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Biochemical Markers in Hematological Disorders: A Review of Diagnostic and Prognostic Relevance in the Indian Pathological Landscape

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ABSTRACT

Anaemia, thrombocytopenia, and haematological malignancies are examples of haematological illnesses that pose a substantial burden to India's public health system. It is nevertheless extremely important to make a diagnosis that is both accurate and early in order to effectively manage and treat these illnesses. Biochemical markers, which include oxidative stress indicators, inflammatory biomarkers, serum ferritin levels, and vitamin D levels, have garnered a significant amount of interest in recent years due to the diagnostic and prognostic usefulness they possess in the field of worldwide medical research. Despite this, their function in the Indian pathological environment is still not fully understood and utilised, particularly in settings where resources are of restricted availability. This paper aims to critically synthesize existing secondary data from peer-reviewed journals, clinical reports, and healthcare bulletins to assess the relevance of biochemical markers in diagnosing hematological disorders prevalent in India. In this study, primary data and statistical methods are not utilised; rather, the emphasis is placed on theoretical assessment and comparative literature analysis. In this study, key biochemical indicators are investigated in connection to their physiological roles, diagnostic thresholds, and the pathological implications they have. The oxidative stress response in

anaemia and malignancies, the involvement of inflammatory cytokines in platelet diseases, the dual function of serum ferritin in iron homeostasis and inflammation, and the contribution of vitamin D to immunological and haematopoietic functions are some of the topics that are discussed in this article. According to the findings, despite the fact that these markers have been extensively researched all over the world, their use in Indian pathology is still restricted. This is because there is a lack of integration in diagnostic procedures, there is heterogeneity in reference values, and there are limits on infrastructure. Based on the findings of the review, it is recommended that uniform diagnostic protocols and theoretical frameworks be developed in order to improve the function that these markers play in pathology laboratories all throughout India. The purpose of this work is to make a contribution to the current body of knowledge by providing a contextualised understanding of biochemical markers and proposing a theoretical underpinning for their more widespread use into diagnostic procedures in India.

1. INTRODUCTION

Medical conditions that affect the blood and its components, such as red blood cells, white blood cells, platelets, haemoglobin, bone marrow, and blood proteins, are referred to as haematological disorders. Haematological disorders are a vast range of illnesses. Anaemia, thrombocytopenia, and haematological cancers including lymphoma and leukaemia are among the most common types of blood disorders. Deficiencies in nutrition, infections, autoimmune illnesses, chronic diseases, and genetic anomalies are all potential causes of these disorders. There is a sizeable section of the population in India that is affected by anaemia on its own, with women, children, and old people being the most susceptible to the condition. Clinical and hospital-based research in metropolitan and semi-urban areas are progressively reporting cases of thrombocytopenia and blood malignancies, despite the fact that these conditions are less common (Shah et al., 2020; Bhandari et al., 2021).

There is a significant contribution that biochemical indicators make to the process of diagnosing, monitoring, and treating these illnesses. The biological and pathological processes that they serve as markers of may be measured quantitatively. The application of biochemical markers in contemporary

pathology has expanded beyond the performance of basic blood counts to incorporate the utilisation of specialised markers such as oxidative stress indicators, inflammatory cytokines, serum ferritin levels, and vitamin D concentrations. These indicators have the ability to assist in early identification, risk assessment, and therapy monitoring, as well as highlight the underlying pathophysiological mechanisms that are responsible for blood diseases (Meena et al., 2021; Raut et al., 2019).

The identification of haematological problems in a timely manner is absolutely necessary in order to initiate appropriate medical intervention and provide better results for patients. The advancement of the disease and the development of complications might be caused by a delayed diagnosis or a misunderstanding of the symptoms. In the context of healthcare in India, diagnostic delays are frequently brought on by a lack of access to sophisticated laboratory equipment and qualified workers, particularly in rural regions. Consequently, biochemical markers provide a method that is both efficient and cost-effective for enhancing the accuracy of diagnostic procedures.

Malondialdehyde (MDA) and glutathione peroxidase (GPx) are examples of markers that represent oxidative stress, which is linked to the loss of red blood cells and the spread of cancer. Similar to the previous point, inflammatory indicators including C-reactive protein (CRP), interleukin-6 (IL-6), and tumour necrosis factor-alpha (TNF-α) play a crucial role in determining immune-mediated platelet diseases. In inflammatory situations, serum ferritin serves as an acute-phase reactant in addition to its function as an indication of the iron status of the cellular population. Even though vitamin D has been known for a long time for its function in maintaining bone health, its connection in erythropoiesis and immunological regulation is becoming more recognised (Thakur et al., 2021; Khanna et al., 2020). These markers are not only relevant for diagnosis but also for prognosis, helping clinicians predict disease trajectory and response to therapy.

The World Health Organisation estimates that more than 1.6 billion individuals throughout the world are affected with anaemia, making it the blood ailment that is reported to be the most prevalent worldwide. According to the findings of the National Family Health Survey-5 (2021) conducted in India, 57% of mothers and 67% of children under the age of five are malnourished. In addition, thrombocytopenia, which frequently results from dengue fever and other diseases, is more prevalent during epidemics that occur throughout specific seasons. According to estimates, roughly 8-10% of all cancers in India are classified as haematological malignancies, and the frequency of these diseases is rapidly increasing (Mitra et al., 2020).

In the field of haematology, recent developments have placed an emphasis on the incorporation of biochemical markers into diagnostic panels. A significant improvement in diagnostic precision has been brought about by the transition away from exclusively morphological and cytological evaluations and towards biochemical and molecular profiling. The use of combinations of markers to identify disease subtypes and assess therapy efficacy is now the focus of research as it pertains to the field. In the context of public health, there is a rising interest in the use of low-cost biomarkers that are already available in India, notably for the treatment of anaemia and chronic inflammatory illnesses (Saxena et al., 2021; Joshi et al., 2019).

It is the purpose of this research to conduct an in-depth analysis of the diagnostic and prognostic significance of major biochemical markers in the context of haematological illnesses in India. These markers include oxidative stress indicators, inflammatory biomarkers, serum ferritin levels, and vitamin D levels. A theoretical framework for integrating these markers into the diagnostic ecosystem is the goal of this project, which will be accomplished by the study of secondary data derived from previously published research. The purpose of this work is to emphasise the importance of the markers, as well as their interpretative limits and potential for inclusion in routine diagnostic protocols in resource-limited Indian settings. This will be accomplished by synthesising existing data.

Review-based theoretical analysis was the approach that was taken in the design of the current study. There were no experimental techniques, primary data collecting, or statistical testing that were involved in this particular endeavour. The research was conceptual and interpretative in character, with the goal of gaining meaning from previously published information that was already in existence.

In this investigation, only secondary sources of information were utilised. Journal papers that had been subjected to peer review, clinical reviews that had been published, official health reports from national agencies, documents from the World Health Organisation, and disease-specific bulletins from Indian medical groups were among these. In order to guarantee that the chosen literature is relevant to the present day, it covered the years 2010 through 2021.

Both narrative and comparative synthesis were utilised in the process of doing the analysis. In the context of certain haematological illnesses, research was conducted to investigate the function that each marker plays in diagnosis and prognosis. Through the use of thematic categorisation, it was possible to discover important insights, prevalent patterns, and theoretical relationships that are pertinent to the Indian healthcare context.

2. OXIDATIVE STRESS MARKERS IN HEMATOLOGICAL DISORDERS

- Analyze oxidative damage and its role in anemia and hematological malignancies.
- Review MDA, SOD, and GPx as biomarkers for disease progression.
- Discuss Indian case studies and research findings using secondary literature.

3. INFLAMMATORY BIOMARKERS AND PLATELET DISORDERS

Platelet problems, and thrombocytopenia in particular, are frequently linked to inflammatory reactions that occur throughout the body. The condition known as thrombocytopenia, which is characterised by an unusually low platelet count, can be brought on by a wide variety of factors, including as autoimmune destruction, viral infections, suppression of bone marrow, and adverse treatment responses. Several of these disorders are characterised by inflammation, which plays a significant part in the pathophysiological process. Key inflammatory biomarkers, including interleukin-6 (IL-6), tumour necrosis factor-alpha (TNF-α), and C-reactive protein (CRP), have been subjected to significant research as diagnostic and prognostic indications in the context of platelet-related illnesses. Thrombocytopenia severity and duration have been connected to these biomarkers, which represent systemic immunological activity and have been associated to both of these factors before (Malik et al., 2021; Roy et al., 2020).

One of the most important cytokines in both acute and chronic inflammation is interleukin-6 (IL-6), which has several functions. Elevated levels of interleukin-6 (IL-6) are frequently reported in patients who have immunological thrombocytopenic purpura (ITP), dengue-related platelet depletion, and chemotherapy-induced cytopenias. These conditions are all linked with thrombocytotoxicity. At the same time as it stimulates the proliferation of megakaryocytes in response to the loss of platelets, it paradoxically has the potential to inhibit efficient thrombopoiesis in the event of acute inflammation. IL-6, working in conjunction with IL-1β and TNF-α, has a synergistic effect, hence increasing the inflammatory cascade and leading to an increase in platelet consumption (Dubey et al., 2020; Srivastava et al., 2019).

Another important pro-inflammatory cytokine, tumour necrosis factor-alpha (TNF-α), has been demonstrated to cause apoptosis in megakaryocytes and to disturb the homeostasis of bone marrow. High levels of tumour necrosis factor-alpha (TNF-α) have been linked to the loss of platelets in patients with autoimmune thrombocytopenia. Additionally, TNF-α has been linked to cases of chronic inflammation and systemic infections. Not only does TNF-α play a role in the breakdown of platelet precursors, but it

also plays a role in enhancing phagocytic activity against circulating platelets in immune-mediated responses (Guha et al., 2021; Shekhar et al., 2020). These mechanisms make TNF-α an important marker in assessing the immune component of thrombocytopenia.

The C-reactive protein (CRP) is a non-specific measure of inflammation that is frequently utilised. It is especially useful in distinguishing viral causes of thrombocytopenia from non-infectious causes of the condition. CRP levels that are elevated are seen in patients who have viral fevers, sepsis, and other systemic inflammatory diseases that are linked with a drop in platelet counts. In clinical settings, the measurement of CRP assists doctors in determining the intensity of the inflammatory response as well as the possible risk of coagulopathies or hemorrhagic consequences. Further, in the case of immune-mediated platelet abnormalities, longitudinal monitoring of CRP might offer valuable insights on the course of the disease as well as the response to treatment (Tripathi et al., 2021; Menon et al., 2021).

In spite of the fact that these biomarkers are recognised to be useful, there is a dearth of thorough research in India that incorporate levels of IL-6, TNF-α, and CRP into diagnostic methods for platelet abnormalities. The majority of clinical evaluations continue to depend mainly on platelet counts and peripheral blood smears, which may not show the underlying inflammatory or immune-mediated aetiology of the conditions being evaluated. The broad adoption of these tests in Indian pathology clinics is further hindered by the absence of standardised reference values, data from regional research, and testing facilities that are available at an affordable price. A further factor that contributes to the lack of uniformity in biomarker interpretation is the fact that different institutions use different laboratory methodologies.

As a result, there is an urgent requirement in India for research that is focused on reviews and efforts that are at the policy level in order to evaluate these inflammatory indicators within the context of local clinical settings. The incorporation of interleukin-6 (IL-6), tumour necrosis factor-alpha (TNF-α), and C-reactive protein (CRP) into standard screening panels for patients who have unexplained thrombocytopenia has the potential to greatly improve diagnosis accuracy and treatment targeting within the Indian healthcare system.

4. SERUM FERRITIN AS A DIAGNOSTIC AND PROGNOSTIC TOOL

Numerous haematological illnesses, in particular anaemia and haematological cancers, are characterised by the presence of oxidative stress, which plays a significant part in the development and evolution of

these disorders. When there is a disparity between the production of reactive oxygen species (ROS) and the capability of antioxidant defence mechanisms, oxidative stress is the outcome. In the case of haematological illnesses, this imbalance results in structural and functional damage to the components of bone marrow, DNA, and red blood cells. A clear connection has been shown between increased oxidative damage and haemolysis in cases of anaemia, as well as genomic instability in cases of cancers such as lymphoma and leukaemia (D'Souza et al., 2020; Rathi et al., 2021). This underlying biochemical dysfunction is reflected in measurable oxidative stress markers, which have emerged as valuable diagnostic and prognostic tools.

Among the most widely studied markers, malondialdehyde (MDA) is the key sign of the presence of lipid peroxidation. In the process of degrading polyunsaturated fatty acids, MDA is produced as a byproduct. The presence of higher amounts of MDA indicates that there is greater oxidative damage to cell membranes. The presence of increased blood MDA concentrations has been regularly confirmed in studies conducted on individuals suffering from iron-deficiency anaemia and sickle cell anaemia. This suggests that oxidative stress plays a role in the fragility of erythrocytes and the early haemolysis that they undergo (Jain et al., 2021; Sultana et al., 2020). In hematological malignancies, MDA elevation corresponds with disease activity, particularly in acute myeloid leukemia, where oxidative damage contributes to DNA mutations and apoptosis resistance.

Superoxide dismutase (SOD) is an essential enzymatic antioxidant that prevents cellular damage by taking superoxide radicals and converting them into hydrogen peroxide. In individuals who suffer from chronic anaemia and leukaemia, it is common to see a decline in the activity of superoxide dismutase (SOD), which in turn affects their capacity to neutralise superoxide radicals. In a number of clinical investigations carried out in India, particularly those carried out in tertiary care facilities, lower levels of superoxide dismutase (SOD) have been found to be connected with the severity of the disease and resistance to therapy in leukaemia patients, hence proving its significance in disease monitoring (Menon et al., 2020; Chakraborty et al., 2019).

Glutathione peroxidase (GPx) is an additional vital antioxidant enzyme that diminishes hydrogen peroxide and lipid hydroperoxides, therefore shielding red cells and bone marrow from the harmful effects of oxidative damage. In situations such as aplastic anaemia, myelodysplastic syndromes, and haemolytic disorders, where oxidative stress hinders haematopoiesis and increases cellular death, decreased GPx activity has been described. In addition, research conducted in India have demonstrated

that there is a correlation between low levels of GPx and an increased need on transfusions among anaemic patients, particularly people who have thalassaemia (Verghese et al., 2021; Joshi et al., 2020).

The findings of this study have been validated by a number of case studies and hospital-based evaluations conducted in India. The hypothesis that oxidative stress exacerbates cellular damage in nutrient-deficiency anaemia was supported by the findings of a research that was carried out at a government hospital in Gujarat. The study found that patients with megaloblastic anaemia had considerably higher levels of MDA, while their levels of SOD and GPx were dramatically altered. Another retrospective study conducted at a cancer hospital in West Bengal looked at the oxidative stress profiles of lymphoma patients. The researchers discovered that greater levels of MDA and lower levels of SOD/GPx were related with more aggressive disease stages and a poor response to treatment (Acharya et al., 2021; Rane et al., 2020).

Exogenous stress indicators are not yet commonly employed in regular diagnostic practice in India, despite the rising body of data supporting their use. Including them in diagnostic algorithms has the potential to enhance early identification, provide direction for treatment, and track the evolution of health conditions. In order to effectively use the potential of these biomarkers in the management of haematological diseases, it would be necessary to provide a larger availability of clinical labs and to standardise the testing techniques.

5. VITAMIN D LEVELS AND HEMATOLOGICAL HEALTH

The importance of vitamin D in sustaining haematological health has just come to light, despite the fact that it has historically been recognised for its involvement in calcium metabolism and bone preservation. Recent research has shed light on its role in erythropoiesis, which is the process of producing red blood cells, as well as in the control of the immune system. These studies have established a connection between vitamin D deficiency and a variety of anaemias and immune-mediated haematological illnesses. Anaemia is commonly reported as a concomitant condition in patients with chronic kidney disease (CKD) and autoimmune disorders including systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA). The consequences of vitamin D deficiency are especially noteworthy in these groups of patients (Deshmukh et al., 2021; Verma et al., 2020).

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The role of vitamin D as an immunomodulator is important to consider in the context of autoimmune illnesses. At the same time as it increases the activity of anti-inflammatory pathways, it decreases the activity of pro-inflammatory cytokines including IL-6 and TNF-α. The important impact that this immuno-regulatory function plays in lowering bone marrow suppression and enhancing the haematopoietic environment cannot be overstated. It has been found that a lack of vitamin D is associated with greater disease activity and a higher prevalence of anaemia in patients with autoimmune haemolytic anaemia and systemic lupus erythematosus. Due to the fact that it modulates immunological responses, research shows that adequate levels of vitamin D may minimise haematologic problems that are associated with autoimmune diseases (Paul et al., 2019; Chhabra et al., 2021).

In addition to its systemic activities, vitamin D has a role in haematopoiesis by stimulating macrophages and monocytes, which in turn have an effect on the microenvironment of the bone marrow. Lower levels of vitamin D are related with greater concentrations of hepcidin, which in turn reduces the amount of iron that is available for erythropoiesis. This factor has an effect on iron metabolism because it regulates the expression of hepcidin. Anaemia and vitamin D insufficiency are both present in inflammatory and chronic illness states, and this process provides an explanation for both of these conditions (Saxena et al., 2020; Josan et al., 2021).

However, despite the fact that these connections have been thoroughly proven, systematic monitoring of vitamin D levels in India continues to be uneven. The lack of understanding among doctors on its haematological significance, the restricted availability of cost-effective tests, and the diversity in testing standards between diagnostic centres are all obstacles that prevent widespread testing from occurring. As a result of the fact that many government and rural healthcare institutions do not include vitamin D testing in conventional anaemia or chronic illness panels, several deficiencies that contribute to the condition are not properly diagnosed. Further complicating the process of establishing conventional reference ranges for the Indian population is the fact that blood vitamin D levels are affected by seasonal

and geographical differences in solar exposure, food habits, and skin pigmentation (Thakur et al., 2020; Pradhan et al., 2021).

In order to address these problems, it is necessary to incorporate vitamin D screening into full anaemia workups. This is especially important for patients who suffer from chronic inflammatory and autoimmune disorders. The diagnosis and management of vitamin D-related haematological disorders in India can be improved by the promotion of research into locally relevant reference values and the subsidisation of testing within public health initiatives.

6. INTEGRATED ANALYSIS: TOWARD A THEORETICAL DIAGNOSTIC FRAMEWORK

A thorough knowledge of haematological problems was achieved with the incorporation of oxidative stress indicators, inflammatory biomarkers, serum ferritin, and vitamin D levels. This was accomplished through the use of a biochemical perspective. Despite the fact that these signals were functionally independent from one another, they together indicated a complex interaction between cellular damage, immunological activity, iron management, and micronutrient balance. Compared to the use of isolated haematological indices alone, the combined diagnostic interpretation of these two factors offered a more nuanced perspective on the illness causes and patient situations.

Through the process of synthesising the functions that these four types of markers play, a theoretical diagnostic framework was established. Oxidative stress markers such as MDA, SOD, and GPx were placed at the centre of this model. These indications indicate the intracellular environment as well as the degree to which cells have been compromised in situations such as anaemia and cancer. These indicators served as early warning signals that indicated the presence of any damage to red blood cells, apoptosis, or suppression of bone marrow. In the context of autoimmune or viral disorders, inflammatory biomarkers including interleukin-6 (IL-6), tumour necrosis factor-alpha (TNF-α), and C-reactive protein (CRP) have been associated with immune-mediated platelet destruction and systemic reactions. The existence of continuous inflammation or immunological dysregulation was confirmed by their increases, which contributed an additional dimension to the diagnostic framework.

Additionally, serum ferritin served as a crucial bridging marker between iron metabolism and inflammation. This was due to the fact that it plays a dual role in iron storage and acute-phase response. The interpretation of this finding, in conjunction with transferrin saturation and inflammatory markers, allowed for the differentiation between iron-deficiency anaemia and anaemia caused by chronic illness. In conclusion, the levels of vitamin D acted as a checkpoint in the framework for both the metabolic and

immunological processes. There was a correlation between its deficit and inhibited erythropoiesis, immunological imbalance, and iron insufficiency occurring as a result of elevated hepcidin levels. By combining these four separate sets of indicators, it was possible to make a differential diagnosis across a wide range of haematological illnesses.

The paradigm that was suggested also theorised advances in clinical decision-making, particularly in situations in India that have limited resources. This biochemical technique made it possible to conduct an evaluation that was both more economical and more easily accessible in situations when typical haematological assays, such as bone marrow biopsy, flow cytometry, or genetic panels, were not available. The combination of monitoring CRP and serum ferritin, for instance, made it possible to differentiate between iron shortage and inflammation-associated anaemia. Serum-based indicators were able to be relied upon by doctors in remote locations where there was a shortage of equipment for complicated cellular diagnostics. These markers allowed clinicians to evaluate disease activity, severity, and possible treatment response.

Furthermore, a stratified diagnostic model was devised and included within this framework. Theoretically, patients who presented with anaemia and increased MDA but normal ferritin were considered to be suffering from oxidative stress–induced anaemia. Individuals who had normal levels of MDA but elevated levels of CRP and IL-6 were classified as having inflammation-mediated disorders. In cases where a shortage in vitamin D was observed alongside low haemoglobin levels and high inflammatory markers, it indicated a combination of dietary and immunological factors as the cause. Without having to rely on expensive technology, practitioners were able to classify patients into diagnostic pathways that could be successfully implemented thanks to this approach.

This approach has important ramifications at the policy level, and those implications were considerable. The theoretical creation of standard diagnostic panels that might be included into public health programs that are focused on the screening of anaemia, maternal health, and the treatment of chronic diseases was made possible as a result of this achievement. With the use of this marker-based approach, policymakers might develop recommendations that are specific to an area in order to enhance early diagnosis and surveillance, particularly in communities who are not being serviced. Integrated diagnostic model offered an organised, cost-effective, and theoretically orientated method to biochemical diagnosis in Indian haematological pathology. This was the overall conclusion of the study.

7. CONCLUSION

This research has theoretically analysed the function of biochemical indicators in the diagnosis and comprehension of haematological diseases, with a focus on their manifestations in India. When taken as a whole, the ideas offered by the various thematic sections shed light on how indicators like serum ferritin, vitamin D levels, oxidative stress indicators, inflammatory biomarkers, and inflammatory stress could improve diagnostic precision and clinical decision-making in contexts with abundant and scarce resources.

The importance of cellular damage in the development of anaemia and haematological malignancies was emphasised in the section on oxidative stress indicators. Important information on the cellular integrity and redox balance of haematopoietic systems was provided by markers such as MDA, SOD, and GPx. The biochemical basis of erythrocyte destruction, suppression of bone marrow, and treatment resistance in blood-related malignancies were better understood with the use of these indicators.

The significance of IL-6, TNF-α, and CRP in identifying immune-mediated platelet abnormalities was highlighted in the examination of inflammatory biomarkers. Results demonstrated that these indicators might detect systemic inflammation, autoimmune reactions, and the development of diseases such persistent infections and thrombocytopenia. Their promise of aiding in early diagnosis and providing prognostic support made them useful in practice, particularly in cases where traditional testing had failed to reveal platelet malfunction.

Serum ferritin's examination confirmed its dual role as an acute-phase reactant and iron storage protein. Researchers found that ferritin levels were a key indicator of whether a patient was suffering from iron-deficiency anaemia or chronic illness anaemia. Additionally, its interpretative flexibility made it a valuable biomarker for tracking the progression of viral and chronic inflammatory illnesses in patients.

Vitamin D's underappreciated but crucial function in immune regulation and erythropoiesis was highlighted in the study of its association with haematological health. Vitamin D insufficiency was linked to anaemia, especially in people with autoimmune diseases and chronic renal illness. Vitamin D insufficiency is common and frequently undiagnosed; this research added weight to the argument that screens for chronic diseases and anaemia should incorporate vitamin D testing. This is especially true in India.

These findings, when added together, demonstrated once again how biochemical markers have the ability to revolutionise haematological diagnosis in India. Theoretical results lent credence to the idea of creating a flexible, integrated diagnostic model that could be used in a variety of healthcare contexts,

including those in underprivileged rural areas, and might save money. By providing a systematic approach, the framework helped doctors make sense of serum-based testing for illness conditions, reducing the need for more costly and inconvenient diagnostic tools.

The research also brought attention to the critical need for further secondary data-based modelling initiatives. Both national policy frameworks that included these indicators into standard protocols and diagnostic recommendations specific to regions were noticeably lacking. Theoretical model validation should be the focus of future research, with an emphasis on structured review articles and thorough meta-analyses of datasets from India. It is possible to develop biomarker panels that are appropriate for various demographics and clinical contexts in India by conducting multicentric secondary-data evaluations.

The study concluded that haematological pathology is best approached using a biochemical, marker-driven method, and it paved the way for more studies, better policies, and evidence-based diagnostic change.

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