods, especially in colder temperatures, and has been found in various sources, including rivers, lakes, wells, and even some municipal water supplies (Cheung *et al.,* 2022). Water can become contaminated with *H. pylori* through fecal matter, making fecal-oral transmission a significant concern in regions with poor sanitation (World Health Organization, 2020). Ingesting contaminated water or using it for food preparation can lead to infection (Molina-Castro *et al.,* 2022). Additionally, *H. pylori* can form biofilms in water distribution systems, making the bacteria more resistant to environmental stresses and disinfection processes (Sugimoto *et al.,* 2020). Epidemiological studies have found associations between *H. pylori* infection and the consumption of untreated or inadequately treated water, suggesting that improving water quality and sanitation can help reduce the prevalence of infection (Cheung *et al.,* 2022). To minimize the risk of waterborne transmission, it is essential to ensure access to clean and safe drinking water, treat and disinfect water supplies, protect water sources from fecal contamination, and promote good hygiene practices (World Health Organization, 2020). While human-to-human transmission remains the primary route for *H. pylori* infection, water is a potential source of transmission, particularly in regions with poor water quality and sanitation (Molina-Castro *et al.,* 2022). Ensuring access to clean water and improving sanitation practices are crucial steps in reducing the spread of *H. pylori* (Sugimoto *et al.,* 2020).

2.3 Routes of Contracting *H. pylori* Infection

Helicobacter pylori (H. pylori) infection is primarily contracted through several routes, most of which involve direct or indirect human-to-human contact (Molina-Castro *et al.,* 2022). The most common route is oral-oral transmission, occurring through direct contact with saliva, such as kissing or sharing utensils, drinking glasses, or other items that come into contact with the mouth (Sugimoto *et al.,* 2020).

Fecal-oral transmission involves ingesting food or water contaminated with fecal matter containing *H. pylori,* facilitated by poor hygiene practices, inadequate sanitation, and contaminated water supplies (Cheung *et al.,* 2022). Gastro-oral transmission can happen when *H. pylori* is regurgitated from the stomach into the mouth through vomiting or reflux, allowing the bacteria to come into contact with another person's mouth (Molina-Castro *et al.,* 2022). Waterborne transmission is another potential route, as *H. pylori* can survive in water sources under certain conditions, leading to infection when contaminated water is ingested or used for food preparation, especially in areas with poor sanitation and inadequate water treatment facilities (Sugimoto *et al.,* 2020). Foodborne transmission can occur through ingestion of contaminated food, particularly undercooked or raw food that has been in contact with contaminated water or surfaces, which is more common in regions with poor food hygiene practices (Cheung *et al.,* 2022). Additionally, environmental contamination plays a role, as *H. pylori* can form biofilms on surfaces, making the bacterium more resistant to environmental stresses and disinfection, leading to indirect transmission through contact with contaminated surfaces in communal areas such as bathrooms or kitchens (World Health Organization, 2020). Overall, improving sanitation, water quality, and food hygiene practices are crucial steps in reducing the spread of *H. pylori* infection (Molina-Castro *et al.,* 2022).

It is still not known exactly how *H. pylori* infections are spread (Sugimoto *et al.,* 2020). The bacterium have coexisted with humans for many thousands of years (Cheung *et al.,* 2022). The infections are thought to spread from one person's mouth to another (Molina-Castro *et al.,* 2022). They may also be transferred from feces to the mouth (World Health Organization, 2020). This can happen when a person does not wash their hands thoroughly after using the bathroom (Sugimoto *et al.,* 2020).

The bacterium is believed to cause stomach problems when they penetrate the stomach mucus lining and generate substances that neutralize stomach acids. This makes the stomach cells more vulnerable to the harsh acids. Stomach acid *H. pylori* together irritates the stomach lining and may cause ulcers in the stomach or duodenum, which is first part of the small intestine (Adesanya *et al.,* 2012).

2.4 Symptoms of *H. pylori* Infection

Most people with *H. pylori* infection are asymptomatic. When the infection lead to an ulcer, symptoms may include abdominal pain, especially the stomach is empty at night or few hours after meals. The pain is usually described as a gnawing pain (severe pain) and it may come and go. Eating taking antacid drugs may relieve this pain (Baako *et al.,* 2016).

A number of other symptoms that may be associated with *H. pylori* infections include excessive burping, feeling bloate, nausea, heartburn, fever, lack of appetite or anorexia, unintended weight loss, trouble swallowing, anemia, blood in stool, vomiting with blood, severe, sharp stomach pain, and halitosis (bad breath) (Harr et al., 2001).

2.5 Risk Factors or People at Risk for *H. pylori* Infection

Children are more likely to develop an *H. pylori* infection. The risk is higher mostly due to close contact and lack of proper hygiene. The risk for infection partly depends on the environment and living conditions. However, several studies have shown that lower socio-economic status, consumption of restaurant food, meat, non-filtered or boiled water and smoking are risk factors *for H. pylori* infection (Mustapha *et al.,* 2007). Poor hygienic practices such as not washing hands regularly, and the use of non-boiled water may contribute to its transmission. A positive family history of peptic ulcer is a risk factor for peptic ulcer. Other studies have shown that an individuals who ate outside three times or more during the week were four times more likely to have *H. pylori* infection compared with individuals who almost never ate outside (Mustapha *et al.,* 2007).

It is now understood that peptic ulcers are caused by this type of bacterium, rather than stress or eating food with high in acid. About ten percent (10%) of people infected with *H. pylori* develop a peptic ulcer, according to the Mayo clinic. Long term use of Non-steroidal anti-inflammatory (NSAIDs) also increases the risk of getting peptic ulcer (Mbengue *et al.,* 2017).

3. LABORATORY DIAGNOSIS of *H. pylori*

The choice of test depends to a large extent on availability, cost and includes a distinction between tests used to establish a diagnosis of the infection and those used to confirm its eradication (Aduful *et al.,* 2017). For the diagnosis of *H. pylori* infection, two types of techniques can be performed, invasive or non-invasive. Nowadays, the diagnosis should only be made in symptomatic cases, and it is not routinely indicated (Pohl et al., 2019).

4. COMPLICATIONS of *H. pylori* INFECTION

- Gastritis is a condition where stomach lining is inflamed. There are three (3) stages of gastritis; acute, chronic and atrophy phase. Acute phase is subclinical stage, where *H. pylori* penetrate through viscid mucous layer reaching epithelial cell where it multiplies. Epithelial cells react to this mucus depletion, cell exfoliation and compensatory regenerative changes. If immune response fails to eradicate the infection, in next 3 to 4 weeks, there will be change from acute phase to chronic phase. In this phase, the production of cytokine and specific *anti-H. pylori* antibodies by B-cell proliferation and plasma cell differentiation results in production of Ig-M antibodies and complement fixing antibody. But still if it fails to eliminate infection (Ogutu *et al.,* 2018)
- Peptic ulcer *H. pylori* causes an inflammatory response in gastric mucosa by inducing epithelium derived cytokines mainly interleukin 8 (IL8) and IL IB by the action of neutrophils, macrophages, lysosomal enzymes, leukotrienes (LT), and reactive oxygen species hampering mucosal defence and initiating the immuno pathogenetic process of ulcer formation. Urease catalyses production of ammonia, when there is an increase in concentration leading to the formation of toxic complex such as ammonie chloride, along phospholipases A and C impairs the phospholipid-rich layer in the mucosa that maintains mucosal hydration and integrity of the gastric epithelial barrier leading to ulcers (Al-Humayed *et al.,* 2010).

- Gastric cancer (GC) is the second cause for cancer related death worldwide, accounting nearly 11% of cancers in male and 7% in female. *H. pylori* infection is recognized a type 1 carcinogen by international agency of research on cancer. Multiple mechanisms are involved in carcinogenesis, among them important are production of relative oxygen species that causes DNA damage and mutation. Hyper methylation of gene promoter (CPG) island is associated with *H. pylori* infection and deregulation of many pathways; among them some are important pathways such as p53 pathway, P13 kinase/Akt pathway, Want pathway and NF-kB pathway (Castro *et al.,* 2018).
- Gastroesophageal reflux diseases (GERD) Is a multifaceted disorder where gastric acid coming up from the stomach into the oesophagus. The Montreal consensus conference defined (GERD) as `` a condition which develops when the reflux of gastric contents causes troublesome symptoms and/or complication. GERD symptoms are seen in 25-40% of the general population, the relationship between GERD and *H. pylori* are documented by many researchers and infection varies by geographic location. Non ulcer dyspepsia or functional dyspepsia; A symptom of upper gastrointestinal distress, without any identified structural abnormalities during diagnosis. Uninvestigated dyspepsia is defined as presence of dyspepsia symptoms for which no further diagnostic evaluation has been performed (Reshentyak *et al.,* 2017).

There are many possible causes for this, like lifestyle factors stress altered visceral sensation, increased serotonin sensitivity, Alteration in gastric secretion, gastric emptying and psycho-social impairment. *H pylori* infection maybe one of the factors among multifactorial etiology of the diseases.

H. pylori infections can lead to peptic ulcers, but the infection or the ulcer itself can lead to more serious complications. Complications may include the following:

- Gastric adenocarcinoma is the most severe consequence of *H. pylori* infection.
- Gastric MALToma: this may be treated with *H. pylori* eradication therapy and has a better prognosis than gastric adenocarcinoma.
- *H. pylori* infection associated with squamous cell esophageal cancer.

- *H. pylori* may play an important role in idiopathic thrombocytopenic purpura. This is due to anti-CagA antibodies that cross react with platelet antigens.
- Internal bleeding: This can happen when a peptic ulcer breaks through the blood vessel and is associated with iron deficiency, leading to an anemia.
- Obstruction: This can also happen when something like tumor blocks the food from living stomach.
- Perforation, which can happen when an ulcer breaks through the stomach wall.
- Peritonitis, which is an infection of the peritoneum, or the lining of the abdominal cavity.

5. TREATMENT of *H. pylori* INFECTIONS

Treatment can cure ulcer, and it may reduce the risk of developing stomach cancer. Normally there is need to take a combination of two different antibiotics, together with another drug that reduces the stomach acid. Lowering stomach acid helps the antibiotics work more effectively. This treatment is sometimes referred to as Triple or quadruple therapy.(*Otegbayo et al.,* 2014). Though, the only condition for which *H. pylori* treatment is indicated in duodenal ulcer which is very uncommon in children. Treatment for RAP or Dyspepsia is not warranted on clinical grounds. There are several treatment regimens available but it appears that at least three drugs including two antibiotics and a proton pump inhibitor are required for satisfactory eradication. In developing countries where the prevalence of infection is very high, well planned double blind cross – over studies are needed before an evidence based answer can be provided for an optimal Therapeutic strategy (Otegbayo *et al.,* 2014).

"Quadruple" therapy (in which triple therapy is combined with use of a PPI) has been shown to be more efficacious and associated with fewer side effects than has routine triple therapy. Such regimens would be especially appealing if the duration of quadruple therapy necessary to accomplish cure rate of 90% proved to be short.

Indeed, a cure rate of 72% with only 1 day of treatment by a regimen that could be considered a variant of quadruple therapy was highly (98%) effective (Adesanya *et al.,* 2012).

Other FDA- approved regimens are the dual therapies consisting of clarithromycin (500 mg three times a day) together with either Omeprazole (40 mg once daily) (cure, 74% or ranitidine bismuth citrate (RBC) (400 mg twice a day) (cure rate, 82% for 14 days. An earlier-touted dual therapy regimen, Omeprazole plus amoxicillin, is neither reliable nor FDA approved and should not be used. The American college of gastroenterology, in recognition of the suboptimal efficacy of the approved dual-therapy regimens, has recommended the addition of other antibiotics to these regimens. Preliminary results of two RBC modifications (a 2-week course of RBC (400 mg twice a day), Metronidazole (250 mg three times a day), and tetracycline (500 mg three times a day); or RBC (400 mg), clarithromycin (500 mg), and amoxicillin 1g) show excellent promise (Aduful *et al.,* 2017).

Among the most effective but not FDA- approved regimens are ``new`` triple-therapy regimens that are quite unlike "traditional" triple-therapy regimens in that the new regimens do not include bismuth compounds. They are known as 3-2-1 regimens: three medicines taken twice a day for 1 week. These regimens have been best studied in the so-called Mach 1 (M, Metronidazole; a, amoxicillin; c, Clarithromycin; *H. pylori;* 1, 1 week) trial Efficacy, defined per protocol but not by intention to treat, was 90 to 96% in this trial. In per protocol analyses, only patients who complete the entire protocol are included. This, patients who drop out due to side effects or other reasons are not included in the final analysis (Aduful *et al.,* 2017).

In contrast, in typical intention-to-studies, results from all patients who enter a given protocol are analyzed. Patients who drop out of intention-to-test studies are considered not to have been treated successfully. Results of intention-to-test analyses, which are more stringent than those of per-protocol analyses, are applicable to real-life situations (Oluwasola *et al.,* 2004).

- Side effects of treatment relate to the particular regimen chosen. Clarithromycin may cause taste disturbances, but this does not usually affect compliance. Metronidazole, particularly at a dose greater than 1g/day, may be associated with side effects.

Traditional triple therapy may be associated with ``mild`` side effects in about 50% of patients; vaginal candidiasis occurs in up to 10% of women. In general, pseudomembranous colitis occurs infrequently, although in one treatment regimen 11% of individuals developed this complication. Overall, discontinuation of therapy related to side effects occurs in less than 5% of patients. At present, the only clear indications for therapy are in patients with peptic ulcer disease or MALTomas. Of interest, extracts of a variety of plants inhibit the growth of *H. pylori* in vitro. Whether such extracts will prove useful in the treatment of infected patients' remains to be demonstrated Mbengue *et al.,* 2017). The aim of this research work is to determine the prevalence of *helicobacter pylor*i infections among patients attending Sir Yahaya Memorial Hospital Birnin Kebbi. However, to determine the prevalence of *H. pylori* with the use of serological test *Helicobacter pylori* Rapid Diagnostic Test (HPRDT), and to determine the *H. pylori* prevalence pattern among various age groups and in according to gender among patients with *H. pylori* ulcers attending Sir Yahaya Memorial Hospital Birnin Kebbi.

6. METHODOLOGIES

Study Area Description

Birnin Kebbi is a city located in Northwestern Nigeria. It is the capital city of Kebbi State. The city had an estimated population of 125,594 peoples. Birnin Kebbi is located within the latitudes 12° 27' 57.8808" N and longitude 4° 11' 58.2864" E, placing it in a tropical region.

Ethical Approval

This research was conducted with ethical approval from the Kebbi State Ministry of Health, Kebbi State Health Research Ethics Committee(KSHREC), dated (9th October, 2024), with approval number (107:059/2024).

Sample Collection

The patients consent was seeked for the blood collection. Fifty (50) blood samples were collected using EDTA container from Sir Yahaya Memorial Hospital, Birnin Kebbi. All the samples were transported to Sir Yahaya Memorial Hospital Birnin Kebbi Laboratory for analysis.

Socio Demographic Data Collection

Experimental Design

A descriptive transversal (John *et al.,* 2000). Epidemiological study, based on the serological determination of the IgG antibodies *H. pylori* was carried out on selected samples of patients without previous history of gastro duodenal antecedent. Patients were diagnosed in this study. Active *Helicobacter pylori* infection was determined using *H. Pylori* rapid diagnostic test (HPRDT)

Test Principle

The *H. Pylori* antibody rapid test cassette (whole blood, serum/plasma) is a qualitative membrane base immunoassay for the detection of *H. pylori* antibodies in whole blood, serum or plasma. In this test procedure, anti-human IgG immobilized in the test region of the test, after specimen were added to the specimen well of the device, it reacted with the *H. pylori* antigen coated particles with the immobilized anti-human IgG. If the *H. pylori* antibodies are present in the serum, a color line appear in the line region indicating a positive result. If the specimen does not contain *H. pylori* antibodies, a color line will not appear in this region indicating a negative result. To serve as a procedural control, a color line will always appear in the control line region, indicating that the proper volume of specimen has been added and membrane wicking has occurred (Megraud *et al.,* 2000).

Procedure

The test kit, specimen, buffer and control were allowed to reach room temperature (15-30^0 C)

Prior to testing was placed. The test cassette was removed from the sealed pouch and used within 1hour.

The cassette was placed on a clean and leveled surface. A dropper was used to transfer 4 drops of serum (approximately 100 micro liter) to the specimen well of the test cassette. The result was observed and recorded at 10 minutes (Loffeld *et al.,* 2000).

7. RESULTS

According to gender, this study have shown that sixteen (16) patients were male (13 positive and 3 negative), and thirty-four (34) patients were female (21 positive and 13 negative). However, in the case of age barrier, the study have identified eight (8) patients were less than <18 (5 positive and 3 negative), and fourty-two (42) patients were greater than>18 (29 positive and 13 negative) respectively.

Table 1. Prevalence of *H. pylori* Among Patients Attending Sir Yahaya Memorial Hospital Birnin Kebbi

No. of Samples	No. of positive (%)	No. of Negative (%)
50	34 (68%)	16 (32%)

Table 2. Prevalence of *H. pylori* According to Gender

Gender	No. Of patients	No. Of positive patients	No. Of negative patients	Percentage (%)
Male	16	13	3	38
Female	34	21	13	62
Total	**50**	**34**	**16**	**100**

Table 3. Prevalence of *H. pylori* According to Age

Age	No. Of patients	No. Of positive patients	No. Of negative patients	Percentage (%)
<18	**8**	**5**	**3**	**15**
>18	**42**	**29**	**13**	**85**
Total	**50**	**34**	**16**	**100**

8. DISCUSSION

The current research examine the prevalence of Helicobacter pylori among patients (male, female, children and adults) attending Sir Yahayya Memorial Hospital Birnin Kebbi which indicates a significant score rate in females (61.675%) and in adults (85.29%). This study aligns with previous studies conducted in developed and developing countries (Davidovic et al.,m 2005, Rosenberg, 2010). Accordingly, those studies have revealed that the H. pylori is the most important causes of peptic ulcer and more serious complication, and resulting in higher hospitalization and mortality rate.

Among the children, the total prevalence rate of H. pylori infection was 14.706%. This finding was in accordance with the study reported among children in other hospital-based studies in South-South (Etukudo et al., 2012) and South-east Nigeria (Emerenin et al., 2021), with prevalence rate of 30.9% and 20% respectively. This variation of prevalence rates reported in these studies could be as a result of difference in environmental settings and socio-economic status. Several studies in the literature have established unclean water as a source of H.pylori. (Aitila et al., 2019).

Socio-demographic characteristics are mostly considered as being associated with H.pylori infection status. Accordingly, low socio economic class is considered as an important factors in terms of H. pylori infection acquisition.

The limitation of this present study is that, the study is hospital-based and sample size of fifty (50) patients, therefore, the prevalence may not be a clear picture of the prevalence of the infection in the larger society.

CONCLUSION

In conclusion, the current study have shown that proper care and attention should be given to patients greater than eighteen (18) years of age to help curtain the chances of getting infected. Similarly, children, women, adults and old age should also be provided with necessary health education more particularly on personal hygiene.

However, environmental sanitation or proper hygiene should be properly observed by patients to help reduce risk of patients getting infected by Helicobacter pylori, and, awareness campaign/or frequent health education should be created and observed by government and non-governmental agencies to educate parents (literate and non-literate) on possible ways to prevent infections.

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CHAPTER 3
GASTRIC DISORDERS AND COLON CANCER: PATHOPHYSIOLOGY, RISK FACTORS, DIAGNOSIS, AND THERAPEUTIC ADVANCES – A COMPREHENSIVE REVIEW

[1]G. DAVID
[2]S. DEEPAK
[3]A. PALANISAMY
[4]C. RAVI

[1]Undergraduate Students, Faculty of Pharmacy, Bharath Institute of Higher Education And Research Chennai, India, daviddarry05@gmail.com, ORCID ID: 0009-0005-0428-9811
[2]Undergraduate Students, Faculty of Pharmacy, Bharath Institute of Higher Education And Research Chennai, India, deepakdpu2004@gmail.com, ORCID ID: 0009-0000-9307-8891
[3]Undergraduate Students, Faculty of Pharmacy, Bharath Institute of Higher Education And Research Chennai,India, palanipalani08050@gmail.com, ORCID ID: 0009-0006-8332-858X
[4]Undergraduate Students, Faculty of Pharmacy, Bharath Institute of Higher Education And Research Chennai,India, raviraviraviravi0686@gmail.com, ORCID ID: 0009-0001-8841-4210

INTRODUCTION

The gastrointestinal (GI) system is responsible for digestion, nutrient absorption, immune regulation, and maintenance of metabolic homeostasis. Disorders affecting this system can significantly impair quality of life and may progress to malignancy if left untreated.

Gastric disorders encompass a wide spectrum of conditions including inflammatory diseases such as gastritis and peptic ulcer disease, functional disorders such as dyspepsia, and neoplastic conditions including gastric and colon cancers. Colon cancer, also known as colorectal cancer, arises from the epithelial lining of the colon or rectum and often develops from precancerous adenomatous polyps (Dekker et al., 2019).

Chronic gastric and intestinal inflammation contributes significantly to carcinogenesis. Persistent inflammatory processes generate oxidative stress, DNA damage, and dysregulation of cellular signaling pathways, creating an environment conducive to malignant transformation (Wang & DuBois, 2015; Ullman & Itzkowitz, 2011).

The aim of this review is to provide a comprehensive overview of gastric disorders with particular emphasis on colon cancer, including epidemiology, molecular mechanisms, clinical presentation, diagnosis, management strategies, and emerging research directions.

1. EPIDEMIOLOGY AND GLOBAL BURDEN

Colorectal cancer is one of the most common malignancies worldwide. According to the World Health Organization and the Global Cancer Observatory, colorectal cancer ranks among the top three cancers in terms of incidence and mortality.(Sung et al., 2021; Bray et al., 2023).

Globally, millions of new cases are diagnosed annually, with significant mortality rates due to late detection. Incidence is higher in developed regions such as North America and Europe; however, developing countries are experiencing rapidly rising rates due to lifestyle transitions.(Arnold et al., 2017).

The disease predominantly affects individuals above 50 years of age, though early-onset cases are increasingly reported. Slight male predominance is observed in many populations.(World Health Organization.,2023; Bray, F., Colombet, M., Mery, L., & Piñeros, M.,2023; Siegel, R. L., Miller, K. D.,2023)

Geographic variation is influenced by dietary habits, environmental exposures, healthcare accessibility, and genetic predisposition. Countries with high red meat consumption and sedentary lifestyles show increased incidence. Early screening programs have reduced mortality in some developed nations, emphasizing the importance of preventive strategies.(Arnold et al., 2020).

2. CLASSIFICATION OF GASTRIC DIORDERS

Gastric disorders represent a diverse group of conditions affecting the stomach and large intestine, ranging from inflammatory and functional disturbances to malignant neoplasms. These disorders differ in etiology, pathogenesis, and clinical severity but often share overlapping risk factors such as diet, infection, stress, and genetic predisposition. Chronic inflammation remains a central mechanism linking many benign gastric conditions to malignant transformation. Proper classification aids in understanding disease progression and designing targeted therapeutic approaches.(Wang & DuBois, 2015)

2.1 Inflammatory Disorders

Inflammatory gastric disorders are characterized by persistent or acute inflammation of the gastrointestinal mucosa. Common examples include gastritis, peptic ulcer disease, and inflammatory bowel disease (IBD). Gastritis involves inflammation of the stomach lining and may result from infections, autoimmune mechanisms, prolonged nonsteroidal anti inflammatory drug (NSAID) use, alcohol consumption, or stress. Chronic inflammation leads to mucosal damage, epithelial cell turnover, and increased susceptibility to neoplastic transformation(Wang & DuBois, 2015). Peptic ulcer disease results from an imbalance between gastric acid secretion and mucosal protective factors. Continuous mucosal injury may lead to ulcer formation, bleeding, or perforation. Inflammatory bowel disease, including Crohn’s disease and ulcerative colitis, involves chronic inflammation of the intestinal tract.

Long-standing IBD significantly increases the risk of colorectal cancer due to repeated cycles of inflammation and regeneration, which promote DNA mutations and dysplasia.(Ullman & Itzkowitz, 2011; Kaser et al., 2010).

Inflammatory processes generate reactive oxygen species (ROS), pro-inflammatory cytokines, and growth factors that damage DNA and disrupt cellular regulation. Over time, this microenvironment fosters genetic instability and tumor development. Therefore, early diagnosis and effective control of inflammatory gastric disorders are essential to prevent long-term complications, including malignancy.(Wang & DuBois, 2015)

2.2 Functional Disorders

Functional gastric disorders are conditions in which patients experience chronic gastrointestinal symptoms without identifiable structural or biochemical abnormalities. These disorders are primarily related to disturbances in gut motility, visceral hypersensitivity, and brain–gut axis dysfunction. Although not directly malignant, persistent functional disorders can significantly impair quality of life and sometimes overlap with inflammatory conditions.

Functional dyspepsia is characterized by upper abdominal discomfort, bloating, early satiety, and nausea. It is thought to arise from abnormal gastric motility, impaired gastric accommodation, and heightened sensory perception. Irritable bowel syndrome (IBS) is another common functional disorder presenting with abdominal pain, altered bowel habits, and bloating. IBS is associated with stress, psychological factors, altered gut microbiota, and immune dysregulation. (Ford et al., 2020; Chey et al., 2015).

Emerging research suggests that subtle inflammatory changes and microbiome alterations may contribute to symptom development. Chronic stress can influence gut motility and immune responses through neuroendocrine pathways. Although functional disorders do not directly cause colon cancer, prolonged dysbiosis and chronic low-grade inflammation may create a permissive environment for disease progression in susceptible individuals.

Management focuses on dietary modifications, stress reduction, pharmacotherapy targeting motility, and probiotics to restore microbial balance.

Understanding functional disorders is important because symptom overlap may delay diagnosis of organic diseases such as colorectal cancer.(Ford, A. C., et al. 2020; Eswaran, S. 2015)

2.3 Neoplastic Disorders

Neoplastic gastric disorders involve abnormal and uncontrolled cell growth within the gastrointestinal tract. These include gastric cancer and colon cancer, both of which represent significant causes of cancer-related mortality worldwide. Neoplasms arise from cumulative genetic mutations, epigenetic changes, and environmental exposures that disrupt normal cell cycle regulation.(Baylin & Jones, 2016).

Colon cancer, commonly referred to as Colorectal cancer, typically develops through the adenoma–carcinoma sequence. This stepwise progression involves transformation of normal epithelium into adenomatous polyps, followed by dysplasia and invasive carcinoma. Key molecular alterations include mutations in tumor suppressor genes and oncogenes that regulate proliferation and apoptosis.(Fearon & Vogelstein, 1990; Dekker et al., 2019).

Gastric cancer follows a similar multistep process involving chronic inflammation, atrophy, intestinal metaplasia, dysplasia, and carcinoma. Environmental factors such as diet, smoking, and chronic infection contribute significantly to neoplastic transformation.(Wang & DuBois, 2015).

Neoplastic disorders are often asymptomatic in early stages, leading to delayed diagnosis and poor prognosis. Screening programs, especially colonoscopy for colorectal cancer, have significantly reduced mortality in developed countries. Early detection and molecular characterization allow for personalized treatment strategies, improving survival outcomes.(Rex et al., 2017; Dienstmann et al., 2017).

2.4 Complications of Gastric Disorders

Gastric disorders may lead to several complications if not diagnosed and treated at an early stage. Persistent inflammation of the gastric mucosa can result in ulcer formation, bleeding, perforation, and obstruction of the gastrointestinal tract.

Peptic ulcer disease is one of the most common complications, where continuous damage to the mucosal lining leads to painful sores that may cause severe bleeding or perforation. Chronic gastritis may also progress to atrophic gastritis, intestinal metaplasia, and eventually gastric cancer due to long-term mucosal damage and cellular mutation (Wang & DuBois, 2015).

In inflammatory bowel diseases such as ulcerative colitis and Crohn's disease, prolonged inflammation increases the risk of colorectal cancer because repeated injury and regeneration of epithelial cells promote genetic mutations (Ullman & Itzkowitz, 2011).

Severe gastric disorders may also cause malnutrition, anemia, and weight loss due to impaired digestion and absorption. Early diagnosis, proper medical management, and lifestyle modification are essential to prevent these complications and improve patient outcomes.

3. COLON CANCER (COLORECTAL CANCER)

3.1 Definition and Types

Colon cancer is a malignant tumor arising from the epithelial cells lining the colon or rectum. It is commonly referred to as colorectal cancer due to the shared pathological features of tumors occurring in both anatomical regions. The majority of cases (approximately 90–95%) are adenocarcinomas, originating from glandular epithelial cells responsible for mucus secretion. (Dekker et al., 2019).

Other histological subtypes include mucinous carcinoma, characterized by abundant extracellular mucin production, and signet-ring cell carcinoma, which contains cells filled with mucin displacing the nucleus. These subtypes are generally associated with more aggressive clinical behavior and poorer prognosis.(Rawla et al., 2019).

Tumors may be classified based on location (right-sided or left-sided colon cancer), stage (I–IV), and molecular characteristics such as microsatellite instability status. Early-stage tumors are confined to the mucosa and submucosa, whereas advanced stages involve lymph node spread and distant metastasis, commonly to the liver or lungs. (Dekker et al., 2019). Understanding tumor classification is essential for determining prognosis and guiding treatment decisions.

Histopathological evaluation remains the cornerstone of diagnosis, while molecular profiling increasingly informs targeted therapeutic approaches.(Dienstmann et al., 2017; Barsouk A.,2019).

3.2 Pathophysiology

The development of colon cancer follows a multistep process known as the adenoma–carcinoma sequence. This progression involves accumulation of genetic alterations that transform normal epithelial cells into malignant cells. One of the earliest events is mutation of the APC, leading to dysregulation of the Wnt signaling pathway and abnormal cell proliferation.(Fearon & Vogelstein, 1990; Clevers, 2006).

Subsequent mutations in the KRAS promote uncontrolled cellular growth through persistent activation of signaling cascades. Later-stage mutations in TP53 impair apoptosis and DNA repair mechanisms, allowing malignant cells to survive and accumulate further mutations.(Prior et al., 2012; Levine, 1997).

Another important mechanism involves microsatellite instability resulting from mismatch repair defects. This pathway is commonly observed in hereditary colorectal cancers and some sporadic cases.(Boland & Goel, 2010; Lynch et al., 2003).

Chronic inflammation contributes significantly to carcinogenesis by generating reactive oxygen species, pro-inflammatory cytokines, and growth factors. These factors induce DNA damage and promote a tumor-supportive microenvironment. Over time, these molecular changes culminate in invasive carcinoma capable of metastasis.(Wang & DuBois, 2015; Grady & Carethers, 2008).

3.3 Risk Factors

Colon cancer is influenced by both modifiable and non-modifiable risk factors. Age remains the most significant risk factor, with incidence rising sharply after 50 years. Dietary habits play a crucial role; low fiber intake and high consumption of red and processed meats increase carcinogen exposure within the colon.(Song et al., 2015; Thanikachalam & Khan, 2019).

Obesity and physical inactivity contribute to insulin resistance and chronic inflammation, both of which promote tumor development. Smoking introduces carcinogenic compounds that damage DNA, while excessive alcohol consumption generates acetaldehyde, a recognized carcinogen.Botteri et al., 2008; Fedirko et al., 2011).

Family history significantly increases risk, particularly in individuals with hereditary syndromes such as familial adenomatous polyposis and Lynch syndrome. Chronic inflammatory bowel

diseases, including ulcerative colitis and Crohn's disease, elevate risk due to persistent mucosal inflammation. (Lynch et al., 2003; Vasen et al., 2013; Ullman & Itzkowitz, 2011)

Understanding these risk factors is essential for implementing preventive strategies, including lifestyle modification and regular screening in high-risk populations.

4. MOLECULAR MECHANISMS

Colorectal carcinogenesis is driven by complex molecular alterations involving genetic mutations, signaling pathway dysregulation, microbiota imbalance, oxidative stress, and epigenetic modifications. One of the central pathways implicated is the Wnt/β-catenin signaling pathway. Mutation of the APC gene disrupts β-catenin degradation, resulting in its nuclear accumulation and activation of proliferation-related genes. This event represents an early and critical step in tumor initiation. (Clevers, H.,2006; Normanno, N., et al.2006; Garrett, W.S.2015)

The epidermal growth factor receptor (EGFR) pathway also plays a major role. Activation of EGFR stimulates downstream signaling cascades such as RAS–RAF–MAPK and PI3K–AKT pathways, promoting cell survival and proliferation. Mutations in KRAS lead to constitutive activation of these pathways, rendering certain targeted therapies ineffective.(Normanno et al., 2006; Prior et al., 2012).

Gut microbiota imbalance (dysbiosis) contributes to chronic inflammation and carcinogen production. Certain bacterial species produce toxins that induce DNA damage and activate inflammatory signaling pathways.

Chronic oxidative stress further generates reactive oxygen species that damage DNA, lipids, and proteins, accelerating malignant transformation.(Garrett, 2015; Schwabe & Jobin, 2013; Kamendulis, 2004).

Epigenetic alterations, including DNA methylation and histone modification, silence tumor suppressor genes without altering DNA sequence. These reversible changes offer promising therapeutic targets. Together, these molecular events interact dynamically, driving colorectal tumor initiation, progression, and metastasis.(Baylin & Jones, 2016).

5. CLINICAL MANIFESTATIONS

Clinical presentation of colorectal cancer varies depending on tumor location, size, and stage. Early-stage disease is often asymptomatic, which contributes to delayed diagnosis. As the tumor grows, patients may experience abdominal discomfort, cramping, and changes in bowel habits such as persistent constipation or diarrhea.(Dekker et al., 2019).

Right-sided colon cancers frequently present with iron-deficiency anemia due to occult bleeding, fatigue, and weakness. Left-sided tumors more commonly cause changes in stool caliber, obstruction, and visible rectal bleeding. Rectal cancers may present with tenesmus and a sensation of incomplete evacuation.(Rawla et al., 2019).

Systemic manifestations such as unexplained weight loss, anorexia, and malaise occur in advanced stages. Metastatic spread to the liver may cause hepatomegaly and jaundice, while lung metastasis may lead to respiratory symptoms.

Because symptoms overlap with benign gastrointestinal disorders, high clinical suspicion is necessary, particularly in individuals over 50 years or those with risk factors. Early recognition significantly improves prognosis. Screening programs play a critical role in detecting asymptomatic disease before progression to advanced stages.(Rex et al., 2017).

6. DIAGNOSTIC APPROACHES

Early and accurate diagnosis is essential for improving survival outcomes in colorectal cancer.

Colonoscopy remains the gold standard diagnostic tool, allowing direct visualization of the colonic mucosa and removal or biopsy of suspicious lesions. Histopathological examination confirms malignancy and determines tumor grade.(Rex et al., 2017).

Imaging techniques such as computed tomography (CT) and magnetic resonance imaging (MRI) are used for staging and assessing metastasis. Endoscopic ultrasound may assist in evaluating rectal tumors.(Van Cutsem et al., 2020).

Tumor markers such as carcinoembryonic antigen (CEA) are useful for monitoring treatment response and detecting recurrence, although they lack specificity for early diagnosis. Molecular diagnostics, including microsatellite instability testing and mutation analysis of genes such as TP53, guide targeted therapy selection. (Dienstmann et al., 2017).

Emerging non-invasive methods include stool DNA testing and liquid biopsy for circulating tumor DNA detection. These approaches offer promising alternatives for early screening and disease monitoring. A multidisciplinary diagnostic strategy combining clinical evaluation, endoscopy, imaging, and molecular analysis provides optimal patient management.(Imperiale et al., 2014; Thierry et al., 2014).

6.1 Biomarkers in Colon Cancer Diagnosis

Biomarkers play an important role in the early detection, diagnosis, prognosis, and monitoring of colorectal cancer. A biomarker is a biological molecule found in blood, stool, or tissues that indicates a normal or abnormal process or the presence of disease. In colorectal cancer, biomarkers help identify malignant changes at an early stage and guide personalized treatment strategies (Dienstmann et al., 2017).

One of the most commonly used biomarkers in clinical practice is carcinoembryonic antigen (CEA). CEA is a glycoprotein involved in cell adhesion that is normally present at low levels in adults but becomes elevated in many patients with colorectal cancer. Although CEA is not sufficiently sensitive for early screening, it is widely used to monitor treatment response and detect recurrence after surgery (Duffy, 2001).

Another important diagnostic approach involves fecal-based biomarkers. Fecal occult blood test (FOBT) and fecal immunochemical test (FIT) detect hidden blood in stool, which may indicate the presence of polyps or cancer. These tests are non-invasive and widely used in population screening programs. Stool DNA testing is a more advanced method that detects genetic mutations and abnormal DNA methylation associated with colorectal cancer (Imperiale et al., 2014).

Molecular biomarkers have become increasingly important with advances in cancer genetics. Microsatellite instability (MSI) is a key biomarker resulting from defects in DNA mismatch repair genes. Tumors with high microsatellite instability show better response to immunotherapy and have different prognostic characteristics compared to microsatellite-stable tumors (Boland & Goel, 2010).

Mutations in genes such as APC, KRAS, NRAS, and TP53 are also used as molecular markers. KRAS mutation testing is particularly important because tumors with KRAS mutations do not respond to certain targeted therapies against epidermal growth factor receptor (EGFR). Therefore, genetic testing helps in selecting the most effective treatment for individual patients (Normanno et al., 2006).

Recent advances have introduced liquid biopsy as a promising diagnostic tool. Liquid biopsy involves detection of circulating tumor DNA (ctDNA), circulating tumor cells, or microRNAs in blood samples. This method is minimally invasive and allows continuous monitoring of tumor progression and response to therapy (Thierry et al., 2014).

Epigenetic biomarkers, including DNA methylation patterns and histone modifications, are also being studied for early detection of colorectal cancer. These changes occur before visible tumor formation and may help identify high-risk individuals (Baylin & Jones, 2016).

Overall, the use of biomarkers has significantly improved the accuracy of colorectal cancer diagnosis and management. Combination of traditional screening methods with modern molecular biomarkers provides better early detection, prognosis evaluation, and personalized treatment planning, ultimately improving survival outcomes.

7. MANAGEMENT AND TREATMENT

Management of colorectal cancer requires a multidisciplinary approach integrating surgery, systemic therapy, radiation, and supportive care. Treatment decisions depend on tumor stage, molecular characteristics, patient performance status, and presence of metastasis.(Dienstmann et al., 2017).

Early-stage disease (Stage I–II) is primarily managed with surgical resection, whereas advanced stages require combined modality treatment. Personalized treatment strategies based on genetic and molecular profiling have significantly improved outcomes in recent years. (Dienstmann et al., 2017).

7.1 Surgical Treatment

Surgery remains the cornerstone of curative treatment for localized colorectal cancer. The primary objective is complete removal of the tumor with adequate margins and regional lymph node dissection. Procedures such as partial colectomy or total colectomy are selected depending on tumor location and extent.(Benson et al., 2023).

Minimally invasive laparoscopic surgery has gained widespread acceptance due to reduced postoperative pain, shorter hospital stay, and faster recovery compared to open surgery. To reduce local recurrence. Surgical intervention also plays a role in palliative care to relieve obstruction or bleeding in advanced disease.(Van Cutsem et al., 2020).

7.2 Chemotherapy

Chemotherapy is administered as adjuvant therapy following surgery to eliminate microscopic residual disease or as primary treatment in metastatic cases. Standard regimens commonly include 5-Fluorouracil, often combined with Oxaliplatin or oral Capecitabine.Longley et al., 2003; André et al., 2004).

These agents interfere with DNA synthesis and induce apoptosis in rapidly dividing tumor cells. Combination regimens such as FOLFOX have demonstrated improved survival rates.(André et al., 2004).

7.3 Targeted Therapy

Targeted therapy is an advanced form of cancer treatment that focuses on specific molecular pathways involved in tumor growth and progression. Unlike conventional chemotherapy, which affects both normal and cancer cells, targeted drugs act selectively on cancer-related proteins, thereby reducing damage to healthy tissues. One of the most important targets in colorectal cancer is the epidermal growth factor receptor (EGFR), which regulates cell proliferation and survival. Monoclonal antibodies such as cetuximab and panitumumab block EGFR signaling and are effective in patients whose tumors do not contain KRAS or NRAS mutations (Normanno et al., 2006).

Another important target is vascular endothelial growth factor (VEGF), which promotes angiogenesis, the formation of new blood vessels that supply nutrients to the tumor. Bevacizumab, a VEGF inhibitor, prevents tumor vascularization and slows cancer progression (Hurwitz et al., 2004). Targeted therapy is often combined with chemotherapy to improve treatment response and survival rates. Molecular testing before therapy is essential to select suitable patients and achieve better clinical outcomes (Dienstmann et al., 2017).

7.4 Immunotherapy

Immunotherapy is an advanced treatment method that works by stimulating the body's immune system to identify and destroy cancer cells. In colorectal cancer, immune checkpoint inhibitors have shown promising results, especially in patients with high microsatellite instability (MSI-H) or mismatch repair-deficient tumors. These drugs block inhibitory proteins such as programmed cell death-1 (PD-1) and programmed death ligand-1 (PD-L1), allowing immune cells to attack tumor cells more effectively. Agents such as pembrolizumab and nivolumab are commonly used in advanced or metastatic colorectal cancer. Immunotherapy is usually recommended when conventional chemotherapy is ineffective and has significantly improved survival in selected patients (Le et al., 2015; Overman et al., 2017).

7.5 Radiation Therapy

Radiation therapy is an important treatment modality mainly used in the management of rectal cancer rather than colon cancer because of anatomical considerations. It uses high-energy radiation to destroy cancer cells by damaging their DNA and preventing further growth and division. Radiotherapy is commonly given as neoadjuvant therapy before surgery to shrink the tumor, making surgical removal easier and reducing the risk of local recurrence. In some cases, it is also used after surgery as adjuvant therapy to eliminate remaining cancer cells. Radiation therapy is often combined with chemotherapy, a method known as chemoradiation, which enhances treatment effectiveness. In advanced stages, radiotherapy may be used for palliative purposes to relieve pain, bleeding, or obstruction, thereby improving the patient's quality of life (Sauer et al., 2004; Benson et al., 2023).

8. PREVENTION AND SCREENING

Prevention strategies for colorectal cancer focus on reducing modifiable risk factors and implementing effective screening programs. Lifestyle modification plays a critical role. Increased intake of dietary fiber, fruits, vegetables, and whole grains reduces contact time between carcinogens and colonic mucosa. (Song et al., 2015; Thanikachalam & Khan, 2019).

Limiting red and processed meat consumption lowers exposure to carcinogenic compounds. Regular physical activity helps regulate body weight and insulin levels, reducing inflammation-associated carcinogenesis. (Bardou et al., 2013; Giovannucci, 1995).

Screening is the most effective strategy for early detection. Colonoscopy remains the gold standard because it allows direct visualization and removal of precancerous polyps, thereby interrupting the adenoma–carcinoma sequence. Non-invasive methods such as fecal occult blood test (FOBT) and fecal immunochemical test (FIT) are widely used for population-based screening. Stool DNA testing is an emerging method detecting molecular alterations associated with cancer.(Rex et al., 2017; Imperiale et al., 2014). High-risk individuals, including those with family history or hereditary syndromes, require earlier and more frequent screening.

Public health initiatives promoting awareness and accessibility of screening programs have significantly reduced mortality in developed countries. Preventive strategies combined with early detection remain the most cost-effective approach to reducing global colorectal cancer burden.(Lynch et al., 2003; Vasen et al., 2013; Arnold et al., 2020).

9. DIET AND LIFESTYLE IN GASTRIC DISORDERS

Diet and lifestyle factors play a crucial role in the development and progression of gastric disorders, including gastritis, peptic ulcer disease, inflammatory bowel disease, and colorectal cancer. Modern dietary habits characterized by high intake of processed foods, red meat, refined sugars, and low fiber contribute significantly to gastrointestinal inflammation and mucosal damage (Song et al., 2015; Thanikachalam & Khan, 2019).

A diet low in dietary fiber slows intestinal transit time, increasing the duration of exposure of the intestinal mucosa to potential carcinogens. Fiber promotes the production of short-chain fatty acids by gut microbiota, which help maintain mucosal integrity and reduce inflammation. Therefore, inadequate fiber intake is strongly associated with increased risk of colorectal cancer and other gastric disorders (O'Keefe, 2016).

High consumption of red and processed meat has been linked to increased formation of N-nitroso compounds and heterocyclic amines during cooking, which are known carcinogens. These compounds can damage DNA in epithelial cells of the colon, leading to mutations that initiate tumor development (Bouvard et al., 2015).

Obesity is another major lifestyle-related risk factor. Excess adipose tissue promotes chronic low-grade inflammation by releasing pro-inflammatory cytokines such as tumor necrosis factor-α and interleukin-6. These mediators contribute to insulin resistance, oxidative stress, and increased cellular proliferation, all of which favor carcinogenesis in the gastrointestinal tract (Bardou et al., 2013).

Physical inactivity further aggravates these effects by reducing metabolic efficiency and impairing immune function. Regular exercise has been shown to decrease inflammation, improve gut motility, and reduce the risk of colon cancer (Giovannucci, 1995).

Alcohol consumption and smoking are also strongly associated with gastric mucosal injury. Alcohol irritates the stomach lining and increases acid secretion, while tobacco smoke introduces carcinogenic substances that cause DNA damage and impair healing of the gastrointestinal mucosa (Fedirko et al., 2011; Botteri et al., 2008).

In addition to harmful habits, protective lifestyle factors include a balanced diet rich in fruits, vegetables, whole grains, and probiotics. Antioxidants such as vitamins C and E help neutralize reactive oxygen species, reducing oxidative damage to the gastric epithelium. Probiotic bacteria help maintain healthy gut microbiota and reduce inflammation (Garrett, 2015).

Overall, diet and lifestyle modification remains one of the most effective and economical strategies for preventing gastric disorders and colorectal cancer. Public health programs emphasizing healthy nutrition, weight control, and regular physical activity are essential for reducing the global burden of gastrointestinal diseases

10. EMERGING THERAPIES AND RESEARCH TRENDS

Rapid advances in molecular biology and biotechnology are transforming colorectal cancer management. Identification of novel biomarkers, including circulating tumor DNA (ctDNA), microRNAs, and epigenetic signatures, offers promising tools for early detection and monitoring treatment response. Liquid biopsy techniques provide minimally invasive alternatives to traditional tissue biopsy.

Personalized medicine has become increasingly important. Molecular profiling enables stratification of patients based on genetic mutations, guiding targeted therapy selection and improving therapeutic outcomes. Immunotherapy combinations and novel immune checkpoint inhibitors are being actively investigated to overcome resistance.

Microbiome research has revealed the influence of gut bacteria on carcinogenesis and treatment response. Modulation of microbiota through probiotics, prebiotics, and dietary interventions is an emerging therapeutic strategy. Nanotechnology-based drug delivery systems aim to enhance precision targeting of chemotherapeutic agents while minimizing systemic toxicity.

Artificial intelligence and machine learning are also being integrated into imaging analysis and risk prediction models. These innovations collectively represent a paradigm shift toward precision oncology and improved patient-specific treatment strategies.

11. CHALLENGES AND FUTURE PERSPECTIVES

Despite significant progress, colorectal cancer management faces several challenges. Late-stage diagnosis remains common, particularly in low- and middle-income countries where screening programs are limited. Lack of awareness and healthcare disparities contribute to delayed presentation.

Drug resistance is a major obstacle, especially in advanced and metastatic disease. Tumor heterogeneity and genetic evolution during treatment lead to resistance against chemotherapy, targeted agents, and immunotherapy. Additionally, treatment-related toxicity affects patient quality of life.

High treatment costs create financial burdens and limit access to advanced therapies. Infrastructure limitations in resource-poor settings hinder implementation of molecular diagnostics and personalized medicine approaches.

Future directions should emphasize affordable screening tools, improved biomarker discovery, and development of novel therapeutics to overcome resistance mechanisms. Integration of genomics, microbiome science, artificial intelligence, and nanotechnology may revolutionize early detection and treatment. A comprehensive, globally coordinated effort focusing on prevention, early diagnosis, and precision therapy is essential to reduce mortality and improve long-term survival outcomes.

CONCLUSION

Gastric disorders and colorectal cancer represent a significant spectrum of gastrointestinal diseases that range from inflammatory and functional disturbances to life-threatening malignancies. Chronic inflammation emerges as a central link connecting benign gastric conditions to colorectal carcinogenesis. Persistent mucosal injury, oxidative stress, genetic mutations, and dysbiosis collectively create a microenvironment that favors tumor initiation and progression.

The adenoma–carcinoma sequence, along with key molecular alterations involving genes such as APC, KRAS, and TP53, highlights the complex, multistep nature of colorectal cancer development.

Globally, colorectal cancer continues to impose a substantial health and economic burden. Although advances in screening and early detection have reduced mortality in many developed regions, rising incidence in developing countries reflects the growing impact of westernized diets, sedentary lifestyles, obesity, and aging populations. Importantly, many risk factors remain modifiable. Dietary improvement, increased physical activity, smoking cessation, and weight management play a vital role in primary prevention.

Significant progress has been achieved in diagnosis and management through colonoscopic screening, molecular profiling, targeted therapies, and immunotherapy. Personalized medicine, microbiome research, and biomarker development are reshaping the therapeutic landscape and offering new hope for improved survival outcomes.

However, challenges such as late diagnosis, therapeutic resistance, limited healthcare access, and high treatment costs persist. A comprehensive strategy integrating prevention, early detection, equitable healthcare access, and innovative research is essential. Continued global efforts in public health policy, clinical research, and translational medicine will be critical in reducing the burden of colorectal cancer and improving patient outcomes in the future.

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ISBN: 978-625-92098-7-6