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Application of cytogenetic studies to assess relapse in patients after allogeneic bone marrow transplantation

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Abstract

Cytogenetics, the study of chromosomes and their structure, plays a vital role in both diagnosing and managing hematological diseases.

Aims: This research aimed to analyse trends, study characteristics, and demographics in cytogenetic studies assessing the relapse after allogeneic bone marrow transplantation. It explored the evolving role of cytogenetics in managing relapse, their impact on treatment outcomes, and their contribution to treatment planning. The study also identified research gaps and future directions.

Study design: A narrative literature review

Place and Duration of Study: From 2019 to 2024

Methodology: A comprehensive PubMed search was conducted for this narrative literature review. The search terms encompassed a blend of keywords (("Cytogenetics" OR cytogenetics OR chromosomal analysis OR karyotyping) AND ("Recurrence" OR recurrence OR relapse OR relapsing) AND ("Transplantation, Homologous" OR "bone marrow transplantation" OR "bone marrow transplant" OR BMT OR "stem cell transplant" OR "hematopoietic stem cell transplantation")), with the intention of pinpointing pertinent research on relapse occurrences and patterns subsequent to transplantation.

Results: The research results highlighted significant advancements and the critical role of cytogenetic monitoring in managing relapse among hematologic malignancy patients. A surge in publications is observed in 2021, indicating rapid technological advancements, particularly in fluorescence in situ hybridisation and comparative genomic hybridisation. The current study findings reflected a diverse global effort, in predicting relapse and informing post-transplant treatment adjustments hence emphasising the effectiveness of cytogenetic techniques and minimal residual disease detection. The patient stratification and relapse management are enhanced as this novel cytogenetic profiling has improved classification and treatment response strategies in acute lymphoblastic leukemia. Nevertheless, challenges persist in effectively managing high-risk subtypes and overcoming resistance mechanisms. This underscores the need for continuous improvement in therapeutic approaches and long-term outcomes in the future.

Conclusion: For monitoring post-allogeneic bone marrow transplantation relapse, and guiding tailored treatments based on genetic profiles, cytogenetic studies are most essential.

Keywords: molecular diagnostics, genetic monitoring, chromosomal aberrations, biomarkers of relapse, minimal residual disease.

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Introduction

Allogeneic bone marrow transplantation has emerged as a life-saving treatment for various hematological malignancies, including leukemia, lymphoma, and myeloma. The relapse remains a significant challenge in spite of significant technical advancements in BMT techniques, and this relapse is affecting approximately 30-50% of patients within the first two after BMT. The early detection and treatments are crucial for improving patient outcomes [1,2].

In allogeneic bone marrow transplantation, healthy blood-forming stem cells are transplanted in order to replace the damaged bone marrow of a patient from a donor related or unrelated to the patient [3]. The main aims and objective are to effectively manage and potentially eliminate specific hematologic diseases and malignancies. This method commences with a conditioning treatment aimed at eliminating any remaining cancer cells in the patient's body and suppressing their immune system to prevent rejection of donor cells. This conditioning may involve chemotherapy, radiation therapy, or a combination of both. The stem cells that are donated are crucial to have a close match in the HLA between the donor and the patient and significantly increases the likelihood of a successful transplant, decreasing the chances of complications and stimulates the growth and development of donor stem cells in the patient's body, resulting in the formation of new blood cells [4,5]. Allogeneic stem cell transplantation can eliminate cancer cells while treating bone and blood, making it a promising alternative treatment for certain types of blood and tumors. However, they may still experience complications such as graft-versus-host disease, a condition in which the patient's immune system attacks the brain after the transplant. Hence, it is imperative for doctors to elucidate the results to enable patients to assess the risks and benefits of allogeneic stem cell transplantation. This treatment also encourages the bone marrow to switch to growing and producing new blood cells, such as red blood cells, white blood cells, and platelets [6, 7].

The effectiveness of bone marrow transplantation varies depending on different conditions, such as the specific disease being treated, the patient's general health condition, and the donor's relationship quality [8]. Allogeneic stem cell transplantation can cure approximately 80% of patients with aplastic anemia. The survival rate of patients in eradication of leukemia ranged from 55% to 68% when interventional agents were used and from 26% to 50% when neutral agents were used. Patients with benign disease have a 70 to 90 percent success rate when they receive a transplant from a sibling with compatible tissue. However, when a referral is received from an unrelated person, the success rate drops to 36% to 65% [9]. Data show that the three-year survival rate for multiple myeloma and Hodgkin lymphoma patients after stem cell transplantation is 79% [10]. Overall, advances in transplant technology, improved the recipient integration, aEnhanced post-transplant care and refined transplant protocols have heightened the success rate of transplantation procedures, consequently enhancing outcomes and survival rates for patients undergoing this treatment.

The relapse of primary disease remains one of the most difficult complications after transplantation having a significant impact on morbidity and mortality even with advances in transplantation and supportive care. Hematological malignancies relapse affects the overall survival and quality of life further emphasising the importance of early detection of relapse [11,12].

The discipline of the proposed scientific research is called cytogenetics, and it studies chromosomes and their organisation. The diagnosis and treatment of blood-related diseases are provided with this knowledge. As the genetics flow in all over the human body, karyotyping is among the most important techniques used in the DNA diagnosis as it helps to identify the abnormalities connected to several disorders and diseases. In the situation when all who are eligible are to undergo cytogenetic methods, it can be used in allogenic bone marrow transplantation (allo-BMT) for minor or major diseases to be detected. These tools facilitate the detection of disease cells that might survive treatment but reemerge as relapse after the transplantation [13,14]. The past few years have seen a major shift in the availability of array-based technologies and molecular cytogenetics, joined by next-generation sequencing, removing many of the detection limits of these methods. The use of this technology, for example, enables scientists to also unveil genes that were not detectable before, which means they had remained hidden in the background [15,16]. Early detection is paramount, serving as the gateway to prompt intervention, prevention of disease progression, and more effective treatment while the condition remains at a subclinical stage. Moreover, this information can be used in the personalisation of treatment strategies as the genetic characteristics of the recurrence may be identified targeting the specific genetic mutations [17,18]. What takes place after a transplant is that we see a major improvement in the blood counts. The post-transplant application of cytogenetic research represents a swiftly evolving domain that holds the potential to reshape the landscape of early treatment, ultimately offering substantial assistance to individuals in need. While this research continues, it tends to increasing distinction of post-transplantation process and the best influencing factor in its optimisation. Finally, this research provided data to make better assessment and management of the patients before they start coping and dealing on their own [19, 20].

This narrative review provided recommendations on utilizing cytogenetic research for post-allogeneic stem cell transplant recovery. This ongoing research is closely tied to numerous unmet needs, highlighting the necessity for patients to undergo continued monitoring and recovery in a more streamlined manner. Cytogenetic analysis has been found to be an important tool in the diagnosis of smallpox, which is an important factor in chromosomal

abnormalities and recurrence. Given the differences in survival outcomes and the potential for early intervention, connections between studies and methods in this field are important. The purpose of this review was to describe the current knowledge, identify gaps, and improve patient care and management by informing future research and practice.

Research Problem

The major obstacle to the use of bone marrow transplantation in the treatment of hematological malignancies is post-transplantation management and prognosis. Despite strides in technology and support, the need for reoperation persists as the primary cause of mortality among transplant recipients. Cytogenetic studies offer solutions by pinpointing chromosomal irregularities that may indicate disease recurrence or predict outcomes. However, the posttransplant use of cytogenetics is complicated by the variability of chromosomal alterations and differences between patients. Thus the main aim of the study was to evaluate the effectiveness of incorporating cytogenetic studies into regular post-transplant follow-up for early detection of relapse. There is a need to verify the accuracy and reliability of cytogenetic markers and develop a standard protocol for timely follow-up. By solving this problem, it is possible increasing the ability to treat after transplantation and reduce the risk of recurrence through early diagnosis and intervention; this voluntarily improves the patient outcomes.

Research Focus

The main purpose of this study was to evaluate the effectiveness of cytogenetic studies in detecting and predicting disease recurrence in patients undergoing allogeneic bone marrow transplantation. This involved examining various chromosomal abnormalities and genetic markers identified by cytogenetic analysis in order to determine the prognosis for relapse. The goal was to incorporate cytogenetic analysis into the post-transplant care process to allow timely treatment based on early signs of relapse. By focusing on the relationship between specific cytogenetic changes and recurrence outcome, this study was designed to develop practical guidelines to guide clinicians in the management of post-transplant patients. Ultimately, this research aimed to improve survival and quality of life by reducing the frequency and impact of relapse through targeted, evidence-based interventions.

Research Aim

1. To analyse temporal trends, characteristics of studies, and demographics of populations included in the research.
2. To explore how cytogenetic analyses have developed in their role to predict and manage relapse in patients post-allogeneic bone marrow transplantation.
3. To assess the impact of cytogenetic techniques on patient treatment outcomes and efficacy.
4. To examine the contribution of cytogenetics to the planning and monitoring of treatment.
5. To identify existing research gaps and propose future directions in the field of cytogenetics for patients after allogeneic bone marrow transplantation.

Research Questions

1. What are the time trends, characteristics of studies, and demographics of populations involved in cytogenetic studies on relapse after allogeneic bone marrow transplantation?
2. How has the role of cytogenetic analyses evolved in predicting and managing relapse in patients following allogeneic bone marrow transplantation?
3. What is the impact of cytogenetic techniques on the outcomes and efficacy of treatments for patients after allogeneic bone marrow transplantation?
4. How do cytogenetic methods contribute to the planning and monitoring of treatment in patients post-allogeneic bone marrow transplantation?
5. What are the current research gaps and what future directions should be pursued in cytogenetic studies related to relapse after allogeneic bone marrow transplantation?

Research Methodology

General Background

Allogeneic bone marrow transplantation is an essential therapy for several types of blood cancers, providing the possibility of treating diseases including leukaemia, lymphoma, and myeloma. This treatment entails the substitution of a patient's sick or malfunctioning marrow with healthy stem cells obtained from a compatible donor, so effectively resetting the hematopoietic system. Despite the procedure's potential to extend life, a significant challenge remains

the risk of relapse, where the original disease returns. This recurrence is often linked to minimal residual disease and genetic abnormalities that persist after the transplant. Cytogenetic studies, which analyse chromosomal changes in cells, have emerged as a crucial tool for detecting these anomalies.

Study Design

This was a narrative review of the literature from 2019 to 2024.

Search Strategy

This narrative literature review was conducted in order to examine the role of cytogenetic analysis in monitoring patient recovery after allogeneic bone marrow transplantation by using the PubMed database for searching relevant literature using a set of keywords "Cytogenetics" OR cytogenetics OR chromosomal analysis OR karyotyping AND "Recurrence" OR recurrence OR relapse OR relapsing AND "Transplantation, Homologous" OR "bone marrow transplantation" OR "bone marrow transplant" OR BMT OR "stem cell transplant" OR "hematopoietic stem cell transplantation".

Study Selection

A rigorous literature search was conducted on PubMed database for the period from 2019 to 2024 as shows in Figure 1. Initially, 2,697 publications were identified. Using the keywords related to cytogenetics, recurrence and mutation. This dataset was narrowed to 658 articles based on relevance, and further reduced to 410 available free full texts. Stringent exclusion criteria were subsequently employed, eliminating Clinical Trials, Observational Studies, RCTs, and Reviews, resulting in 91 articles. The selection was refined to 77 articles by including only those involving human subjects. Finally, a detailed assessment of these articles identified 7 key studies that provided critical insights into the predictive value of cytogenetic markers and chromosomal dynamics post-transplant, essential for informed clinical decision-making and effective patient management. This approach allowed the selection of the most important and influential studies to provide a better understanding of the cytogenetic impact on the patient after transplantation.

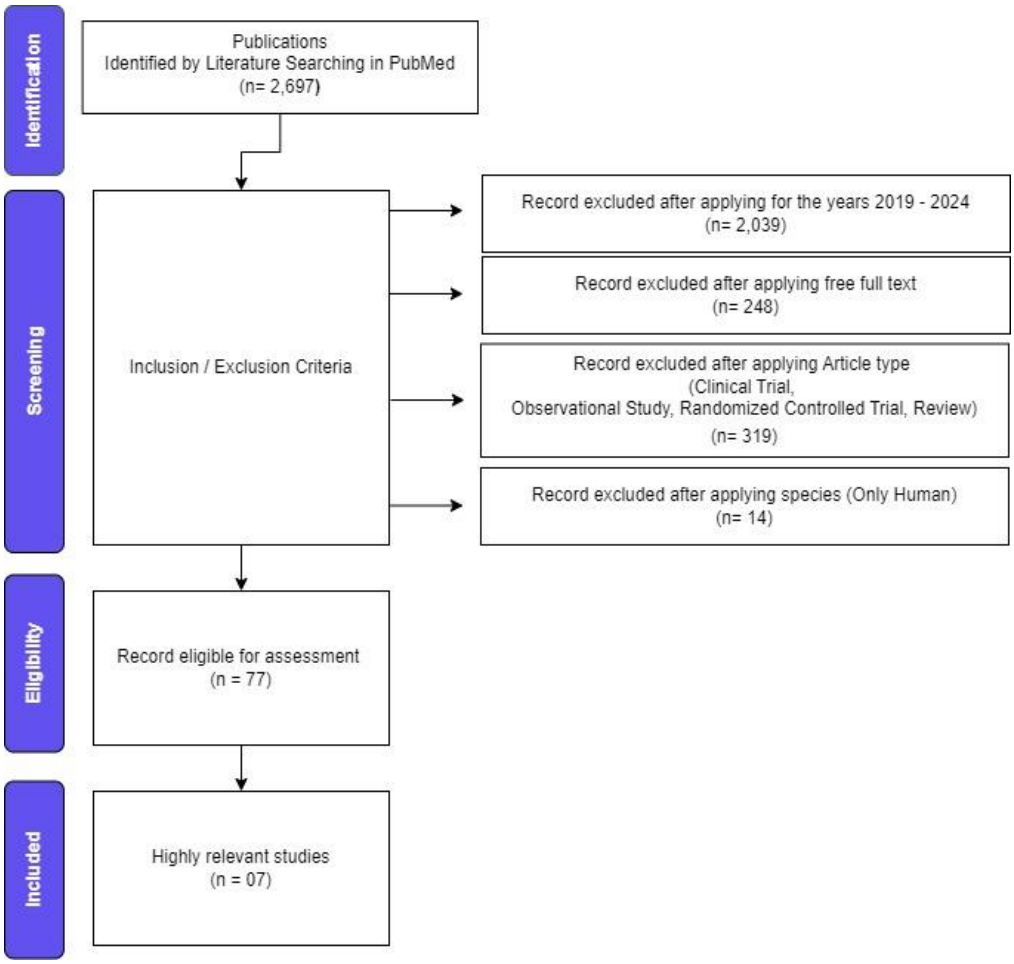

Figure 1. PRISMA Flow Diagram of Literature Search.

Research Results

The results presented in Figure 2 outline the annual publication count from 2000 to 2024 and reflect the evolving interest and research intensity. The initial consistent, moderate volume of publications from 2000 to approximately 2010 implies an exploratory phase of research in this domain. A significant surge in interest and publications from 2011 onward, peaking in 2021, indicates a period of increased focus and likely advancements in cytogenetic technologies and methodologies. This may be associated with the advancement and verification of more advanced cytogenetic techniques, such as fluorescence in situ hybridisation and comparative genomic hybridisation, which improve the identification of chromosomal abnormalities that indicate relapse. The fact that publication output has not continued at the pace and level attained in 2021 through to 2024 might indicate some expertise and knowledge aging, a revisited field or more sophisticated insights, or an external force effect on life and health. This trend illustrates that the field of science is changing all the time and in lymphoma diagnosis cytoanalytics, specifically studies in cytogenetics, definitely have an important part to it while helping with early relapse detection.

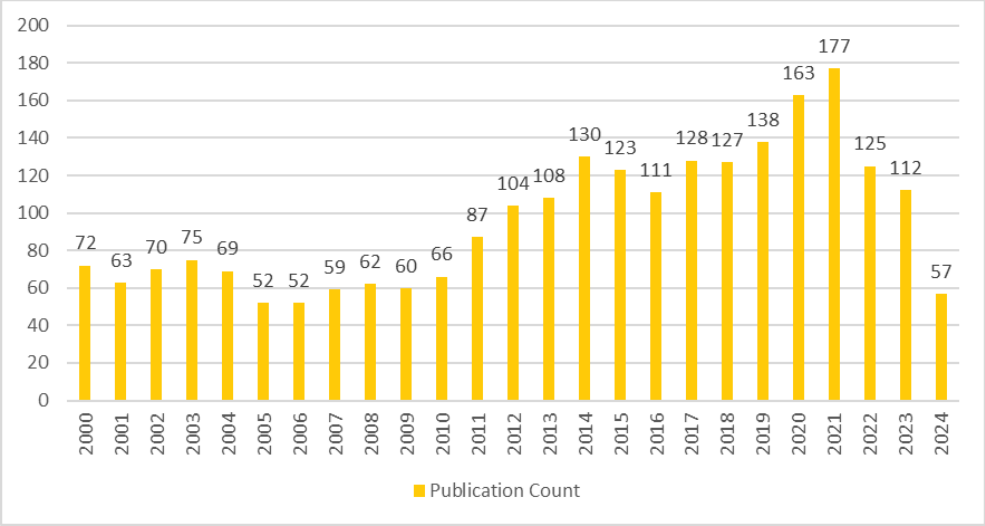

Figure 2. Publication Trends in Cytogenetic Studies, 2000-2024.

Figure 3 encompasses a broad spectrum of studies conducted between 2019 and 2024, all of which are incorporated in the present narrative review. This review features a combination of randomised controlled trials, clinical trials, a retrospective study, and a recent review, each contributing unique insights into the utility of cytogenetic analyses in the post-transplant setting. Starting with the most recent, Yoon et al. (2024) provides a comprehensive review that likely synthesises the latest advancements and summarises the key data on how cytogenetic studies are used to monitor relapse [21]. Following this, Döhner et al. (2022) presents a randomised controlled trial, offering robust evidence on the efficacy of particular cytogenetic markers or techniques in predicting relapse [22]. The clinical trials conducted by Jain et al. (2021), Thol et al. (2020), Shadman et al. (2020), and Bezerra et al. (2019) explore various aspects of cytogenetic testing, such as the application of new techniques, the correlation of specific cytogenetic abnormalities with patient outcomes, and potentially comparing these findings against other biomarkers [23–26]. Cantoni et al. (2019) presented a retrospective study of historical data to identify long-term changes or associations between cytogenetic changes and patient outcomes and found the importance for understanding the longevity and risk of cytogenetic markers in clinical practice [27].

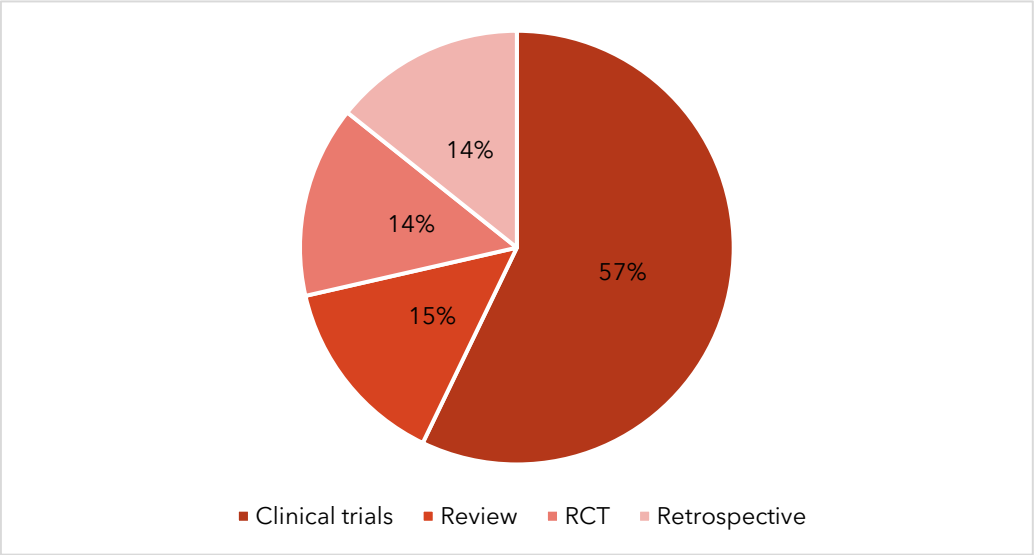

Figure 3. Study Characteristics

Table 1 summarised the findings from various studies in the narrative review on the application of cytogenetic studies to assess the relapse in patients post-allogeneic bone marrow transplantation cover a broad spectrum of geographic regions and patient demographics from 2019 to 2024. Key insights include the latest advancements in the monitoring techniques for adult patients with ALL across the U.S., Europe, and Korea [21], the effectiveness of these studies in older populations internationally [22], and approaches tailored to diverse genetic backgrounds in younger populations in India [23]. Studies also highlight specific challenges and monitoring protocols in Western populations for Acute Myeloid Leukemia patients [24], the detailed analysis possible in smaller cohorts [25], and targeted treatment responses and relapse monitoring for Philadelphia chromosome-positive (Ph+) ALL and Chronic Myelogenous Leukemia patients in the U.S. [26,27]. Collectively, these studies offer a thorough overview of the implementation of cytogenetic monitoring across various settings and leukaemia types, uncovering critical insights that can enhance post-transplant care and outcomes.

Table 1. Population Characteristics.

Author's	Geographic Context	Population and Size	Year
Yoon et al. 2024 [21]	U.S, Europe, Korea	Adult patients with ALL	2024
Döhner et al. 2022 [22]	International	Patients aged 55 years or older	2022
Jain et al. 2021 [23]	India	Adolescents and adults aged >14	2021
Thol et al. 2020 [24]	U.S. and Europe	AML patients	2020
Shadman et al. 2020 [25]	-	60 patients	2020
Candoni et al. 2019 [27]	Nationwide	Adults with Ph+ ALL	2019
Bezerra et al. 2019 [26]	U.S.	40 CML patients	2019

Table 2 summarised the results that underscored the evolving role of cytogenetic analyses in managing and predicting relapse in patients following allogeneic bone marrow transplantation. The first study emphasised the importance of detailed cytogenetic profiling in classifying ALL into subtypes and the necessity of using advances in molecular cytogenetics and MRD detection to guide therapy, although relapses remain common in subtypes with poorer prognoses like Ph-like and ETP-ALL [21]. The second study highlighted that how localised cytogenetic assessments combined with MRD monitoring can produce a better relapse-free survival rates when treatments such as oral azacitidine are applied, reflecting the value of personalised treatment plans based on cytogenetic insights [22]. Similarly, two other studies indicated that despite the implementation of sophisticated flow cytometry techniques, relapse remains a significant risk, especially in elderly or high-risk patients [23, 24]. In contrast, one of the studies provided a more optimistic outlook, showing that treatment adjustments based on high-risk cytogenetic factors like del17p or complex karyotypes can substantially reduce relapse rates [25]. Two included studies further corroborate the critical role of MRD detection in prognosis, with findings that suggested MRD positivity at HSCT is a strong predictor of relapse risk and that sensitive techniques like RT-PCR for BCR-ABL mRNA can significantly decrease relapse rates [26, 27]. In summary these studies emphasised the vital role of continual advancements in cytogenetic and MRD technologies and in improving patient outcomes through tailored therapeutic interventions.

Table 2. Cytogenetic Techniques and Detection of Minimal Residual Disease

Author's	Cytogenetics and MRD Detection	Relapse and Refractoriness
Yoon et al. 2024 [21]	Detailed cytogenetic profiles are used to classify ALL into various subtypes, such as Ph-positive, Ph-like, and ETP-ALL. Advances in molecular cytogenetics and the application of MRD detection are highlighted as critical in assessing disease status and guiding therapy.	Still occurring, particularly in poor prognosis subtypes like Ph-like ALL and ETP-ALL
Döhner et al. 2022 [22]	Local cytogenetic and molecular assessments at diagnosis, MRD assessed by multiparameter flow cytometry	Oral-AZA associated with improved relapse-free survival
Jain et al. 2021 [23]	10-color flow cytometry	23% of patients experienced an event, including relapse and induction failures
Thol et al. 2020 [24]	Frequent updates during treatment, especially at relapse	Common, especially in elderly or high-risk patients
Shadman et al. 2020 [25]	High-risk cytogenetics (del17p or complex karyotype)	Lower relapse rate at 3 years in rituximab-treated group (17%) vs. controls (31%)
Candoni et al. 2019 [27]	G-banding for cytogenetics, real-time qPCR for BCR-ABL transcripts	Higher risk with MRD positivity at HSCT; persistent challenge in active disease at HSCT
Bezerra et al. 2019 [26]	Qualitative RT-PCR for BCR-ABL mRNA, sensitivity 10(-5)	12.6% cytogenetic or clinical relapse at 4.5 years, significant decrease from historical 42%

Figure 3 describes different strategies' effectiveness for blood cancers and also discusses novel strategies that may cause a high relapse rate after the autologous bone marrow transplantation. In a study by Yoon et al. (2024), an article discusses advancements in the classification and treatment of acute lymphoblastic leukaemia. This study highlights the importance of molecular residual disease (MRD) detection and subsequent patient allocation based on risk estimates to decrease the incidence of relapse [21]. Moreover, Döhner et al. (2022) identify Oral-AZA as a supportive therapy in the model of survival improvement for AML patients with NPM1 and FLT3 mutations, implying the preventive role of this drug in sustaining remission and prolonging the disease-free periods following the transplantation [22]. Jain et al. (2021) reports the efficacy of a regimen that combines the administration of Bortezomib and Rituximab with chemotherapy drugs. This combination showed high-survival rates and tolerability in patients suggesting that the targeting and reduction of disease relapses can be achieved through initial management of the disease in patients during transplantation [23]. While Toll et al. (2020) focused on the challenges of suffering from r/r AML without understanding the outcome, but proposed an idea that further research could be one of many driving forces for the weak groups [24]. Shadman et al. (2020) aimed to assess whether rituximab, if added to CBT in patients with high-risk cytogenetics, could drop the relapse and contribute to more survival while there was no effect on return-to-work mortality; this showed that rituximab had only a less important role to play in the first process [25]. Further, HSCT therapeutic features were revealed by Cantoni et al. (2019), especially for Ph + ALL that had been proven beneficial in MRD negative pre-transplantation setting, which assists in determining the risk assessment [27]. Lastly, Bezerra et al. (2019) looked into the utility of interferon (IFN) after HCT for the treatment of CML, primarily in patients who have developed resistance or intolerance to tyrosine kinase inhibitors (TKIs), thereby introducing an additional strategy to prevent disease relapse [26].

Table 3. Outcomes and Efficacy

Author's	Overall Survival	Research Outcome
Yoon et al. 2024 [21]	Improvement noted with the new treatment modalities	Improved understanding and classification of ALL subtypes, enhanced detection of MRD, and better treatment outcomes with the integration of novel therapies into standard care protocols

Döhner et al. 2022 [22]	Improved in Oral-AZA arm versus placebo, especially in NPM1mut or FLT3mut subgroups	Oral-AZA significantly improves survival in patients with NPM1 and FLT3 mutations, showing effectiveness as maintenance therapy in AML remission
Jain et al. 2021 [23]	78.7% at 21 months	Bortezomib and rituximab with chemotherapy shown to be effective and tolerable; plans for further evaluation in phase 3 trial
Thol et al. 2020 [24]	Generally poor in r/r AML, varies by specific treatments and patient subgroups	Ongoing studies are crucial for improving outcomes in r/r AML, several promising results noted in targeted therapy trials
Shadman et al. 2020 [25]	OS at 3 years: 53% in rituximab-treated vs. 50% in controls	Rituximab addition to conditioning regimen reduced relapse rates, especially among high-risk cytogenetics, without significant improvement in OS or NRM
Candoni et al. 2019 [27]	Improved with current therapies, especially with MRD negativity pre-HSCT	Confirming HSCT as a potentially curative treatment in Ph+ ALL, highlighting the importance of achieving MRD negativity before HSCT
Bezerra et al. 2019 [26]	Median OS not reached; data suggest long-term survival with IFN	IFN may be a viable option for CML post-HCT, particularly in TKI-resistant or intolerant cases

Table 4 summarising unresolved issues and future research directions in hematologic malignancies highlights several crucial areas requiring further investigation. Yoon et al. (2024) emphasise the challenges in treating refractory or relapsed cases of ALL, specifically in subtypes like Ph-like ALL and ETP-ALL, calling for novel therapeutic targets and strategies to improve outcomes [21]. Similarly, Döhner et al. (2022) discuss the impact of baseline and treatment-emergent mutations in acute myeloid leukaemia outcomes, noting a particular gap in understanding the role of Oral-AZA in different FLT3 mutations and treatment regimens [22]. Jain et al. (2021) highlights a lack of data on the comparative effectiveness of bortezomib and rituximab, particularly concerning infection rates associated with these treatments [23]. Thol et al. (2020) identify a need for more robust data on combining novel agents with traditional therapies to address the resistance mechanisms and optimise therapy for specific mutations [24]. Shadman et al. (2020) points out the high non-relapse mortality and the necessity of long-term follow-ups in hematopoietic cell transplantation to better understand late relapse dynamics [25]. Candoni et al. (2019) argue for more comparative studies to explore post-HCT strategies, especially concerning the use of TKIs and the role of HCT in patients who are minimal residual disease negative [27]. Lastly, Bezerra et al. (2019) note high early treatment discontinuation rates due to interferon toxicity in CML, suggesting a need for improved formulations and an evaluation of modern TKIs in post-transplant outcomes [26]. While these insights collectively underscore substantial gaps in various treatment strategies and patient monitoring for hematologic cancers, they also have broader implications for clinical practice, particularly in improving long-term patient outcomes and customising treatment approaches. However, none of these studies directly address the specific application of cytogenetic studies in monitoring relapse after allogeneic bone marrow transplantation, indicating a potential gap in the literature that would merit direct investigation to enhance predictive capabilities and post-transplant care in hematologic malignancies.

Table 4. Unresolved Issues and Future Research Directions

Author's	Unresolved Issues	Research Gap
Yoon et al. 2024 [21]	Relapse and refractoriness in subtypes like Ph-like ALL and ETP-ALL	Identification of novel therapeutic targets and strategies that could further improve outcomes, particularly in refractory or relapsed ALL
Döhner et al. 2022 [22]	Influence of baseline and treatment-emergent mutations on outcomes, impact of Oral-AZA in different AML treatment regimens	Effects of Oral-AZA on different types of FLT3 mutations, long-term outcomes, and alternative treatment regimens
Jain et al. 2021 [23]	Differentiation of benefits between bortezomib and rituximab; higher infection rates	Comparative effectiveness of bortezomib and rituximab combination versus rituximab alone not established

Thol et al. 2020 [24]	Optimal combinations of novel therapies, resistance mechanisms, targeted therapy for specific mutations	Need for more data on combining novel agents with each other and with traditional therapies
Shadman et al. 2020 [25]	High NRM, need for longer follow-up to evaluate late relapses	Long-term follow-up, comparative studies between HCT and other novel treatments
Candoni et al. 2019 [27]	Optimal post-HSCT strategies, including the use of TKIs and the role of HSCT in MRD-negative patients	Comparative studies on HSCT versus non-HSCT consolidation strategies in MRD-negative patients
Bezerra et al. 2019 [26]	High rates of early treatment discontinuation due to IFN toxicity; new formulations may be needed	Impact of modern TKIs and updated treatment modalities on post-HCT outcomes in CML

Discussion

This narrative review on cytogenetic studies in relapse control in patients after allogeneic bone marrow transplantation was a study that illustrated diverse types of research designs, noticeably, randomised controlled trials, clinical trials, one retrospective study and a recent review. In essence, this method revealed the complexity involved in interpreting cytogenetic assessments as the most valid tools used in the prevention and in monitoring of relapses in allogeneic bone marrow transplant recipients. This review provided similarities, for example, with other narrative review analysis, which uses CML-TAP changes in chronic myelomonocytic leukaemia transplant score model to determine non-relapse mortality with patients with chronic myelomonocytic leukaemia. The clinical criteria used comprised ASXL1 or NRAS mutations, the level of bone fractures, and the HCT-CI Score used complemented the analysis of cytogenetic studies in the prognosis of a non-relapse of tapering off and death [28]. Another research illustrated that up to a third of all samples of MDS patients with these somatic mutations (TP53 mutations) had failed to benefit from the allogeneic transplantation. In addition; the absence of TP53 mutations was correlated to the overall outcome. This is why the biospecificity of the gene transfer in the context of the stem cell transplantation cannot be overestimated [29]. Furthermore, studies point to the possible stem cell transplantation (AlloSCT) as a way to prolong life span. As per Simonidis et al., patients who achieved complete remission and underwent alloSCT experienced a longer duration of remission compared to those who achieved partial remission [30]. The conclusion made in this paper indicated the significance of testing this disease in predicting allogenic stem cell transplantation outcome and therefore should be applied widely as a prognostic tool for patients undergoing allogenic bone marrow transplant.

This review highlighted the importance of cytogenetic monitoring after allogeneic bone marrow transplantation in cancer patients, specifically focusing on advances in diagnostic technology for adults with ALL in the United States, Europe, and Korea. This review also showed the effectiveness of these procedures in adults worldwide, treatment strategies for young Indian patients with different genetic backgrounds, challenges in treating acute myeloid leukaemia in western populations, and subgroup-specific strategies. It is also important for clinical response and follow-up in Philadelphia chromosome-positive ALL and acute myeloid leukaemia in the United States. + der (22)t(9; 22) and 9/9p are negatively predictive in adults with Philadelphia chromosome-positive ALL [31]. These finding was further explored in another study published in the American Journal of Haematology, which not only confirmed these negative manifestations but also discussed the challenge of the tyrosine kinase inhibitor-resistant population and emphasized the need for a more in-depth understanding of BCR-ABL kinases [32]. Furthermore a study shows the importance of identifying tyrosine kinase inhibitor protection mechanisms through genetic for the better treatment of CML [33]. Furthermore, the significance of precise diagnosis, evaluation of clinical manifestations, and continuous monitoring of residual disease is emphasised by another study that explored the factors contributing to resistance, relapse, or progression of chronic myeloid leukaemia (CML) [34]. Overall, these studies highlight the importance of cytogenetic monitoring in the diagnosis, prognosis and treatment of leukaemia. They highlighted the need to identify cytogenetic abnormalities (such as BCR::ABL fusion genes) and understand mechanisms of resistance to tyrosine kinase inhibitors, particularly in the treatment of CML. Descriptions and case studies highlight the need to develop treatment strategies tailored to the different genetic backgrounds and critical challenges facing AML in Western populations.

The current review has emphasised the growing significance of cytogenetic analyses in managing and predicting the relapse post-allogeneic bone marrow transplantation and underscored the crucial role of detailed cytogenetic profiling in classifying Acute Lymphoblastic Leukaemia into subtypes and customising treatment strategies. The advancements in molecular cytogenetics and MRD detection were emphasised as essential for guiding therapy, although relapses are still common in aggressive ALL subtypes. Studies indicate that integrating cytogenetic assessments with MRD monitoring, particularly using treatments such as oral azacitidine, can enhance relapse-free survival rates. Despite this, other research finds that even with advanced techniques like flow cytometry, the risk of

the relapse remains significant, especially among elderly or high-risk patients. On a more optimistic note, adjusting treatments based on high-risk cytogenetic factors can significantly reduce the relapse rates. Additionally, the importance of MRD positivity at the time of hematopoietic stem cell transplantation as a strong predictor of relapse is noted, with sensitive detection methods like RT-PCR for BCR-ABL mRNA significantly lowering these rates. Collectively, these observations underscored the vital role of continuous advancements in cytogenetic and MRD technologies for improving patient outcomes, though challenges in completely mitigating relapse risks persist. Another study suggested a novel risk stratification model for B-cell ALL that combines cytogenetic aberrations with MRD status and demonstrates that among high-risk patients, those achieving molecular remission show significantly lower relapse rates, highlighting the importance of both cytogenetic and MRD status in treatment decisions [35]. Further emphasising the value of MRD, another study discusses the application of next-generation DNA sequencing for MRD monitoring in AML and study findings indicated that NGS techniques at days +90 and +180, along with pre-hematopoietic stem cell transplantation MRD levels, were highly predictive of relapse and overall survival. However, due to its cost and complexity, this method is currently recommended only within clinical trials [36]. Another study also highlighted challenges in MRD monitoring, which emphasised the necessity of complementing flow cytometry-based MRD assessment with reverse transcriptase PCR. This combination is crucial for detecting rare events such as myeloid lineage switch after anti-CD19 therapies, illustrating the complexity of MRD detection in ALL [37]. According to the findings of another study, differential cytometry MRD analysis is crucial at three specified intervals prior to allogeneic hematopoietic stem cell transplantation. Consequently, if moderate response is not attained with primary drugs following initial treatment of mild disease, the physician may contemplate secondary drug options based on this study [38]. Lastly, another research, however, concerns several approaches with the aid of which to detect minimal residual disease of AML is tracked. Nevertheless, these methods should be used and further research is needed for this. Support the research aimed towards making MRD more effective. It provides a clearer understanding of its role in various scenarios, which can be utilized to delineate shifts in patient treatment trajectories or the results of clinical trials [39]. Another study shows the role of better advances of cytogenetics, MRD technology and other methods alongside leukaemia therapy which play an important role in controlling the occurrence of relapse and also ensures improved outcomes of the ALL treatment. However, there are challenges that still remain in predicting and preventing a relapse of the disease.

The current review also revealed that the transplantation of allogeneic hematopoietic stem cells may reduce the relapse rate and improve outcomes in acute lymphoblastic leukaemia and chronic myeloid leukemia and these findings support the use of new therapies to improve minimally invasive disease detection in ALL, the use of oral azacitidine to control remission in AML patients with specific mutations, and the combination of bortezomib and rituximab with chemotherapy has potential in primary disease control. Similarly, another study provides a historical perspective on the development and success of allogeneic hematopoietic stem cell transplantation for the treatment of malignancies and discusses the development of stem cells and the resulting important cancer treatment, expanding and reducing the indications for allogeneic hematopoietic stem cell transplantation on the use of cold storage with emphasis on donor selection and conditioning. Together, these factors highlight the role of cytogenetic studies in the evaluation of recurrence and help reduce morbidity and mortality [40]. Additionally, a retrospective analysis was also performed in order to evaluate the effectiveness of allo-HSCT in children with leukemia, shows that allo-HSCT is still the best option for treating high-risk or relapsed ALL and AML and further emphasizes the importance of taking steps to prevent graft-versus-host disease and infection and providing full support during transplantation. [41]. Another review conducted to evaluate the effectiveness of bone marrow transplantation in the treatment of AML and revealed that BMT not only improved symptoms of the patients but also delayed disease progression, relapse and prolonged lifespan, providing strong evidence supporting the use of cytogenetic studies to assess recovery and ongoing development of BMT [42]. In summary, this study provided evidence affirming the significance of cytogenetic studies in assessing enhancements in the efficacy and efficiency of allogeneic hematopoietic stem cell transplantation, novel therapies, refinement of treatment modalities, and the advancement of supportive care. The current review also addressed the challenges in treating hematological malignancies, the role of mutations and the effectiveness of some drugs in acute myeloid leukemia, and bortezomib et al. and rituximab. Additionally, there are on-going concerns regarding combined HCT prophylaxis methods, mortality, effectiveness of post-HCT strategies, and treatment costs due to CML drug toxicity. Other studies also show the vulnerability of hematological malignancies to the immune system, continuous monitoring of the immune system in the blood, and the ability of cancer cells to enhance immunity. This review also supports the use of cytogenetic studies to assess the risk of early recurrence. However, the use of immunotherapy for hematological malignancies has drawbacks, including that malignant cells can be activated by the inflammatory response and cytokine environment, and malignancies can heal the body against diseases that must be overcome [43]. Another research investigation examined the latest progress in comprehending different types of immunotherapies used to treat blood cancers, such as stem cell transplantation, immune checkpoint inhibitors, antigen-targeted antibodies, antibody-drug conjugates, tumour vaccines, and adoptive cell therapies. However, it emphasizes the necessity of cytogenetic studies in the evaluation of early recurrence and treatment [44]. Additionally, other studies have explored the potential for using large-scale genomic analysis in hematological malignancies including identification of somatic changes, treatment potential, and better patient care by comparison with the original model. Studies

demonstrated the need for accurate identification of markers to measure minimal/residual disease and avoid false positives [45]. In conclusion, although progress has been made in the field of hematological malignancies, especially in immunotherapy and genomic analysis, significant problems remain. The methods in which diseases can be treated are therefore improved, including the administration of drugs, the overcoming of drug resistance, the reduction of treatment-related death, and proper management of comorbidities. Addressing these challenges is likely the most effective approach to enhancing patient outcomes in this cancer type.

Conclusions and Implications

Cytogenetic studies play a significant role in the assessment of post grafting relapse, development of targeted therapy focusing on an identified genetic abnormality and identification as well as classification of blood cancers like acute lymphoblastic leukemia and acute myeloid leukemia. Innovations like non-surgical exploratory testing and the integration of PCR output into the patient in situ are achievable alongside other efforts in AML treatment like the goal of curable goal using oral azacitidine. Conversely, the administration and management of relapsing diseases can remain problematic, as seen in the case of chronic myeloid leukemia (CML), where the efficacy of tyrosine kinase inhibitors may be compromised due to the presence of anti-resistant mechanisms. There is a need for patient-specific treatment regimens considering genetic features and also minimal invasion status as main tools to get the advancement. To summarise, future study should be directed towards the creation of clinically relevant disease monitoring and cytogenetic assays which are also reliable and affordable, together with integrative immunotherapy through the use of existing treatments, and sophisticated whole genome analyses to find novel targets for treatment. It is vital to train practitioners to utilise cytogenetic methods, MRD detection techniques as these form the cornerstone of clinical practice and enhance the competence of doctors trained in them. Unexpected values coming under ethics and economics worry, including the work on total treatment, correctness, and justice. Such values are patient consent, data confidentiality, genetic discrimination based on data, and technology costs. As a result, this enhances patient outcomes and advances the treatment of hematological malignancies through bone marrow and other cord blood transplants, leveraging further developments in cytogenetic and molecular techniques.

Declarations

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Conflicts of Interest

The author declare no conflict of interest regarding this study.

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