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# An Attempt to Determine Hematological Malignancies in Selected Patients: A Cytogenetical Approach

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***Abstract***

*Diagnosis and treatment of hematological malignancies, a diverse category of tumors that begin in the blood and bone marrow, are extremely difficult. Our knowledge of these conditions has been revolutionized by the development of cytogenetics, the study of chromosomes and genetic abnormalities. A total of 180 patients with benign and malignant hematological malignancy had peripheral bone marrow or blood samples obtained using the standard G-banding procedure. Fifty-one percent of patients had normal karyotypes. In addition, thirty individuals (15%) had a complicated karyotype whereas eighty-five percent (85%) had a normal one. Three-hundred and three percent of patients were diagnosed with Pre-B Acute Lymphoblastic Leukemia (Pre-B ALL), followed by twenty percent with Chronic Myelogenous Leukemia (CML), and fourteen percent with Acute Lymphocytic Leukemia.*

**Keywords:** *Hematological, Cytogenetics, Leukemia, Chronic, Acute*

## 1. Introduction

Hematological malignancies, a diverse group of cancers that originate in the blood and bone marrow, present a significant challenge to patients and clinicians alike. These disorders encompass a wide spectrum of diseases, including leukemia, lymphoma, and myeloma, each characterized by the uncontrolled proliferation of abnormal blood cells. The management of hematological malignancies has witnessed remarkable progress in recent decades, thanks in large part to advances in cytogenetic techniques. Cytogenetics, the study of chromosomes and their abnormalities, has revolutionized our understanding of the genetic underpinnings of these diseases. By delving deep into the genetic landscape of hematological malignancies, cytogenetics has not only provided valuable insights into disease mechanisms but has also paved the way for tailored therapies and improved patient outcomes.

The relationship between genetics and hematological malignancies has long fascinated researchers and clinicians alike. These disorders, often insidious and challenging to diagnose, have puzzled medical practitioners for centuries. The advent of cytogenetics, however, has shed new light on these enigmatic diseases. Through the systematic examination of chromosomal abnormalities and genetic alterations, cytogenetic studies have unveiled critical information about the origins and progression of hematological malignancies.

One of the hallmark features of hematological malignancies is the genetic diversity they exhibit. This diversity is not only reflected in the numerous subtypes of these diseases but also in the intricate patterns of chromosomal aberrations observed in affected individuals. Cytogenetic analysis has proven indispensable in categorizing these disorders, aiding in their precise diagnosis, prognosis, and treatment selection. By identifying specific genetic markers and abnormalities associated with different types of hematological malignancies, clinicians can now tailor their therapeutic approaches to individual patients, maximizing the chances of a successful outcome.

From conventional karyotyping to fluorescence in situ hybridization (FISH) and, more recently, next-generation sequencing (NGS), each of these approaches plays a unique role in deciphering the genetic intricacies of blood disorders. Karyotyping, the oldest and most established technique, involves the microscopic examination of stained chromosomes to identify structural abnormalities and numerical changes. FISH, on the other hand, employs fluorescent probes to target specific genetic regions, allowing for precise detection of chromosomal rearrangements and abnormalities with high sensitivity.

NGS, a cutting-edge technology, offers a comprehensive view of the entire genome, enabling the identification of novel genetic mutations and alterations in a high-throughput manner.

In addition to its diagnostic and prognostic utility, cytogenetics has also contributed to our understanding of the underlying mechanisms driving hematological malignancies. The identification of specific genetic alterations has led to the discovery of critical pathways involved in cell proliferation, differentiation, and survival. For instance, the BCR-ABL1 fusion protein in CML activates signaling pathways that promote cell division and inhibit apoptosis. Targeted therapies designed to disrupt these pathways have revolutionized the treatment of CML, turning it from a once-fatal disease into a manageable chronic condition. Similarly, the discovery of mutations in genes like FLT3 and NPM1 in AML has shed light on the dysregulated signaling pathways in this aggressive leukemia, paving the way for the development of targeted therapies currently under investigation.

Moreover, cytogenetics has unraveled the clonal evolution of hematological malignancies, revealing the dynamic nature of these diseases. As patients progress through various stages of their illness or in response to treatment, cytogenetic analysis can identify new genetic abnormalities or shifts in the clonal makeup of malignant cells. This insight has significant implications for treatment strategies, as it may necessitate adjustments to therapy in order to effectively target evolving subclones.

The impact of cytogenetics on hematological malignancies extends beyond the realm of clinical diagnosis and treatment. It has also played a pivotal role in research, enabling scientists to unravel the molecular mechanisms underlying these diseases and paving the way for the development of novel therapeutic approaches. For instance, the discovery of the JAK2 V617F mutation in myeloproliferative neoplasms (MPNs) has led to the development of JAK inhibitors, such as ruxolitinib, which specifically target the dysregulated JAK-STAT signaling pathway. This represents a paradigm shift in the treatment of MPNs, offering patients a targeted therapy that addresses the underlying molecular defect.

Furthermore, cytogenetic research has contributed to our understanding of clonal hematopoiesis of indeterminate potential (CHIP), a phenomenon where individuals harbor somatic mutations in hematopoietic stem cells without clinical evidence of hematological disease. These mutations, often detected through NGS, increase the risk of developing hematological malignancies and cardiovascular diseases. By identifying and monitoring these early genetic changes, cytogenetics has opened new avenues for early intervention and risk stratification, potentially preventing the progression to overt disease.

**Review of Literature**

Yahya, Dinnar et al., (2022) For many years, cytogenetic analysis has been standard practice for evaluating patients with haematological malignancies. The purpose of this study is to summarize and evaluate the conventional cytogenetic examination of bone marrow samples from patients with various haematological diagnoses performed by the Cytogenetic sector of the Laboratory of Medical Genetics - Varna. One more goal is to develop some conclusions and pass on our knowledge by analyzing the patterns that have emerged over the past eleven years. All samples taken from bone marrow at our facility between 2010 and 2020 were analyzed retrospectively. Totaling 2,653 patients ranging in age from 0 to 93 years old, we analyzed the data. According to the most recent guidelines from Europe and the International System for Human Cytogenomic Nomenclature, samples were stained using the G-banding method. GraphPad Prism (version 8.3.0) was used to conduct a temporal trend analysis statistically. Acute myeloid leukemia, myelodysplastic syndrome, acute lymphoid leukemia, chronic myeloid leukemia, and multiple myeloma were the most common types of hematological malignancy (90.9%). 2,215 (83.5%) samples passed through the analyzer successfully, with pathology being detected in 723 (32.6%) and a normal karyotype being discovered in 1492 (67.4%). Complex karyotype (29.9%), Philadelphia chromosome (21%), trisomy 8 (6.1%), and deletion of the long arm of chromosome 5 (4.4%) were the most prevalent abnormalities in this category. Standard workup for haematological malignancies continues to include this technique because to its significant impact on disease assessment. The scientific community is aware of the limitations of cytogenetic analysis, and our own observations corroborate this requirement for a more precise genetic technique.

Mohi-Ud-Din Malla, Tahir et al., (2022) The purpose of this article is to offer a comprehensive review of the cytogenetic methods currently employed for the diagnosis and prognosis of hematological malignancies. Since the Philadelphia chromosome was shown to be the only aberration in chronic myeloid leukemia, cytogenetics has become more important in the diagnosis of blood cancers. Advanced cytogenetic techniques like Fluorescent In-Situ Hybridization, Spectral Karyotyping, and Comparative Genomic Hybridization have eliminated the problems associated with traditional cytogenetics, such as culture failures, poor chromosome morphology, and a low mitotic index, making

the identification of clones and the monitoring of the response to drug therapy much simpler. There is strong evidence that chromosomal abnormalities serve as early warning signs of the development of a hematological disease. In addition to helping in the identification of individual clones, conventional cytogenetics, when supplemented with molecular cytogenetic techniques, immunophenotyping, and real-time PCR, can aid in the characterization of hematological malignancies, the prediction of prognoses, and the evaluation of minimal residual disease during the course of their treatment. We conclude that cytogenetic procedures, even in the age of array diagnostics, remain a dependable tool for the correct diagnosis, characterisation, and prognosis of hematological malignancies. This review focuses on the use of cytogenetic methods in the detection and evaluation of blood cancers. It also sheds light on the technological difficulties and potential solutions while doing such research.

El-Jawahri, Areej et al., (2020) Patients with hematologic malignancies have varying palliative and end-of-life care demands since this diverse group of illnesses has different illness trajectories, treatment paradigms, and possibilities for cure. Both the disease itself and the often-intense therapies that produce considerable toxicities and adverse effects place a heavy burden on the minds and bodies of patients with hematologic malignancies. Patients with hematologic malignancies are more likely to die in the hospital, spend more time in the critical care unit, and be sent to hospice at a lower rate than patients with solid tumors. Hematologic malignancy patients often exaggerate their prognosis and have inflated views of the potential advantages of their therapy. Late effects, post-treatment problems, and post-traumatic stress symptoms all affect survivors of hematologic malignancies, reducing their quality of life. Patients with hematologic malignancies seldom seek the advice of specialised palliative care providers, despite the fact that they have significant unmet requirements. Palliative care integration and excellent end-of-life care face obstacles in this group due to a variety of causes. However, new data has shown that incorporating palliative care to enhance the quality of life and care for patients with hematologic malignancies and their carers is feasible, acceptable, and effective. To establish generalizability and define a sustainable clinical delivery strategy, further research is required to design and evaluate population-specific palliative and supportive care treatments. Future research should also design less resource-intensive integrated care models to meet the varying demands of this group, as well as find moderators and mediators of the impact of integrated palliative care models on patient-reported outcomes.

Oechsle, Karin (2019) Studies addressing the possible impact of integrated palliative care for patients with hematologic malignancies (HM) are very uncommon. Comprehensive information on their current end-of-life treatment, including the first data on integrated specialist palliative care (SPC) and possible impediments, is included in this narrative review. While HM patients' overall symptom load and distress seem to be on par with that of other cancer patients, their performance status and particular symptoms are much worse. Until a person's last days or weeks, they tend to be preoccupied with trying to extend their life as much as possible. Even though they are twice as likely to die in the hospital as other cancer patients, they are just half as likely to get specialized palliative or hospice care. Prospective research shows that integrated SPC is well-accepted and has beneficial consequences, including but not limited to: better treatment outcomes; improved quality of life; and reduced rates of depression, anxiety, symptom load, and PTSD. Not enough is being done to promote interdisciplinary collaboration, prompt talks regarding SPC referral, and the use of markers to 'flag' patients in need of SPC. In conclusion, further research is needed to determine what variables might be used to identify HM patients who would benefit from SPC. It is important to conduct prospective trials of other models of early integrated palliative care and implement the most promising ones into standard clinical practice.

Alves, Angelica et al., (2018) Cancers of the blood and bone marrow often result from chromosomal abnormalities and mutations in hematopoietic cells. The immune system weakens, the bone marrow stops producing new blood cells, and a small percentage of the old (2-3%, on average) have chromosomal anomalies due to clonal mosaicism. The goal of this article is to provide a detailed description of the epidemiology and cytogenetic profile of hematological malignancies, focusing on the prevalence of age-related chromosomal changes in these neoplasms. Method Between 1998 and 2016, the Cytogenetic Laboratory of the Blood Center at the Faculdade de Medicina de Marilia (FAMEMA) conducted retrospective cross-sectional research analyzing the results of karyotype examinations. The Onco-hematology Outpatient Clinics at the regional blood center, hospitals, and external clinics gathered blood samples from children and adults being treated for a variety of hematological malignancies. The findings of karyotype examinations were examined for 746 individuals with a mean age of 54.7 years (23.1). Hematological malignancies were most common among the elderly (50.9%), followed by adults (38.3%), and then young persons (10.7%), with the greatest prevalence seen among old women (55.0%). Among the aged population, normal karyotypes (46,XX/46,XY) were more prevalent than aberrant karyotypes (56.4% vs. 61.8%). Atypically high rates of aberrant karyotypes

(67.4%) were seen in myeloproliferative neoplasms. Hematological malignancies are more common in the elderly, and this trend may be explained by a decline in genomic processes and hematopoiesis that results in the production of cells with the chromosomal changes seen in these diseases.

Tadesse, Abilo (2013) Leukemia, lymphoma, and plasma cell dyscrasia are all examples of hematological malignancies, which are primary tumors of the blood and blood-forming organs (the bone marrow and lymphoid tissues). Hematological malignancies are increasing across the board in the United States and Europe, and are also thought to be on the rise in Africa. The lack of data on the clinical features of hematological malignancies in Ethiopia prompted the researchers to perform this investigation. The purpose of this research is to characterize the prevalence and variety of hematological malignancies in the area. Patients hospitalized to Gondar University Hospital with a hematological malignancy diagnosis between January 2008 and December 2011 were the focus of this retrospective descriptive analysis. During the research period, 67 individuals were hospitalized with a hematological malignancy. Patients with hematological malignancies had mean and median ages of 42 and 45 years old. Out of the 67 cases of hematological malignancy, 22 (32.8%) were caused by non-Hodgkin's lymphoma (NHL), 17 (25.4%) by chronic myeloid leukemia (CML), and 13 (19.4%) by chronic lymphocytic leukemia (CLL). The aggressive character of NHL is reflected in the fact that the vast majority of patients come with advanced disease, high-grade type, and B-symptoms (68%). Chronic leukemia (CML and CLL) cases reported with tiredness, weight loss, and organomegally on admission, while patients with acute leukemia, especially acute lymphoblastic leukemia (ALL), exhibited characteristics of cytopenia (fatigue, fever, and bleeding propensity). On admission, 12/17 (71%) patients with CML were in chronic phase, 4/17 (23%) were in accelerated phase, and 1/17 (6%) were in blast phase. Nine of the thirteen patients admitted with CLL had Binet C disease (69%) and ten of the thirteen (76%) had advanced illness (Rai stages III and IV). This study's findings on the prevalence and presentation of different hematological malignancies are generally consistent with those from previous research conducted in other African nations.

Haus, Olga et al., (2012) In order to properly identify and categorize hematologic malignancies, cytogenetic analysis is required, as stated by European LeukemiaNet—Workpackage Cytogenetics. The gold standard of genetic diagnostics in hemato-oncology is still conventional cytogenetic analysis, which can detect both balanced and unbalanced chromosomal rearrangements. The process of detecting and analyzing recurring genetic abnormalities, however, may now be complemented by a number of fast growing state-of-the-art molecular and cyto-molecular approaches. Hematologic malignancies now routinely use cytogenetic analysis as part of the diagnosis procedure. It aids in the categorization of diseases, the provision of vital prognostic and predictive data, the shaping of treatment plans by providing rationale for individualized approaches that target cancer-specific genetic abnormalities or their products, and the evaluation of therapy efficacy by revealing genetic remission or progression.

## 2. Materials And Methods

This research was a cross-sectional descriptive study. Patients were referred from adult and pediatric hematology units at public and commercial hospitals around the country. Patients with acute/chronic leukemia, lymphoma, CMPD, or MDS were also included for a total of 180. All cases of hematological cancer are identified in accordance with WHO standards.

All samples were analyzed cytogenetically over the course of the study (January 2019 through December 2019), and the results were published using the International System for Human Cytogenetic Nomenclature (ISCN). Frequencies and descriptive statistics were calculated using SPSS software.

## 3. Results and Discussion

The highest prevalence of these hematological disorders among the inclusive patients was found to be Pre-B Acute Lymphoblastic Leukemia (Pre-B ALL), followed by 20% Chronic Myelogenous Leukemia (CML), 14% Acute Lymphoblastic Leukemia (ALL), 14% Acute Myeloid Leukemia (AML), 7% Chronic Lymphocytic Leukemia (CLL), 6% MDS, 2.4% Multiple Myeloma (MM) and other abnormalities 3%, respectively, as shown in Table 1.

**Table 1: Prevalence of hematological malignancies in patients**

| Hematological Malignancies | Percentage |
|---|---|
| Acute Lymphoblastic Leukemia | 14.0 |
| Acute Myeloid Leukemia | 14.0 |

| | |
|---|---|
| Pre-B Acute Lymphoblastic Leukemia | 33.0 |
| Chronic Lymphocytic Leukemia | 7.0 |
| Chronic Myelogenous leukemia | 20.0 |
| Myelodysplastic Syndrome | 6.0 |
| Multiple Myeloma | 2.5 |
| Other's (Burkit Lymphoma, Jack 2 kinase mutation, Pancytopenia) | 3.0 |

We have also looked at the chromosomal abnormalities that are present in these hematological cancers. The translocation was the most common kind of chromosomal aberration, occurring in 24.8% of patients. This was followed by 5% monosomy, 6.9% hypotriploidy, 4% trisomy, 3.5% hyperdiploidy, and 2.5% deletion. On the other hand, as shown in Table 2, a total of 51% of patients exhibited no abnormal chromosomal behavior and were considered to be normal. These karyotypes have also been measured by a number of other hematological cancers, as can be shown in Table 2.

**Table 2 Chromosomal aberrations in different hematological malignancies**

| | | Hematological Malignancies | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Chromosomal Abnormalities** | **%** | **ALL** | **AML** | **CLL** | **CML** | **MDS** | **MM** | **Pre-B-ALL** | **Others** |
| Deletion | 2.5 | 60% | | | | 20% | | 20% | |
| Dicentric chromosomes | 0.5 | | | | | | | 100% | |
| Hyperdiploidy | 3.5 | 43% | 14% | | | | | 43% | |
| Hypodiploidy and monosomy | 1.0 | | | | | | | | 100% |
| Heteroploidy | 0.5 | 100% | | | | | | | |
| Hypotriploid | 6.9 | 57% | | | | | | 43% | |
| Monosomy | 4.0 | | 40% | 10% | | | | 40% | 10% |
| Normal | 51.0 | 6% | 14% | 12% | 20% | 8% | 5% | 32% | 3% |
| Tetrasomy | 0.5 | | | | | | | | 100% |
| Translocation | 24.8 | 8% | 18% | | 2% | 40% | 6% | | 26% |
| Trisomy | 5.0 | 30% | 10% | | | | | | 60% |

## 4. Conclusion

Cytogenetics has been instrumental in deciphering the enigmatic genetic landscape of hematological malignancies. Its historical evolution, closely intertwined with the unraveling of DNA's structure and the subsequent development of advanced laboratory techniques, has led to groundbreaking discoveries. The identification of characteristic chromosomal abnormalities, such as the Philadelphia chromosome in CML, has not only provided diagnostic markers but has also guided the development of targeted therapies, ultimately changing the trajectory of patient care. Cytogenetics has redefined our approach to hematological malignancies. It has transitioned from a scientific curiosity to an indispensable pillar of clinical practice. Its impact on diagnosis, prognosis, and treatment selection has improved patient outcomes and holds the potential to further enhance care in the years to come. As we navigate the ever-evolving landscape of hematology, cytogenetics remains a steadfast guide, illuminating the path toward precision medicine and better lives for those affected by hematological malignancies.

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