Review Article
http://mjiri.iums.ac.ir
Medical Journal of the Islamic Republic of Iran (MJIRI)

Med J Islam Repub Iran. 2025 (23 Apr);39.59. https://doi.org/10.47176/mjiri.39.59

A Study of the Effectiveness of Apoptosis Biomarkers in the Diagnosis of Gastric Cancer in Kazakhstan: A Review of Systematic Evidence

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Received: 15 Oct 2024 Published: 23 Apr 2025

Abstract

Background: Gastric cancer in Kazakhstan shows low survival rates due to late diagnosis. This study aimed to explore apoptosis biomarkers to improve early detection and diagnostic accuracy. By investigating biomarkers like p53, RAS, miRNAs, and inflammation markers, the study sought to identify potential indicators for better prognosis and survival outcomes.

Methods: This systematic review was conducted using the keywords "apoptosis biomarkers" OR "gastric cancer" AND "Kazakhstan" OR "Kazakhstani" in the PubMed and Google Scholar databases, yielding 2,025 records. After filtering, 24 studies were selected for analysis. Quality was assessed using the Newcastle-Ottawa Scale, and data were extracted and synthesized for critical findings.

Results: This systematic review on apoptosis biomarkers in gastric cancer diagnosis in Kazakhstan highlights key findings across diverse studies. Biomarkers with the strongest diagnostic potential include p53, RAS, miRNAs (e.g., miR-21, miR-34a), and inflammation markers like NLR (neutrophil-to-lymphocyte ratio), PLR (platelet-to-lymphocyte ratio), and SII (systemic immune-inflammation index). Cytokines, including IL-2 and TNF, were linked to prognosis. DNA repair markers such as γ-H2AX and 53BP1 correlated with improved survival rates. Male predominance was consistent, with 63.1% to 66.4% of participants being male. Key environmental risk factors include Helicobacter pylori infection and heavy metal contamination. Survival rates ranged from 7.3% (Stage IV) to 50.5% (Stage I). The study also observed a statistically significant reduction in mortality rates from 14.0 to 8.9 per 100,000 ($p<0.001$), reflecting improvements in cancer management and diagnostic interventions.

Conclusion: This review underscores the pivotal role of apoptosis biomarkers in gastric cancer diagnosis in Kazakhstan. Biomarkers such as p53, RAS, and inflammation indices are integral to prognosis. Personalized diagnostic approaches, early detection, and targeted treatments can significantly improve survival outcomes and cancer management in this population.

Keywords: Gastric cancer diagnosis, Survival rates, Early detection, Gender disparities, Oncology Diagnostics, Cancer Molecular Markers

Conflicts of Interest: *None declared*
Funding: *Implemented within the framework of grant funding for the scientific project: IRN No. AP23490776 "Prognostic value of gastric cancer biomarkers in relation to the Lauren classification", Aktobe, Kazakhstan.*

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Cite this article as: Tulyayeva A, Iztleuov Y, Kereyeva N, Aitmagambetova M, Akhmetova S. A Study of the Effectiveness of Apoptosis Biomarkers in the Diagnosis of Gastric Cancer in Kazakhstan: A Review of Systematic Evidence. *Med J Islam Repub Iran.* 2025 (23 Apr);39:59. https://doi.org/10.47176/mjiri.39.59

Introduction

Cancers of the stomach still rank among the leading global causes of death associated with cancer (1). In Kazakhstan, the prevalence is particularly high because of diet, infection with Helicobacter pylori, and environmental factors (2). A major challenge in the fight against gastric cancer (GC) is the delay in diagnosis, often leading to advanced-stage detection when treatment options are limited and less effective. Apoptosis, also known as programmed

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↑What is "already known" in this topic:
Gastric cancer in Kazakhstan is associated with low survival rates due to late-stage diagnosis. Several apoptosis biomarkers have been explored for their diagnostic potential, including p53, RAS, and miRNAs. Environmental factors, such as Helicobacter pylori infection, also play a significant role in the disease's progression.

→What this article adds:
This study synthesizes the role of apoptosis biomarkers in improving early diagnosis and prognosis of gastric cancer in Kazakhstan, highlighting potential biomarkers for targeted treatments and personalized diagnostic approaches to enhance survival outcomes.

cell death, is a process vital for the conservation of cellular stability. It is thus apparent that knowing the signification of apoptosis biomarkers will dramatically alter the detection and prompt treatment of gastric cancer (3). Several pathologies, including tumors, are characterized by malfunction in the apoptosis process, resulting in excessive cell growth (4, 5). Gastric cancer (GC) continues to be a problem around the world, especially in countries such as , Kazakhstan, where late diagnosis is prevalent and contributes to a high-impact fatal outcome (6). The apoptosis biomarkers assist in improving the measures taken against the disease and, even more importantly, its early detection and intervention (7). Gastric cancer is asymptomatic until it is advanced, and therefore prognosis is poor. The fraction classified as having more advanced stages of disease have 5-year survival losses of less than 30%, while this figure can easily be increased to over 90% with early detection (8).

Gastric cancer is a common solid tumor that now accounts for a large share of cancer death rates all over the world (9). No matter the advances in cancer treatment and the use of adaptive learning technologies, the prognosis of patients with gastric cancer remains poor, suggesting that state-of-the-art prevention strategies are lacking (10, 11). Nonetheless, new research have noticed an alarming increase in the incidence rates of younger adults 50 years or less (12).

The statistics reveal that more than half of the patients suffering from the complications caused by gastric cancers belong to developing nations, with varying risk distribution (13). High-risk countries are East Asia (China, Japan), Eastern Europe, Central Asia, and South America (14). Regions with low risks are Southern Asia, North/East Africa, North America, Australia, and New Zealand (15). Disparities on a geographical basis emphasize the need for an investigation into the apoptosis biomarkers for aiding in the early detection of pre-adenocarcinomas such as atrophic gastritis and hence effectuating personalized therapies to enhance treatment response rates and the rate of survival as well (16).

Apoptosis biomarkers can also be utilized to monitor disease progression and response to treatment, providing valuable information for clinicians (17). At present, the biomarkers that are routinely used in gastric cancer diagnostics with the greatest accuracy are carcinoembryonic antigen (CEA) and carbohydrate tumor markers, CA19-9 and CA72-4, among others (18). Nevertheless, these indexes have positive predictive value and do not, however, excel in the early diagnosis of gastric cancer (19). Furthermore, they do not help in the diagnosis of GC precursors such as atrophic gastritis, intestinal metaplasia, and dysplasia. Thus, looking for novel biomarkers is important for better outcomes and for increasing sensitivity for early diagnosis (20).

The literature examined the improvement in the diagnosis of gastric cancer in Kazakhstan, and advocated the adoption of European standards in healthcare, utilization of sophisticated technologies for increasing early diagnosis, decreasing diagnostic mistakes, and improving patient prognosis (21).

Kazakhstan encounters issues regarding healthcare services, particularly in the field of gastric cancer detection, due to a lack of screening, scarce diagnostic means, and insufficient number of oncologists. Additionally, geographical areas, especially rural ones, slow down the process of early diagnosis and treatment as well as the outcome of the patient (22, 23)

The introduction of gastric cancer screening using a gastroscopy in Kazakhstan in 2013 and its withdrawal in 2018 meant a deficit concerning early detection. Low participation in cancer screenings, when in action, stands at 15%, seeking, more public awareness and education as a way of improving the coverage of screening (24, 25). Gastric cancer is associated with genetic alterations such as p53, HER2, and RAS, which influence survival and treatment. In spite of their involvement, issues like tumor heterogeneity, inconsistencies in biopsies, and poor predictive value still exist, showing the promise of apoptosis biomarkers to enhance diagnosis and therapies (26–28).

In Kazakhstan, spastic gastric cancer takes its toll due to environmental risk factors, genetic load, and demographic elements. The differences in healthcare resources between rural and urban areas also determine the occurrence and treatment of the disease, underlining the importance of local approaches to public health (29, 30).

AI is revolutionizing the diagnosis of gastric cancer by making biomarker analysis more efficient, which in turn improves accuracy and establishes personalized treatments. It assists in early detection, biomarker validation, and clinical application. However, issues such as standardization, ethics, and penetration of technology need further investigation (31, 32).

Research conducted in Kazakhstan focused on the importance of apoptosis biomarkers in the diagnosis of gastric cancer by emphasizing their lower cost, technological requirements, and ease of use, which translates to better chances of early treatment for patients suffering from gastric cancer (33, 34). This leads to the crucial research question: Are there novel apoptosis biomarkers resulting from the existing studies that can help to detect gastric cancer in Kazakhstan patients early, and what specific measures must be taken to apply these findings into practice?

Research Problem

The increasing incidence and poor survival rates of gastric cancer in Kazakhstan highlight a critical need for improving diagnostic and therapeutic strategies. Despite these limitations, however, apoptosis biomarkers hold the potential to improve the sensitivity and specificity of gastric cancer diagnosis. However, recent reviews of such biomarkers are limited by translating these biomarkers' applications in preclinical studies to clinical settings, especially addressing how genetic mutations, immune responses, and inflammation markers contribute to the progression and prognosis of the disease. Furthermore, there are few studies devoted to the demographic and environmental characteristics of Kazakhstan, gender-related trends, and the differences in cancer incidence and mortality rates within the regions of the country.

Research Focus

The purpose of this research work will involve assessing the options available in using apoptosis biomarkers in diagnosing gastric cancer among Kazakh patients and involves the assessment of genetic mutations biomarkers such as p53, RAS, TNF, immune biomarkers such as IL-2, TNFα, inflammation ratio biomarkers such as NLR, PLR, and protein biomarkers such as HER2, c-myc. There is equal focus on age and gender in given populations, an evaluation of the impact of environmental factors like Helicobacter pylori as a factor in cancer development, and how these elements play out in affecting the progression of and survival from cancer. Furthermore, the emphasis is placed on the biomarkers' potential in the early stage of identification and better tailoring of treatment plans.

Research Aim

Therefore, the purpose of this study is to examine the diagnostic potential of the apoptosis biomarkers in the population of Kazakh gastric cancer patients, with the consideration of optimal biomarkers that might reflect the diagnostic efficacy, patient prognosis, and particular therapeutic management.

Methods

Study Design: A systematic literature review.

Search Strategy

As part of the study, a systematic literature search was conducted using the search terms "apoptosis biomarkers" OR "gastric cancer" AND "Kazakhstan" OR "Kazakhstani" for two databases: PubMed and Google Scholar. The choice of PubMed and Google Scholar was justified by their extensive coverage of biomedical research, clinical studies, and interdisciplinary articles, ensuring access to a wide range of literature relevant to the study's objectives. In the beginning, there were 2,025 records found, of which 145 were from PubMed, and 1880 were from Google Scholar. To refine the selection process, a year filter (2018-2024) was applied, resulting in the removal of 885 records. Duplicate records, which were removed, totaled 11. A follow-up evaluation was done on the remaining 1,129 articles to confirm the relevancy of certain keywords, and 1,084 studies were excluded due to irrelevance. This left 45 studies eligible for full-text assessment, and 24 studies were identified as highly relevant for further research, as presented in Figure 1.

Inclusion and exclusion criteria

The consideration process for the literature search was oriented towards selecting studies published between 2018 and 2024 and available in the English language, which considered studies on apoptosis biomarkers and gastric cancer, specifically on Kazakhstan or Kazakhstani populations.

Inclusion criteria were established to select studies that specifically evaluated cell apoptosis mechanisms in gastric cancer, provided detailed data on biomarkers associated

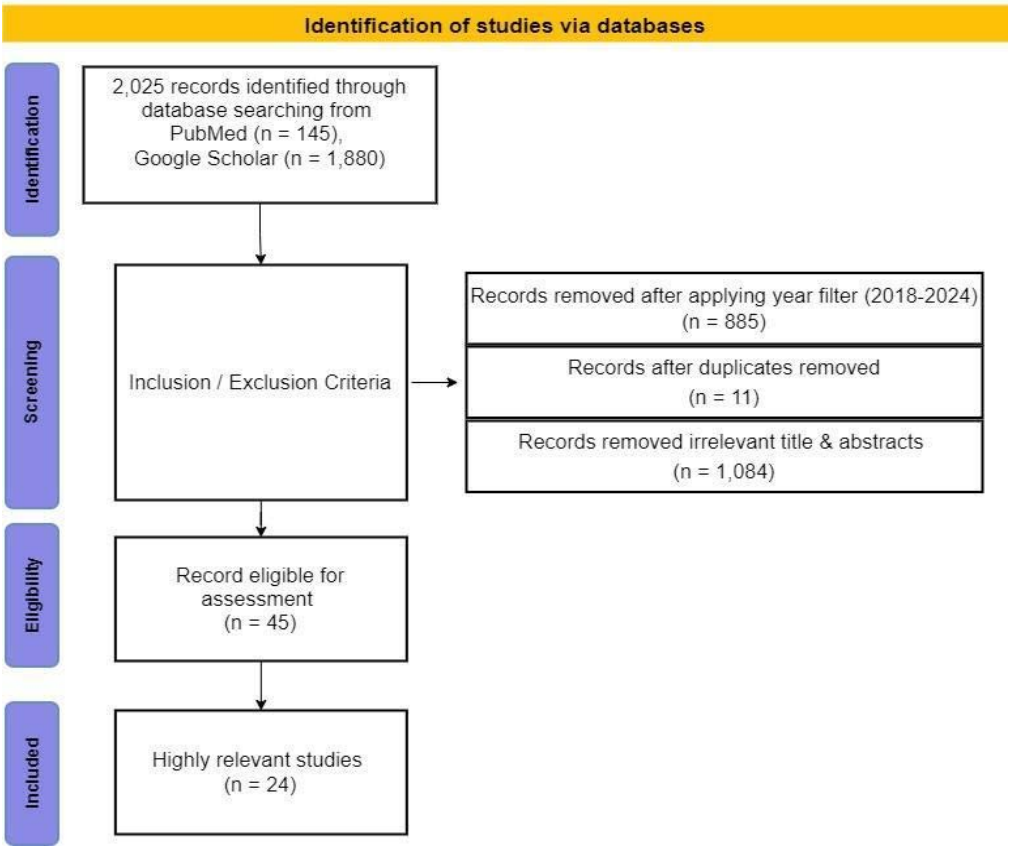

Figure 1. PRISMA flow diagram

with gastric cancer in patients from Kazakhstan, and utilized validated methods to measure and report apoptosis biomarkers. Biomarkers were defined and evaluated based on their roles in regulating programmed cell death (e.g., p53, RAS, miRNAs, cytokines such as IL-2 and TNF), with a focus on their diagnostic and prognostic potential. Relevant studies provided quantitative or qualitative analysis of these biomarkers and their association with patient outcomes.

Exclusion criteria eliminated duplicate studies from different databases, articles published in languages other than English, studies published before 2018, and those irrelevant to the themes of apoptosis and gastric cancer, including non-cancer-related apoptosis or other cancer types. Additionally, studies focusing on regions outside Kazakhstan, such as Kyrgyzstan, and articles with off-topic titles or abstracts lacking a focus on apoptosis biomarkers in gastric cancer were excluded. Only studies with logically dominant relevance to the research theme—apoptosis biomarkers in gastric cancer patients from Kazakhstan—were retained for content analysis. The inclusion criteria ensured that selected studies comprehensively addressed biomarkers relevant to apoptosis, such as DNA repair markers (γ-H2AX, 53BP1), inflammation indices (NLR, PLR, SII), and their diagnostic or prognostic value in gastric cancer.

Data analysis

Data analysis was performed within a form that directly corresponded to one prepared by the reviewers in an Excel spreadsheet. The form aimed to extract the main characteristics of each study, which include year of publication, study design, number of subjects, age range of subjects, gender distribution, biomarkers analyzed for apoptosis, survival rates, and main outcomes assessment. Having selected the twelve studies, great care was taken in reading them, and the necessary data was captured in the Excel sheet for comparison and integration. The review team assessed the types of biomarkers evaluated, recorded how the studies were designed, and noted how the survival rates and other outcomes varied among the studies. In this way, it provided both accurate, thorough analysis of the key features of the presentation of main biomarkers associated with apoptosis and their clinical relevance in esophageal cancer management in the Kazakhstan region. Findings were then triangulated, looking for similarities, differences, and things that needed to be studied further.

Results

Quality assessment

For this study, the assessment of quality was undertaken using the Newcastle-Ottawa Scale (NOS), an internationally accepted instrument for evaluating systematic errors in studies. This tool evaluates studies based on their selection, comparability, and outcomes. In the assessment Figure 2, most reviewed studies were rated with a bias risk of Low Risk, particularly in domains such as representation of cohorts (D1), selection of external control (D2), and outcomes (D4, D7). However, certain studies exhibited Unclear Risk in domains like sufficient follow-up time (D8) and adequacy of follow-up (D9), and High Risk in comparability of cohorts (D6) and incomplete outcome data (D5). These findings highlight the overall high quality of the studies while also identifying methodological concerns in specific

Figure 2. Quality assessment (Newcastle-Ottawa Scale) of selected studie

areas that may require cautious interpretation of the outcomes.

Table 1 shows the results of the current systematic review on the effectiveness of apoptosis biomarkers in the diagnosis of gastric cancer in Kazakhstan based on a diverse set of studies featuring varying designs, sample sizes, age ranges, and gender distributions. Large-scale retrospective studies involved sample sizes of 27,467 and 19,672, respectively, focusing on older populations aged 60-85+ years. These studies revealed a consistent male predominance, with 63.1% of participants being male in one study and 64.2% male in another. Another study similarly reported 66.4% of males in their sample of 1,458 participants aged 18 and above, further emphasizing gender-related patterns. Case-control studies reported that 52.4% of gastric cancer cases and 81.1% of controls were male in a sample of 498 individuals aged around 55 years. Descriptive studies, which involved 22 participants, revealed a gender split of 59% males and 41% females, while other smaller-scale experimental studies lacked complete gender data. Additionally, cross-sectional studies reported that 59% of their 166 participants aged 40-64 were male. Overall, this review emphasizes the significant role of apoptosis biomarkers in gastric cancer diagnosis, with male predominance consistently observed across most studies. The large sample sizes and demographic data provide valuable insights into the variations in biomarker effectiveness based on gender and age in the Kazakh population, reinforcing the importance of tailoring diagnostic approaches to these demographic factors.

Table 2 shows the investigation of apoptosis biomarkers in the diagnosis of gastric cancer in Kazakhstan, which has focused on several key biomarker types, each explored in various studies. Genetic mutations and polymorphisms have been a primary focus, with biomarkers such as p53, RAS, TNF, KRAS, and miRNAs playing a crucial role in understanding the genetic foundations of gastric cancer. Studies (36,40,47,52,54) specifically addressed these genetic components, providing a detailed exploration of how mutations and gene variations contribute to cancer progression. Among these, p53 and miRNAs have shown particular promise in diagnosing gastric cancer at early stages, especially in male patients.

Cytokines and immune response markers have also been extensively studied, particularly cytokine levels like IL-2, TNFα, and IFNγ, as well as immune response markers and

Table 1. Overview of Study Designs, Sample Characteristics, and Gender Distribution

Author's & Year	Study Design	Sample Size	Age Range	Gender Distribution
Taszhanov et al. 2022 (35)	Retrospective	27,467	60-74 years	63.1% male and 36.9% female
Yermekova et al. 2023 (36)	Experimental	433	40 to 75 years	-
Sharip et al. 2024 (37)	Descriptive	22	48-74 years	13 males (59%) and 9 females (41%).
Kassymbekova et al. 2024 (38)	Observational	2 million	0 to 85+ years	-
Balmagambetova et al. 2020 (39)	Retrospective	1,458	18 and ≥70 years	66.4% males (968) and 33.6% females (490).
Kulmambetova et al. 2020 (40)	Case-control	498	55 years	52.4% males in GC cases and 81.1% males in controls
Umurzakov et al. 2022 (41)	Retrospective	6,779	-	-
Zhandossov et al. 2018 (42)	Experimental	62	-	-
Tulyayeva et al. 2021 (43)	Retrospective	793	18 - 60+ years	34.9% female and 65.1% male
Isajevs et al. 2021 (44)	Cross-sectional	166	40–64 years	59.0% males and 41.0% females
Mezmale et al. 2021 (45)	Cross-sectional	166	40 to 64 years	59% male and 41% female
Komekbay et al. 2024 (46)	Observational	109	27 to 81 years	70.6% male and 29.4% female
Rakhimbekova et al. 2024 (47)	Observational	214	-	-
Uzun et al. 2020 (48)	Retrospective	262	-	males 64.4% and females 35.6%; males 70.3% and females 29.7%
Igissinov et al. 2022 (49)	Retrospective	19,672	30 to 85+	Males 64.2% and Females 35.8%
Mezmale et al. 2019 (50)	Cross-sectional	157	40 to 64	Female 40.1% and Male 59.9%
Igissinov et al. 2019 (51)	Retrospective	12,946	50 - 70+ years	-
Akimniyazova et al. 2021 (52)	-	69	-	-
Tulyayeva et al. 2024 (53)	Comparative	60	-	-
Kulmambetova et al. 2018 (54)	Case-control	158	±6 years	-
Taszhanov et al. 2020 (55)	Retrospective	27,468	-	-
Zakiryanova et al. 2019 (56)	Experimental	19	39–84	15 men, 4 women
Şahinli et al. 2020 (57)	Retrospective	95	22-84 years	females 27.4% and males 72.6%
Kerimkulov et al. 2024 (58)	Retrospective	136	-	-

Table 2. Summary of Biomarkers and Analytical Methods Used in Studies on Gastric Cancer Diagnosis in Kazakhstan

Biomarkers	Description	Studies
Genetic Mutations and Polymorphisms	Biomarkers related to gene mutations, polymorphisms, and candidate genes (p53, RAS, TNF, KRAS, miRNAs).	(36,40,47,52,54)
Cytokines and Immune Response Markers	Cytokine levels (IL-2, TNFα, IFNγ), immune response markers, and antibodies to Helicobacter pylori.	(42,45,54,56)
DNA Damage and Repair Markers	Biomarkers related to DNA damage and repair (γ-H2AX and 53BP1).	(53)
Protein and Histological Biomarkers	Histology types, protein expression (HER2, c-myc), gastric atrophy (Pepsinogen I/II), and PSA screening.	(39,41,44,46,50)
Inflammation and Survival Markers	Inflammation ratios (NLR, PLR, SII), Kaplan-Meier survival curves, DALYs, and gene expression (DEGs).	(37,38,43,50,57)

antibodies to Helicobacter pylori. Studies (42,45,54,56) highlighted the significant role that immune responses play in the development and progression of gastric cancer. These studies examined the immune system's interaction with the tumor environment, showing the potential of cytokines and immune markers as diagnostic and prognostic tools. In particular, elevated TNFα levels have been linked to advanced-stage gastric cancer, offering potential for use in both diagnostic and prognostic models.

DNA damage and repair markers, such as γ-H2AX and 53BP1, were examined in the study (53). These biomarkers are critical in understanding how DNA damage and the body's repair mechanisms influence cancer development. The focus on DNA repair mechanisms provides insights into how the integrity of genetic material is compromised in cancerous cells and how these mechanisms could be targeted for treatment. Among DNA repair markers, γ-H2AX is particularly relevant in high-risk populations, correlating with poorer survival outcomes.

Protein and histological biomarkers were studied in detail across multiple studies (39,41,44,46,50), focusing on histological types, protein expression (e.g., HER2, c-myc), gastric atrophy (Pepsinogen I/II), and PSA screening. These studies offered insights into how changes at the protein level and histological alterations in gastric tissues can be used to diagnose and track the progression of gastric cancer. HER2 overexpression, particularly in younger patients, has demonstrated strong diagnostic potential in early-stage gastric cancer.

Finally, inflammation and survival markers were another area of focus, with studies (37,38,43,50,57) investigating inflammation ratios such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic immune-inflammation index (SII). These markers, along with survival metrics like Kaplan-Meier curves and disability-adjusted life years (DALYs), provide valuable information about patient outcomes and the progression of the disease. Gene expression markers (DEGs) were also considered as part of this category, contributing to a deeper understanding of how gene expression patterns correlate with inflammation and survival in gastric cancer patients. The NLR and PLR ratios have shown high sensitivity in predicting poor survival in advanced stages of gastric cancer, particularly in older male patients.

In summary, the extensive range of biomarkers studied, spanning genetic mutations, immune response, DNA repair, protein expression, and inflammation markers, demonstrates the complexity of diagnosing and treating gastric cancer in Kazakhstan. These biomarkers provide critical insights into the mechanisms underlying cancer progression and offer potential pathways for improving diagnostic accuracy and therapeutic strategies.

Table 3 provides a comprehensive overview of survival rates across studies investigating apoptosis biomarkers in gastric cancer. The survival outcomes vary significantly, reflecting different stages of the disease and patient conditions. One study reports a poor prognosis, with 5-year survival rates ranging from 10-25%, indicating the aggressive nature of gastric cancer in this population (37). Another study shows a 5-year survival rate of 28.4% and a median survival of 8 months, with the best outcomes observed at Stage I, where survival reaches 50.5%, and the worst at Stage IV, where it drops to 7.3% (39). This highlights the critical role of early-stage diagnosis in improving survival rates.

Another report presents data on both prostate cancer (PCa) and testicular cancer (TCa), with 5-year survival rates for PCa ranging from 20.7% (2016) to 32.5% (2011), while TCa shows better survival outcomes, ranging from 55.6% (2010) to 62.2% (2019) (41). These differences underscore the variability in cancer survival based on type and year of diagnosis. Meanwhile, another study reports a 1-year survival rate of 33.1% and a 5-year survival rate of just 8.4%, highlighting the severe prognosis for gastric cancer

Table 3. Survival Rates in Studies Investigating Apoptosis Biomarkers

Author's & Year	Survival Rates
Sharip et al., 2024 (37)	The 5-year survival rate typically ranges from 10-25%.
Balmagambetova et al., 2020 (39)	Five-year survival rate = 28.4%, Median survival = 8 months. Best survival at Stage I (50.5%), worst at Stage IV (7.3%).
Umurzakov et al. 2022 (41)	PCa: Five-year survival ranged between 20.7% (2016) and 32.5% (2011). TCa: Five-year survival ranged from 55.6% (2010) to 62.2% (2019).
Tulyayeva et al., 2021 (43)	One-year survival is 33.1%, and Five-year survival is 8.4%.
Isajevs et al., 2021 (44)	Focused on the prevalence and subtypes of IM rather than patient outcomes.
Uzun et al., 2020 (48)	With and without lymph node involvement had a survival rate of 32.6% and 75.9, respectively. Lymph node involvement is a significant prognostic factor.
Igissinov et al. 2022 (49)	The overall 5-year survival rate was not explicitly mentioned, but the study indicates that most cases (70%) are diagnosed at late stages, contributing to low survival rates.
Igissinov et al. 2019 (51)	Mortality-to-incidence ratio (M/I ratio) varies by age group, with higher ratios observed in the 70+ age group: M/I for esophageal cancer: 0.92 (70+ years) M/I for stomach cancer: 0.97 (70+ years)
Taszhanov et al. 2020 (55)	The study shows a significant decline in mortality from GC, with the annual mortality rate decreasing from 14.0 per 100,000 in 2009 to 8.9 per 100,000 in 2018 (p=0.000). Reflects progress in treatment and prevention strategies.
Şahinli et al. 2020 (57)	Median overall survival (OS): 33 months. Disease-free survival (DFS): This was not reached in some groups but was shorter in those with higher NLR, PLR, and SII values (e.g., the PLR high group had 13 months of DFS). Higher PLR associated with poorer DFS
Kerimkulov et al. 2024 (58)	1-year survival: 78.6% 3-year survival: 34.9% Disease-free survival: 76.8% (1 year), 39% (3 years)

patients in this cohort (43).

One study shows a stark contrast in survival based on lymph node involvement, with a survival rate of 75.9% for patients without lymph node involvement compared to 32.6% for those with lymph node involvement, emphasizing the prognostic importance of lymph node status (48). Lymph node status is critical in predicting survival and highlights the need for targeted treatment strategies**.** Another study did not explicitly state the overall 5-year survival rate but noted that 70% of cases were diagnosed at later stages, contributing to low survival rates (49). Similarly, a report on mortality-to-incidence ratios (M/I) found M/I for esophageal cancer at 0.92 and stomach cancer at 0.97 in patients aged 70+, indicating a high mortality rate in elderly populations (51).

One report highlights a significant improvement in gastric cancer outcomes, with the annual mortality rate decreasing from 14.0 per 100,000 in 2009 to 8.9 per 100,000 in 2018 (P=0.000) (55), reflecting progress in treatment or prevention. This suggests the potential impact of advancements in treatment protocols and early detection methods**.** Another study reports a median overall survival (OS) of 33 months, with shorter disease-free survival (DFS) in patients exhibiting higher inflammatory markers such as NLR, PLR, and SII, where the high PLR group had a DFS of 13 months (57). The association between high PLR levels and shorter DFS indicates the importance of inflammatory biomarkers in prognosis.

Lastly, another study presents a 1-year survival rate of 78.6% and a 3-year survival rate of 34.9%, with disease-free survival at 76.8% after 1 year and 39% after 3 years, showing a sharp decline over time (58). Overall, these statistics illustrate the variation in survival outcomes based on cancer stage, biomarker expression, and patient conditions, highlighting the importance of early detection and individualized treatment strategies for improving survival in gastric cancer patients.

Table 4 shows the results of the current systematic literature review on apoptosis biomarkers in gastric cancer diagnosis in Kazakhstan and highlights several key findings across various research areas. Genetic mutations and biomarkers were identified in several studies (36,40,52,54), revealing significant mutations in genes such as p53, RAS, and miRNAs, along with genetic polymorphisms in TNF, IL10, and TP53, all of which are recognized as risk factors for gastric cancer. These genetic alterations are critical in understanding the development of the disease. Among these biomarkers, p53 mutations and miRNAs show strong diagnostic potential, particularly in advanced stages of gastric cancer.

In the area of immune response and inflammation, studies (37,42,57) demonstrated an increased immune response, particularly in chemoimmunotherapy, identifying key immune pathways like IL-2 and TNFα. Inflammatory markers such as NLR, PLR, and SII were also associated with poorer prognoses, highlighting the detrimental impact of heightened inflammation in cancer progression. NLR and PLR have been shown to be particularly relevant in predicting outcomes for patients with advanced-stage disease.

The review also noted a decline in gastric cancer incidence and mortality according to several studies (35,38,39,49,51,55), which emphasized regional differ-

Table 4. Summary of Findings on Apoptosis Biomarkers in Gastric Cancer Diagnosis: A Systematic Literature Review in Kazakhstan

Main Group	Sub-Group	Studies
Genetic Mutations and Biomarkers	Studies identified significant gene mutations (p53, RAS, miRNAs) and genetic polymorphisms (TNF, IL10, TP53) as risk factors for gastric cancer. p53 mutations and miRNAs show strong diagnostic potential, particularly in advanced stages	(36,40,52,54)
Immune Response and Inflammation	Studies reported increased immune response in chemoimmunotherapy, identification of immune pathways (IL-2, TNFα), and high inflammatory markers (NLR, PLR, SII) as poor prognostic factors NLR and PLR are particularly relevant in predicting outcomes for patients with advanced-stage disease.	(37,42,57)
Gastric Cancer Incidence and Mortality	Studies show a decrease in gastric cancer incidence and mortality, highlighting regional differences, demographic factors, and improvements in early diagnosis. Targeted early detection programs, particularly for older males, could help further reduce mortality.	(35,38,39,49,51,55)
Survival and Prognosis	Studies revealed poor survival outcomes for advanced-stage gastric cancer, with better survival linked to specific types (intestinal, lymph node-negative), and biomarkers of DNA damage/repair (γ-H2AX, 53BP1). H2AX and 53BP1 biomarkers hold significant promise for improving prognosis, particularly in early-stage gastric cancer	(41,43,48,53)
Environmental and Risk Factors	Studies highlighted Helicobacter pylori infection, heavy metal soil contamination (copper, lead), and pepsinogen levels as risk factors for gastric cancer. Helicobacter pylori infection remains a major risk factor, especially in younger populations, underscoring the need for targeted screening and prevention measures.	(45,47,50)
Treatment and Effectiveness	FLOT chemotherapy, HER2 positivity, c-myc expression, and IM subtyping were effective diagnostic or treatment tools for gastric cancer in high-risk patients. FLOT chemotherapy and HER2 positivity have shown significant effectiveness in treating high-risk gastric cancer patients, particularly those with advanced stages.	(44,46,56,58)

ences, demographic factors, and improvements in early diagnosis as contributing to these reductions. This trend indicates progress in the management and detection of gastric cancer. These findings suggest that early detection programs targeting high-risk demographics, such as older males, could help further reduce mortality.

In terms of survival and prognosis, studies (41,43,48,53) indicated that survival outcomes remain poor for advanced-stage gastric cancer. However, better survival rates were observed for specific cancer subtypes, such as intestinal and lymph node-negative cases. Biomarkers related to DNA damage and repair, such as γ-H2AX and 53BP1, were linked to better prognostic outcomes, providing new avenues for treatment and monitoring. γ-H2AX and 53BP1 biomarkers hold significant promise for improving prognosis, particularly in early-stage gastric cancer.

Environmental and risk factors were also explored, with studies (45,47,50) identifying Helicobacter pylori infection, heavy metal contamination (copper, lead), and elevated pepsinogen levels as significant contributors to gastric cancer risk, emphasizing the role of environmental exposures in disease development. Helicobacter pylori infection remains a major risk factor, especially in younger populations, underscoring the need for targeted screening and prevention measures.

Finally, in terms of treatment and effectiveness, several studies (44,46,56,58) found that FLOT chemotherapy, HER2 positivity, and c-myc expression were effective treatments, particularly in high-risk patients. Additionally, intestinal metaplasia (IM) subtyping emerged as a valuable diagnostic tool, aiding early detection and improving treatment outcomes for gastric cancer. FLOT chemotherapy and HER2 positivity have shown significant effectiveness in treating high-risk gastric cancer patients, particularly those with advanced stages.

Overall, the findings provide a comprehensive understanding of the interplay between genetic, environmental, and immune factors in the diagnosis and treatment of gastric cancer, with implications for improving survival and prognosis in Kazakhstan.

Discussion

The current study summarizes the systematic literature review on apoptosis biomarkers in diagnosing gastric cancer in Kazakhstan, revealing diverse research designs and sample sizes that enhance the findings' robustness. Most studies focused on middle-aged to elderly populations, correlating with the higher incidence of gastric cancer in these age groups, while a notable predominance of male participants was observed. Despite gaps in gender and age data in some studies, the review suggests a solid framework for assessing these biomarkers. Overall, the findings highlight the need for targeted research to refine diagnostic accuracy and improve therapeutic outcomes for gastric cancer patients in Kazakhstan. Similarly, larger studies demonstrate greater robustness against biases, such as selection bias or variability in participant characteristics, which are common in smaller studies. This robustness is crucial for assessing biomarkers that may vary in expression or effect based on demographic factors (59). However, it is essential to critically evaluate the feasibility of such large-scale studies in regions with limited research funding and medical infrastructure, as well as the ability to recruit a representative sample**.** Another study highlights that gastric cancer, often diagnosed at advanced stages, poses significant treatment challenges, particularly for men. The overall survival rates have not increased as a result of conventional therapies, which calls for the search for new biomarkers and targets for treatment. The development in the field of bioinformatics and functional genomics has made it possible to examine biomarkers that are associated with treatment response, survival, and recurrence, which can enable early detection and appropriate course of treatment for patients. However, the practical integration of bioinformatics tools into clinical workflows remains a significant hurdle, especially in settings with limited technical expertise or infrastructure (8).

Another study assesses the prognostic value of systemic inflammation-based score and immune inflammation metrics in the population of gastric cancer patients undergoing minimally invasive gastric surgery. Among 412 patients, the independent prognostic factors for overall survival (OS) estimate were ASA-PS, tumor grade, pTNM stage, and CEA levels. The SII was noted to be a significant prognostic indicator, particularly among inflamed OS patient populations, while no such prognostic relevance was found for non-inflamed populations. This implies that SII is most helpful in cases of inflammatory gastric cancer. However, the clinical utility of SII in routine practice must be further validated through prospective studies, and its applicability in low-resource settings where patients may not have access to the necessary immunologic testing needs to be explored (60). Another study shows that the SII has been proposed as a comprehensive marker reflecting the balance between immune response and inflammation. Studies have shown that lower SII values are associated with better tumor differentiation and improved survival rates post-surgery. For instance, patients with low SII exhibited significantly longer median OS compared to those with high SII values (61). The clinical utility of SII, though promising, requires careful consideration in real-world settings where patient heterogeneity, particularly in resource-poor regions, may complicate its interpretation and be used as a reliable biomarker**.**

The need to emphasize the new role of liquid biopsy in gastric cancer, diagnosed in advanced stages, is illustrated in another review received. Using a liquid biopsy allows tracking of tumor changes and evaluation of the treatment effectiveness without surgical interventions by studying circulating tumor cells (CTCs), for example, circulating tumor DNA (ctDNA), free circulating DNA (cfDNA), and exosomes. Recent improvements in liquid biopsy systems and biomarkers, as well as developments in ongoing clinical studies, highlight the potential of liquid biopsy in enhancing early detection and systemic individual therapy for gastric cancer patients. However, significant barriers to translating liquid biopsy technologies into routine clinical practice in low-resource settings remain, particularly due to high costs, lack of infrastructure, and insufficient trained personnel to manage such sophisticated techniques (62). AI

is significantly improving early gastric cancer diagnosis through machine-learning models like WeightedEnsemble, CatBoost, and RandomForest. These models enhance diagnostic accuracy by analyzing clinical features and biomarkers, aiding in early detection and effective disease staging. AI's ability to process large datasets enables better identification of disease patterns, supporting timely interventions. In clinical applications, AI helps clinicians make informed treatment decisions, improving patient outcomes. Future research will refine these technologies and explore integrating novel approaches like liquid biopsies or AI-driven diagnostics to further strengthen clinical applicability and precision (63, 64).

Long noncoding RNAs (lncRNAs) were also found to be effective predictors and therapeutic targets in the case of gastric cancer, which remains one of the most common life-threatening cancers with one of the lowest 5-year survival rates of around 30 -35%. Early stages provide a better chance of taming the cancer, and there is an urgent need to find new biomarkers. Particularly, lncRNA H19, HOTAIR, UCA1, PVT1, and LINC00152 are underlined as promising diagnostic and prognostic indicators. Global studies have identified apoptosis-related biomarkers, such as NME2, which suppresses apoptosis by upregulating anti-apoptotic genes like miR-100, RIPK1, STARD5, and LIMS1. Additionally, the long non-coding RNA DHRS4-AS1 inhibits gastric cancer cell proliferation and promotes apoptosis by destabilizing the protein DHX9 (65, 66). Additionally, ec-CEBPA, MLK7-AS1, and TUG1 have been investigated for their ability to regulate the epigenetics and drug resistance of gastric cancer, which is important for the further application of this compound in targeted therapies. While these lncRNAs present a promising avenue for early diagnosis and targeted therapies, the complexity of their clinical implementation must be carefully considered. This includes challenges such as the cost of testing, the need for specialized equipment, and the training required for clinicians to interpret these markers effectively in real-world settings (67). In conclusion, these results stress the importance of further studies aimed at increasing the accuracy of diagnostics and the efficacy of treatment for patients suffering from gastric cancer, especially through the discovery and utilization of innovative biomarkers. However, the potential of these biomarkers will only be realized if challenges such as the lack of infrastructure, training, and financial resources in low-resource settings are addressed. More research is needed to develop strategies for integrating these biomarkers into practical diagnostic and therapeutic protocols, ensuring their broad applicability and effectiveness in diverse healthcare settings

The current review demonstrates the different biomarkers and the different strategies used in studies concerning the diagnosis of gastric cancer in Kazakhstan, implying the nature of the problem. Of particular note, these encompassed many studies of genetic mutations affecting the main cellular pathways as well as gene expression analysis using RNA sequencing, which changed the understanding of gastric cancer. Furthermore, patients' factors like histological type, single nucleotide polymorphism, and geographical location, were found to have significant contributions to cancer risk. Such comprehensiveness highlights the need to produce diverse biomarkers and techniques in order to improve the diagnostic capabilities of gastric cancer in the region and its therapies. However, a critical challenge remains in translating these advancements into clinical practice, especially in low-resource settings like Kazakhstan, where access to advanced diagnostic technologies and treatments may be limited. This discernment imagines that this use of different analytical methods is necessary for overcoming the exact problem that has been identified, which is the clinical effects. Despite the promising findings, the application of these biomarkers in routine clinical settings may face significant barriers, including the lack of infrastructure and trained personnel to implement such sophisticated diagnostic methods**.** The synthesis of these results from various studies demonstrates the difficulty that is met in the diagnosis and treatment of gastric cancer in Kazakhstan. Similarly, there are a wide range of approaches, beginning with genetic study and ending with biomarker search, to provide a well-rounded approach that is necessary in tackling this common disease. The results further fit into the growing picture within the scope of global research, whereby biomarkers such as serum pepsinogen stand out in terms of their predictive usefulness in populations at risk (68). Nonetheless, these diverse approaches may not be equally accessible or practical in clinical settings where resources are scarce, thus limiting their widespread application. A study involving 657 subjects showed that patients undergoing curative surgery had significantly lower NLRs compared to those receiving palliative treatment. Specifically, median NLR values were 2.9 for curative surgeries versus 3.79 for palliative surgeries, highlighting the correlation between NLR and treatment outcomes. Furthermore, elevated NLRs were linked to advanced tumor stages (T3 and T4), reinforcing their role as a prognostic marker (19). Additionally, the emphasis on treating molecular characteristics such as HER2 and PD-L1 expression is by fractionation for targeted therapies, highlighting the importance of molecular profiling in making treatment decisions (69). However, the clinical implementation of such molecular profiling requires substantial investment in both technology and training, which may not be feasible in all healthcare settings.

The harmonization of the local results with global standards is critical for incorporating Kazakhstan's diagnostic and therapeutic strategies into the global narrative on the management of gastric cancer. The present research reveals differences in the overall survival rates for gastric cancer patients in Kazakhstan, pointing out the necessity for measures to be taken for early diagnosis and adequate treatment. The study reveals a sharp decline in gastric cancer survival rates, with a 1-year survival rate of 78.6% dropping to 34.9% at 3 years and disease-free survival rates of 76.8% at 1 year and 39% at 3 years. The significant variation in survival outcomes warrants further exploration to understand the underlying reasons. For instance, differences in patient demographics, cancer stages at diagnosis, and healthcare infrastructure could be contributing factors to the observed disparities. Similarly, another study shows

an increase in 5-year survival rates from 38.3% (2007-2011) to 42.9% (2017-2021), but emphasizes that survival varies by stage, exceeding 70% for localized cancer but falling to 10% for distant-stage patients (70). This stage-dependent variation further emphasizes the critical role of early diagnosis in improving survival outcomes and highlights the need for targeted interventions at different stages of cancer. Furthermore, a study highlights factors such as younger age and tumor differentiation as influencing better outcomes, aligning with the initial study's findings on biomarker expression (71). Additionally, a study underscores that multimodal treatment, including adjuvant chemotherapy, improves survival, reinforcing the need for personalized treatment based on cancer stage and patient characteristics (72). The impact of treatment strategies on survival, particularly in advanced stages, varies, highlighting the need for tailored therapeutic approaches. Attention in the literature is then given to negative outcomes of treatment, but mainly in advanced cancer stages. On the other hand, it is noted that the present-day approaches do not adequately help in the current treatment of such diseases. Added studies highlight the key role of lymph node involvement in staging. The variability in treatment effectiveness across studies may also be attributed to differences in treatment regimens, healthcare access, and patient response to therapy. These findings demonstrate the need for other potential predictors of failure, including apoptosis-related biomarkers that can help better guide treatment and enhance outcomes for patients with gastric cancer in Kazakhstan. The exploration of relevant factors, like circulating tumor DNA (ctDNA), microRNAs, and other factors, also offers a good scope for non-invasive diagnostics in the future. These biomarkers could potentially explain the observed survival differences by offering more precise tools for early detection and individualized treatment planning. These potential biomarkers could identify individuals at high risk for the disease before clinical symptoms develop, thereby enabling treatments to take place at a critical time (73). Likewise, different research calculated gastric cancer gender-related mortality adjustment by higher age groups 2009 -2018 showed a clear reduction of mortality rates trends over the years, although cases noted regions countries where traditionally higher case rates were observed. This adjustment highlights the impact of demographic factors on survival rates but also suggests that significant regional disparities still exist that need more targeted public health strategies. This points out that while it may be the case that there are some improvements in trends across regions, some specific challenges still exist that need more specific measures (49). Also, the healthcare system of Kazakhstan frequently does not have enough resources, for instance, advanced diagnostic equipment or trained personnel. Or even worse, such deficiency may give rise to a relatively poor screening of gastric cancers or an even worse situation where less screening is performed on gastric tumors than on screening for breast and cervix cancers whose programs have been quite established (74). The lack of adequate healthcare resources, especially in rural or underfunded regions, can contribute to delayed diagnoses and poorer survival outcomes, underscoring the need for infrastructure improvements in diagnostic and treatment facilities. The study makes a case that efforts to fill these gaps in infrastructure should be prioritized as they will correspondingly lead to better outcomes regarding gastric cancer in the region. Another study established a new prognostic model of gastric cancer (GC) using univariate and LASSO regression analyses based on 12 genes that relate to apoptosis. The model was able to identify differences in the molecular mutations, signaling pathways, and immune characteristics of low-risk and high-risk subgroups; low-risk group was more sensitive to chemotherapy. This model is better than the traditional TNM staging in prognostic assessment and has potential applications in individualized treatment of GC (75). Based on this analysis, the improved accuracy of this model is an important step forward in the individualization of gastric cancer therapy. The improved prognostic models, particularly those incorporating apoptosis-related biomarkers, could significantly enhance personalized treatment strategies, leading to better patient outcomes. A systematic review and meta-analysis of the 12 studies consisting of 2477 patients sought to evaluate the prognostic significance of X-linked inhibitor of apoptosis protein (XIAP) in cancers of the gastrointestinal tract. In this case, higher expression of XIAP was linked to poorer overall survival (HR: 1.64, 95% CI: 1.27–2.13) but not recurrence-free survival (HR: 1.06, 95% CI: 0.96-1.16). It can be concluded that XIAP may be a prognostic factor and a target for treatment, which indicates the significance of apoptosis control in cancer development (76). In summary, the inhibition of XIAP would enhance the survival in patients with gastrointestinal malignancies. The role of XIAP and similar biomarkers in cancer prognosis highlights the potential for apoptosis modulation as a therapeutic target, offering promising avenues for improving survival rates in gastric cancer patients. In conclusion, the observed variability in survival outcomes across studies underscores the complexity of gastric cancer prognosis. Differences in survival rates can be attributed to multiple factors, including stage at diagnosis, patient demographics, treatment regimens, and healthcare infrastructure. Addressing these factors and incorporating advanced biomarkers into clinical practice could lead to improved survival and personalized care for patients in Kazakhstan.

The current systematic review highlights key findings on apoptosis biomarkers in gastric cancer diagnosis in Kazakhstan. Genetic mutations (p53, RAS, miRNAs) and polymorphisms (TNF, IL10, TP53) are identified as risk factors for the disease. Increased immune responses and inflammatory markers (NLR, PLR, SII) correlate with poorer prognoses. A decline in gastric cancer incidence and mortality suggests improvements in early diagnosis and management. Biomarkers linked to DNA damage (γ-H2AX, 53BP1) show potential for better prognostic outcomes. Environmental factors like Helicobacter pylori and heavy metal exposure increase risk. FLOT chemotherapy, HER2 positivity, and c-myc expression prove effective in high-risk cases, enhancing treatment strategies. The review identifies genetic mutations such as p53, RAS, and various miRNAs as significant risk factors for gastric cancer. Sim-

ilarly, recent studies corroborate this, showing that mutations in TP53 are prevalent in Kazakh populations, impacting prognosis and treatment responses (77). Research on biomarkers for gastric carcinoma in Kazakhstan is limited. In general, p53 immunohistochemistry has high sensitivity (90.9%) and specificity (95.4%) for detecting TP53 mutations. The other miRNAs, particularly miR-210, miR-21, and miR-126, also seem to be valid diagnostic markers with good sensitivity and specificity (78,79). Additionally, polymorphisms in genes like TNF, IL10, and TP53 have been linked to increased susceptibility to gastric cancer, highlighting the genetic landscape's role in disease risk (80). Biomarkers associated with DNA damage, specifically γ-H2AX and 53BP1, show promise for better prognostic outcomes. Recent research has highlighted their potential utility in predicting treatment responses and overall survival rates (81). Likewise, another recent review of the existing scientific literature concerning genetic factors also confirms that Single-Nucleotide Polymorphisms (SNPs) are known to contribute to the gastric carcinogenesis risk in various ethnic groups, of which Kazakhs are included. Recognition of these genetic markers is already of great importance to designing screening and prevention efforts, providing insight into the significance of genetic testing for high-risk populations (82). Despite these promising findings, the integration of genetic testing into clinical practice faces obstacles such as limited access to genetic counseling services and a lack of awareness among healthcare professionals. Furthermore, the heterogeneity of genetic markers across different populations presents additional challenges in developing universal screening guidelines, particularly in a diverse region like Kazakhstan. Cancer Stem Cells (CSCs) are one of the few identifiable populations that exist in tumors and are characterized by their ability to self-renew, differentiate and metastasize. Even with the progress made in the characterization of these CSCs, most of the cells are still drug-resistant, leading to cancer relapse. The review explores CSCs' interactions with the tumor microenvironment (TME), involving lymphoid cells (T, B, NK cells), myeloid cells (macrophages, neutrophils, MDSCs), and mesenchymal cells (fibroblasts, adipocytes, endothelial cells). The role of CSCs in the ECM and their impact on cancer progression are also discussed. Emerging therapies targeting CSCs within the TME, including CAR-T, oncolytic viruses, and CSC -vaccines, show promise for innovative immunotherapy strategies, presenting new frontiers in cancer treatment (83). While these new therapies show great promise, they also pose significant challenges in terms of accessibility, cost, and complexity, especially in resource-limited settings. The application of CAR-T therapies, oncolytic viruses, and CSC-targeting vaccines requires highly specialized facilities, trained personnel, and substantial financial resources, which may not be available in Kazakhstan or other low-income countries. Another study highlights that while global incidence and mortality rates of gastric cancer have generally declined over the past decade, certain countries, especially those with younger populations, show increasing trends. By 2035, despite predicted declines in mortality rates, the absolute number of gastric cancer deaths may rise due to population growth, particularly in Israel, Chile, France, and Canada among females. This trend suggests that while progress has been made, ongoing efforts are needed to adapt cancer prevention and management strategies to evolving demographic shifts (84). This demographic shift presents a dual challenge: while improved prevention and treatment strategies may reduce overall mortality rates, the increasing number of cases due to aging populations and demographic changes necessitates more scalable, sustainable solutions. As such, an emphasis on early detection, targeted therapies, and public health interventions, especially in regions with limited resources, will be critical in managing the growing burden of gastric cancer**.** These findings highlight the necessity of a comprehensive and adaptable approach to cancer control, one that integrates genetic, environmental, and demographic factors to effectively address the complexities of gastric cancer on a global scale. The ongoing evolution of healthcare infrastructure and the prioritization of cancer research funding, especially in emerging economies, will be pivotal in realizing the full potential of these biomarkers and therapeutic strategies.

Potential Limitations

While the method adopted was robust, certain limitations were noted. The search strategy was limited to two databases (PubMed and Google Scholar), potentially missing relevant studies indexed in other databases. Additionally, language bias was introduced by restricting the search to studies available in English, which excluded potentially valuable research in other languages. Publication bias was another limitation, as studies with significant findings were more likely to have been published, possibly skewing the results. Lastly, while the data extraction process was thorough, no advanced statistical techniques, such as meta-analysis, were conducted, which limited the generalizability of the findings. Acknowledging these limitations proved the need for a cautious interpretation of the results and highlighted areas for improvement in future reviews.

Conclusion

This study reviewed research using diverse designs and population groups, offering a solid foundation for understanding gastric cancer patterns in Kazakhstan. However, the inconsistency in data reporting highlights the need for a standardized research protocol. Genetic variants in apoptosis, including mutations and SNPs, show potential as biomarkers for early detection and treatment, emphasizing the necessity for cross-validation of results across studies.

The data reveals a focus on diagnosis timeliness, with advanced cancer stages becoming more common due to factors that hinder survival. Environmental risk factors such as heavy metal and salt intake, alongside Helicobacter pylori infection, underscore the need for policy interventions. Practical recommendations include implementing biomarker-based screening, improving diagnostic techniques, and addressing environmental health gaps to enhance early detection and treatment strategies.

Implications

By detecting particular genetic and molecular markers, more effective diagnostic criteria will be developed for gastric cancer, resulting in an earlier detection stage and better patient management.

1. Since some biomarkers for HER2 overexpression and tumour suppression-associated SNPs have been identified, targeted therapy can be given to particular pathology-related patient groups.

2. The link between the environment and cancer registration data makes it clear that appropriate health promotion measures that influence the risk factors that can be changed, such as policies limiting environmental pollution and encouraging changes in diet, such as less salt consumption, are needed. These could include national policies for reducing Helicobacter pylori infection rates, limiting environmental pollution, and encouraging dietary changes, such as reducing salt consumption.

3. The results indicate that there is a high possibility of the introduction of national screening programs along with other measures aimed at improving awareness and early diagnosis of gastric cancer, particularly in high-risk populations and areas with high pollution levels.

4. Developing robust public health campaigns targeting risk factors such as Helicobacter pylori and dietary habits is crucial for reducing gastric cancer incidence.

Recommendations

Set specific guidelines for biomarker research in gastric cancer, including sample size, demographics, and analytic method, to enable comparison and meta-analysis. Initiate countrywide screening programs for gastric cancer for early diagnosis and prevention in targeted regions, such as older males. Design policy rest for relevant intervention implications focused on genetic and nutritional aspects of stomach cancer risk. Conduct further research to validate the identified apoptosis biomarkers in larger, more diverse populations and explore their potential role in personalized medicine and targeted therapies for gastric cancer. Enhance cancer care services in Kazakhstan, particularly in regions with high cancer incidence, to ensure timely diagnosis, effective treatment, and comprehensive patient support, ultimately improving survival outcomes and quality of life for gastric cancer patients. Strengthen initiatives to control Helicobacter pylori infections through public health measures and integrate its screening into national programs for gastric cancer prevention. Expand research into longitudinal and cohort studies focusing on underrepresented populations to address gaps in data and provide a more comprehensive understanding of gastric cancer in Kazakhstan.

Authors' Contributions

All authors participated in formulating the concept, executing the implementation, processing the results, and composing the manuscript.

Ethical Considerations

Not applicable.

Acknowledgment

Declared none.

Conflict of Interests

The authors declare that they have no competing interests.

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