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MedEst|2026 | Vol.6: e577| ISSN: 2789-7567 |RNPS: 2524| NARRATIVE REVIEW ARTICLE

Plasma proteins and protein electrophoresis: composition, function, and applications in human pathology. A narrative review

Proteínas plasmáticas y proteinograma: composición, función y aplicaciones en patología humana. Revisión Narrativa

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RESUMEN

Introducción: Las proteínas plasmáticas constituyen un conjunto heterogéneo de moléculas con funciones esenciales para la homeostasis del organismo. Su estudio mediante proteinograma representa una herramienta diagnóstica de amplia utilidad clínica, aunque persisten controversias sobre su interpretación en contextos específicos y ante la irrupción de nuevas tecnologías analíticas. **Objetivo:** Sintetizar el conocimiento actual sobre las proteínas plasmáticas, integrando su composición, origen, funciones fisiológicas y valor diagnóstico mediante el proteinograma. **Métodos:** Se realizó una búsqueda en distintos buscadores académicos, utilizando términos como "plasma proteins", "serum protein electrophoresis", "proteinograma", "monoclonal gammopathy" y "nephrotic syndrome". Se incluyeron artículos originales, revisiones, capítulos de libro y guías clínicas publicados entre 2015 y 2026, en español e inglés. La selección priorizó la relevancia temática y la calidad metodológica, con preferencia por metaanálisis, revisiones sistemáticas y estudios de alto nivel de evidencia. **Resultados:** Las proteínas plasmáticas, sintetizadas en hígado y sistema inmune, se organizan en albúmina, α1, α2, β y γ-globulinas, con funciones en transporte, inmunidad, coagulación y presión oncótica. El proteinograma por electroforesis identifica patrones típicos de síndrome nefrótico, cirrosis, inflamación y gammapatías. La electroforesis capilar y la proteómica amplían el potencial diagnóstico, aunque la electroforesis convencional sigue siendo la técnica de cribado de referencia. **Conclusiones:** El proteinograma sigue siendo fundamental en el laboratorio clínico. Su correcta interpretación, con consideración de variaciones fisiológicas y contexto clínico, junto con tecnologías avanzadas, ofrece una visión integral del estado de salud y enfermedad. La proteómica promete medicina personalizada, aunque su implementación rutinaria enfrenta desafíos de costo y complejidad técnica.

ABSTRACT

Introduction: Plasma proteins constitute a heterogeneous set of molecules with essential functions for the homeostasis of the organism. Its study by proteinogram represents a diagnostic tool of wide clinical use, although controversies persist about its interpretation in specific contexts and in the face of the emergence of new analytical technologies. **Objective:** Synthesize current knowledge about plasma proteins, integrating their composition, origin, physiological functions and diagnostic value through the proteinogram. **Methods:** A search was carried out in different academic search engines, using terms such as "plasma proteins", "serum protein electrophoresis", "proteinogram", "monoclonal gammopathy" and "nephrotic syndrome". Original articles, reviews, book chapters and clinical guidelines published between 2015 and 2026, in Spanish and English, were included. The selection prioritized thematic relevance and methodological quality, with preference for meta-analysis, systematic reviews and studies with a high level of evidence. **Results:** Plasma proteins, synthesized in the liver and immune system, are organized into albumin, α1, α2, β and γ globulins, with functions in transport, immunity, coagulation and oncotic pressure. The electrophoresis proteinogram identifies typical patterns of nephrotic syndrome, cirrhosis, inflammation and gammopathies. Capillary electrophoresis and proteomics expand the diagnostic potential, although conventional electrophoresis remains the gold standard screening technique. **Conclusions:** The proteinogram continues to be essential in the clinical laboratory. Its correct interpretation, with consideration of physiological variations and clinical context, together with advanced technologies, offers a comprehensive vision of the state of health and disease. Proteomics promises personalized medicine, although its routine implementation faces challenges of cost and technical complexity.

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INTRODUCTION

Plasma proteins are essential components of blood and crucial for a multitude of biological functions that maintain the body's homeostasis. They represent a heterogeneous population of more than 300 types of proteins, with a total serum concentration ranging between 60 and 80 g/L under normal conditions [1]. These molecules not only constitute the structural scaffolding of plasma but are also the primary effectors of processes such as substance transport, immunity [2], coagulation, and the inflammatory response.

The synthesis of these proteins occurs, for the most part, in the liver, although a significant group, the immunoglobulins, are produced by B lymphocytes [3]. Albumin, which alone constitutes approximately 55 % to 65 % of total proteins, is the most abundant and is essential for maintaining oncotic pressure, preventing edema formation, and acts as a nonspecific transporter of hormones [4], drugs, and other metabolites. The remaining proteins are classified as globulins, which are subdivided into fractions (α1, α2, β, and γ) according to their mobility in an electric field, a technique known as electrophoresis [5] that gives rise to the proteinogram.

The proteinogram is, therefore, a semiquantitative method that provides an overall picture of the patient's protein profile. Its clinical value is immense, since various pathologies characteristically alter the synthesis, catabolism, or distribution of these proteins, generating recognizable patterns associated with hepatic, renal, inflammatory, and neoplastic diseases, among others [6]. For example, a decrease in albumin together with an increase in the α2-globulin fraction is highly suggestive of nephrotic syndrome, while a polyclonal increase in γ-globulins is frequent in chronic liver diseases [7].

Despite the widespread clinical use of the proteinogram, controversies persist in its interpretation in specific contexts, such as in elderly patients with multiple comorbidities or in populations with particular ethnic characteristics [8]. The emergence of new analytical techniques—such as capillary electrophoresis and proteomics—raises questions about the positioning of conventional electrophoresis in the current diagnostic algorithm. These considerations justify an integrative synthesis that updates the available knowledge and guides the clinician in the interpretation of protein patterns.

The objective of this review is to synthesize current knowledge about plasma proteins, integrating their composition, origin, physiological functions, and diagnostic value through the proteinogram, to offer an updated reference for the clinician and the laboratory medicine specialist.

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The choice of a narrative review as a methodological approach responds to the breadth and heterogeneity of the topic addressed, ranging from fundamental biochemical aspects to clinical and technological applications. A systematic approach with meta-analysis would be inappropriate given the diversity of study designs, populations, and outcomes reported in the literature, as well as the predominantly descriptive nature of the available evidence in this field.

METHODS

Study design

A narrative review of the scientific literature was conducted, adopting an integrative approach that combines the synthesis of classical knowledge with contemporary advances in the study of plasma proteins. This methodological design proved most appropriate given the multidimensional nature of the topic, ranging from fundamental biochemical aspects to clinical and technological applications, with predominantly descriptive and heterogeneous evidence in terms of study designs, populations, and reported outcomes.

Bibliographic search strategy

An exhaustive search of the scientific literature was carried out during the month of July 2026, prioritizing publications from the period between January 2015 and June 2026 to ensure the currency of the information.

The information sources consulted included:

- **Bibliographic databases:** PubMed, ScienceDirect, and PubMed Central (PMC).
- **Institutional repositories:** SciELO, Redalyc, and portals of renowned universities.
- **Gray literature:** Master's and specialty theses, consensus documents, and clinical guidelines from scientific societies (Spanish Society of Clinical Biochemistry and Molecular Pathology, International Myeloma Working Group, American Association for Clinical Chemistry).

The search terms were organized into strategies combined with Boolean operators (AND, OR) and adapted to each database:

Main strategy in English:
"plasma proteins" OR "serum proteins" OR "proteinogram" OR "serum protein electrophoresis"
Combined with: "composition" OR "function" OR "clinical applications" OR "diagnostic patterns"

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And specific terms: "nephrotic syndrome" OR "liver cirrhosis" OR "monoclonal gammopathy" OR "inflammation"

Main strategy in Spanish:
"proteínas plasmáticas" OR "proteinograma" OR "electroforesis de proteínas"
Combined with: "fracciones proteicas" OR "patrones electroforéticos" OR "gammapatías"
And specific terms: "síndrome nefrótico" OR "cirrosis hepática" OR "hipoalbuminemia"

Additionally, a manual search was conducted by tracking the bibliographic references of selected articles (snowballing) to identify additional relevant sources not captured in the initial search.

Eligibility criteria

Inclusion criteria: Review articles (systematic reviews, meta-analyses, and narrative reviews) addressing relevant aspects of plasma proteins or the proteinogram. Original studies with diverse methodological designs: randomized clinical trials, cohort studies, case-control studies, cross-sectional studies, and descriptive observational studies. Chapters from reference textbooks in clinical biochemistry and laboratory medicine. Clinical guidelines, consensus documents, and recommendations from scientific societies. Publications in Spanish and English. Studies conducted exclusively in human populations. Works with full-text availability or extensive abstracts allowing adequate information extraction.

Exclusion criteria: Studies in experimental animals or in vitro models without direct clinical translation. Isolated case reports without significant relevance to the general synthesis of knowledge. Publications without full-text access when the abstract did not provide sufficient information. Opinion articles, editorials, or letters to the editor without empirical support. Documents not peer-reviewed or with questionable methodological quality. Duplicate studies in different databases.

Source selection process

Document selection was carried out following a structured two-phase process, executed independently by two reviewers (ARR and LMH):

Phase 1: Initial screening (titles and abstracts): The reviewers independently examined the titles and abstracts of all identified references. Documents that clearly did not meet the inclusion criteria were excluded. Disagreements were resolved through discussion and

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consensus; when agreement was not reached, a third expert reviewer (MARC) was incorporated for the final decision.

Phase 2: Critical reading (full text): Full texts of all preselected references from phase 1 were obtained. The reviewers critically evaluated each document and applied the eligibility criteria. Reasons for exclusion were recorded for documents that did not pass this phase.

Process documentation: A detailed record was kept of the number of references identified, preselected, and finally included, specifying the main reasons for exclusion. The selection process was documented to ensure transparency and reproducibility.

Methodological quality assessment

Given the heterogeneous nature of the included sources (different study designs and publication types), evaluation criteria were adapted according to the type of document:

For systematic reviews and meta-analyses: The comprehensiveness of the search, clarity of inclusion criteria, risk of bias assessment, and adequacy of synthesis methods were evaluated.

For original studies: The relevance of the methodological design to answer the research question, sample size, validity of the analytical methods used, and clarity in the presentation of results were considered.

For clinical guidelines and consensus documents: The representativeness of expert groups, updating of the evidence considered, and clarity of recommendations were assessed.

For book chapters: The reputation of the authors and publisher, as well as the updating and comprehensiveness of the content, were evaluated.

Quality assessment was used to weight the level of evidence of each source in the synthesis process, prioritizing those with greater methodological rigor.

Data extraction and synthesis

A data extraction form was designed that included the following categories:

1. **Bibliographic data:** Author(s), year of publication, title, journal or source, language.
2. **Study design:** Type of study, sample size (when applicable), study population.
3. **Main objective:** Research question or purpose of the study.

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4. **Relevant content:** Specific information on plasma protein composition, functions, physiological variations, analytical methods, or electrophoretic patterns.
5. **Main results:** Key findings related to the objective of this review.
6. **Limitations:** Main methodological or scope limitations stated by the authors.
7. **Level of evidence:** Classification according to study design (when applicable).

Extraction was performed by the two main reviewers (ARR and LMH) and cross-verified to minimize errors. Disagreements in extraction were resolved by consensus.

Synthesis strategy:

The extracted information was organized into the following thematic categories to structure the presentation of results:

1. Composition and origin of plasma proteins
2. Functions of protein fractions
3. Physiological variations in different age groups and special situations
4. Analytical methods for protein determination
5. Characteristic electrophoretic patterns in diseases

The synthesis approach was mainly descriptive-analytical, identifying:

- **Common patterns:** Consistent findings reported across multiple sources.
- **Contradictions or discrepancies:** Differences in results or interpretations among studies.
- **Evolution of knowledge:** Changes in the understanding of concepts over time.
- **Knowledge gaps:** Areas where evidence was insufficient or controversial.

The inclusion of high-level evidence (meta-analyses, systematic reviews, randomized clinical trials) was prioritized when available. When information came mainly from observational studies, expert consensus, or textbooks, this circumstance was explicitly noted and the implications for the robustness of the conclusions were discussed.

Ethical considerations and transparency statement

As this is a bibliographic review that does not involve human or animal participants, nor sensitive personal data, approval by an institutional ethics committee was not required. Nevertheless, compliance with the principles of scientific integrity was guaranteed, including:

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- **Transparency in the process:** All phases of the review were documented to allow replicability.
- **Conflict of interest declaration:** The authors explicitly declared the absence of conflicts that could bias the interpretation of results.
- **Proper attribution:** All consulted sources were duly cited, respecting copyright.
- **Declaration of AI use:** The authors declared that generative artificial intelligence was not used in the writing of the manuscript, ensuring human authorship of the content.

Methodological limitations

The narrative review presents limitations inherent to its design: The absence of a preregistered protocol, typical of systematic reviews, limits the reproducibility of the process. The non-systematic search may have omitted relevant studies, particularly those published in languages other than Spanish and English or in databases not consulted. Source selection, although performed by two independent reviewers, is subject to a certain degree of subjectivity in the interpretation of eligibility criteria. A formal risk of bias assessment was not performed using standardized tools (e.g., ROBINS-I, QUADAS-2), which could affect the weighting of evidence. The narrative synthesis does not allow a quantitative analysis of findings or the estimation of combined effects.

These limitations have been considered in the interpretation of results and in the formulation of conclusions, adopting a prudent stance in the extrapolation of findings.

RESULTS

Composition and origin of plasma proteins

Blood plasma is a complex biological matrix in which thousands of different proteins have been identified. The total protein concentration in serum (plasma once coagulation factors have been removed) normally ranges between 6,6 and 8,7 g/dL [10]. These proteins can be broadly classified into three major groups according to their structural function: albumin, globulins, and fibrinogen (the latter being absent in serum) [11].

Albumin is the most abundant protein, representing between 50 % and 60 % of the total, with a normal concentration of approximately 30–50 g/L. It is synthesized exclusively by the liver and has a half-life of approximately 19 days [12]. Globulins constitute the remainder of the proteins and are subclassified, according to their electrophoretic

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mobility, into α1, α2, β, and γ globulins [13]. Finally, fibrinogen is a glycoprotein synthesized in the liver and is key to the blood coagulation process; it constitutes the main protein difference between plasma and serum [14].

The origin of these proteins is, for the most part, hepatic. The liver is responsible for the synthesis of albumin, fibrinogen, and most α and β globulins. The γ-globulin fraction, composed primarily of immunoglobulins (antibodies), is produced by activated B lymphocytes in response to antigenic stimuli [15].

Functions of plasma proteins

The functions of plasma proteins are diverse and vital for the maintenance of homeostasis. Table 1 summarizes the main functions of each fraction.

Table 1: Main functions of plasma protein fractions

Protein Fraction	Main Components	Specific Functions
Albumin	Albumin	Maintenance of oncotic pressure, transport of hormones, drugs, fatty acids, and bilirubin, amino acid reserve
α1-Globulins	α1-antitrypsin	Protease inhibition (prevents tissue damage), positive acute-phase reactants (increase with inflammation)
α2-Globulins	α2-macroglobulin, haptoglobin, ceruloplasmin	Protease inhibition (α2-macroglobulin), binding to free hemoglobin (haptoglobin), copper transport (ceruloplasmin)
β-Globulins	Transferrin, LDL, complement C3, fibrinogen (in plasma)	Iron transport (transferrin), cholesterol transport (LDL), innate immune function (complement C3), coagulation (fibrinogen)
γ-Globulins	Immunoglobulins (IgG, IgA, IgM, IgD, IgE)	Adaptive immune defense (antibodies). Specific humoral response against antigens

Source: Own elaboration based on Whitfield JB [16].

In addition to the specific functions described, plasma proteins collectively fulfill general roles such as blood pH regulation through

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buffer systems, protection against infections (through antibodies and complement proteins), and prevention of blood loss through coagulation [17].

Physiological differentiation in different age groups and situations

The concentration and profile of plasma proteins are not static throughout life but vary physiologically depending on age, sex, and special situations such as pregnancy [18].

Newborns and children: Infants present lower total protein and IgG concentrations than adults, since the transfer of maternal IgG across the placenta is the main initial contribution. The child's own synthesis progressively increases during the first months of life. Essential amino acid requirements per kilogram of body weight are higher in children to support growth and development [19]. Cohort studies have documented that total protein concentrations in newborns are approximately 20–30 % lower than in adults, reaching similar values around 2–3 years of age [20].

Pregnancy: During gestation, a state of physiological hemodilution occurs, where the increase in plasma volume is greater in proportion than the increase in erythrocyte mass and protein synthesis. This leads to a relative decrease in hematocrit and in total protein and albumin concentration [21]. The reduction in serum albumin can reach between 0,5 and 1,0 g/dL compared to prepregnancy values, without necessarily reflecting a pathological state [22].

Adults and the elderly: In healthy adults, values remain relatively stable within reference ranges. In the elderly, although studies are inconsistent, some suggest that essential amino acid requirements may be altered, and it is common to observe a slight decrease in serum albumin, sometimes associated with subclinical conditions of malnutrition or chronic diseases [23]. Multiple studies report a progressive decrease in serum albumin of approximately 0,5–1,0 g/dL per decade after 60 years of age, related to changes in hepatic synthesis and nutritional status [24]. Sarcopenia (loss of muscle mass) associated with aging may also affect the general pool of amino acids available for protein synthesis.

Methods for the determination of proteins and their fractions

The classic and most widespread method for the study of protein fractions is electrophoresis. This technique separates proteins based on their net electrical charge, size, and shape when subjected to an electric field [25]. Traditionally, separation was performed on supports

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such as cellulose acetate or agarose. Once separated, proteins are stained with dyes (e.g., Coomassie Blue) and quantified semiquantitatively with a densitometer, obtaining a graph (proteinogram) with five or six main bands: albumin, α1, α2, β, and γ globulins [26].

A significant technological evolution is capillary electrophoresis. In this system, the sample is passed through a very narrow capillary and proteins are separated by a strong electroosmotic voltage. Quantification is performed by measuring absorbance at 214 nm of the peptide bond. This technique offers advantages such as greater speed, automation, precision, and resolution [27]. Comparative studies have shown that capillary electrophoresis presents approximately 35 % higher resolution than conventional agarose electrophoresis and reduces analysis time by 60 % [28].

For the precise quantification of specific proteins (such as a particular immunoglobulin or an acute-phase reactant like C-Reactive Protein), immunochemical methods such as nephelometry or immunoturbidimetry are required [29].

In recent years, mass spectrometry-based proteomics techniques have allowed the scanning of thousands of proteins in a single plasma sample, identifying a "core dataset" of more than 3,000 plasma proteins with high confidence [30]. These approaches, although not yet routine in the clinical laboratory, are revolutionizing biomarker discovery and enabling the development of health and disease prediction models based on protein expression patterns [31].

Table 2: Comparison of analytical techniques for the study of plasma proteins

Technique	Principle	Advantages	Limitations	Main Application
Agarose electrophoresis	Separation by charge and size	Low cost, standardized	Limited resolution, semiquantitative	Initial screening
Capillary electrophoresis	Electrophoretic separation in capillary	High resolution, automated, rapid	Higher instrumental cost	Screening and monitoring

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Immunofixation	Precipitation with specific antibodies	Identifies monoclonal Ig type	Less sensitive than modern methods	M-spike characterization
Nephelometry/Immunoturbidimetry	Detection of antigen-antibody complexes	Precise quantification	Requires specific antibodies	Quantification of individual proteins
Mass spectrometry	Identification by mass/charge	High sensitivity, multiplexing	High cost, technical complexity	Research, biomarker discovery

Source: Own elaboration by the authors based on consulted sources [27,28,29,30].

Most characteristic proteinogram patterns in diseases

The alteration in the synthesis, catabolism, or loss of plasma proteins in various pathologies generates recognizable patterns in the proteinogram, guiding clinical diagnosis.

1. **Inflammatory pattern:** This is one of the most frequent findings (approximately 45 % of alterations in the proteinogram). It is characterized by an increase in positive acute-phase reactants, which migrate in the α1 and α2 fractions (e.g., α1-antitrypsin, haptoglobin), and a decrease in negative acute-phase reactants such as albumin and transferrin [32]. If inflammation becomes chronic, it is also common to observe a polyclonal increase in γ-globulins due to persistent stimulation of the immune system [33].
2. **Nephrotic syndrome pattern:** This pattern is a consequence of massive renal loss of low molecular weight proteins. A marked decrease in albumin (often ≤2,5 g/dL) and a compensatory increase in the α2-globulin fraction are observed, where high molecular weight proteins such as α2-macroglobulin, which are not lost through the damaged kidney, are found [34]. This pattern occurs in approximately 88 % of patients with established nephrotic syndrome [35].
3. **Liver cirrhosis pattern:** Chronic liver damage affects the liver's synthetic capacity. The typical pattern shows a decrease in albumin (due to synthesis failure) and a polyclonal increase in γ-globulins (especially IgA), producing a broad, "stair-step" curve that can join the β and γ fractions [36]. This increase is due to the lack of degradation of intestinal-origin antigens and

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hyperactivation of the immune system. It is observed in 78 % of cases of advanced liver cirrhosis [37].

Gammopathies: These are alterations in the γ fraction, composed of immunoglobulins.

1. **Polyclonal gammopathy:** A diffuse, broad-based increase in the γ region is observed. It indicates activation of the immune system and is common in chronic infections (e.g., leishmaniasis, tuberculosis), autoimmune diseases, and liver diseases [38].
2. **Monoclonal gammopathy:** A narrow, tall peak ("M-spike") appears in the β or γ region, reflecting the proliferation of a clone of B cells producing a single type of immunoglobulin. It is characteristic of neoplasms such as multiple myeloma (generally IgG or IgA) or Waldenström's macroglobulinemia (IgM), but may also be a Monoclonal Gammopathy of Undetermined Significance (MGUS) [39]. The prevalence of monoclonal gammopathies in the population over 50 years of age is estimated at approximately 3 %, and IgG M-spike is the most frequent (55 % of cases) [40].

Table 3: Summary of the most characteristic electrophoretic patterns

Pattern	Albumin	α1-Globulin	α2-Globulin	β-Globulin	γ-Globulin
Normal	Normal	Normal	Normal	Normal	Normal
Acute/Chronic Inflammation	↓	↑	↑	Normal / ↑	↑ (Polyclonal, in chronic)
Nephrotic Syndrome	↓↓	↓ / Normal	↑↑	Variable	↓ / Normal
Liver Cirrhosis	↓	Normal / ↓	Normal / ↑	Variable	↑↑ (Polyclonal, "stair-step")
Monoclonal Gammopathy	Normal / ↓	Normal	Normal	Normal / ↑ (depends on Ig)	↑ (Narrow M-spike)

Source: Own elaboration by the authors based on consulted sources [32,33,36,39].
Note: ↑ = increase; ↓ = decrease; ↑↑ = marked increase; ↓↓ = marked decrease.

DISCUSSION

The analysis of plasma proteins through the proteinogram maintains an indisputable relevance in clinical diagnosis. Its value lies in its ability to offer a broad "snapshot" of the patient's physiological or

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pathophysiological state, integrating information on liver function, immune response, and the presence of inflammatory or neoplastic processes.

The usefulness of the pattern is undeniable. The inflammatory pattern, with its increase in acute-phase reactants, is often the most common finding and constitutes a nonspecific but sensitive marker of organic pathology. More specifically, classic patterns such as those of nephrotic syndrome (hypoalbuminemia and hyper α2-globulinemia) or cirrhosis (hypoalbuminemia and polyclonal hypergammaglobulinemia) decisively guide clinical investigation toward a specific organ system [41]. The correct identification of a monoclonal peak, on the other hand, is crucial for referring the patient to hematology and ruling out a B-cell neoplasm [42].

The findings of this review agree with those reported in other narrative syntheses on the subject [43,44], which highlight the usefulness of the proteinogram as a first-line screening test. However, unlike previous works that focused exclusively on the electrophoretic technique, this review incorporates the analysis of new emerging technologies (capillary electrophoresis, proteomics) and their potential impact on clinical diagnosis.

It is essential to emphasize that the interpretation of the proteinogram must be contextual. The physiological variations discussed, such as hemodilution in pregnancy or low IgG levels in newborns, are factors that must be considered to avoid diagnostic errors. A decrease in albumin in a pregnant woman, for example, may be a normal adaptation and not an indicator of malnutrition or liver disease [21]. Likewise, in the elderly patient, the coexistence of multiple pathologies can generate atypical patterns that require more cautious interpretation [24].

The implementation of the proteinogram in the diagnostic algorithm shows a solid clinical utility. The reviewed studies indicate a utility of 94 % for liver diseases, 89 % for chronic inflammatory disorders, and 96 % for gammopathy screening [33,41]. Combination with complementary techniques such as immunofixation increases the sensitivity for detecting monoclonal components from 82 % to 97 %, which is crucial for the early diagnosis of B-cell dyscrasias (45). Prospective studies demonstrate that integrating the proteinogram with clinical and laboratory parameters improves overall diagnostic accuracy by 32 % compared to isolated clinical evaluation [46]. This evidence consolidates the proteinogram not as an isolated test, but as a fundamental piece within an integrated diagnostic approach.

Limitations of the present review

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This review presents methodological limitations inherent to its narrative design. The non-systematic search may have omitted some relevant studies, especially those published in languages other than Spanish and English or in databases not consulted. Source selection, although performed by two independent reviewers, is subject to a certain degree of subjectivity inherent to narrative synthesis. A formal risk of bias assessment of the included studies was not performed, so the conclusions should be interpreted with caution.

Clinical implications

Despite these limitations, the findings of this review have important practical implications:

- The proteinogram remains a first-line screening test in the study of hepatic, renal, and hematological diseases.
- Interpretation should always consider the clinical context and physiological variations.
- Capillary electrophoresis offers advantages over conventional electrophoresis in terms of resolution and speed, so its progressive implementation is recommended.
- The combination of the proteinogram with immunochemical techniques (immunofixation, light chain quantification) significantly increases diagnostic sensitivity in gammopathies.

Knowledge gaps and future research

The review identifies several areas where evidence is insufficient and future research is required:

- Prospective studies evaluating the utility of the proteinogram in populations with diverse ethnic and geographic characteristics.
- Research determining specific reference values for different age groups and physiological conditions.
- Studies rigorously comparing the diagnostic cost-effectiveness of capillary versus conventional electrophoresis in different healthcare settings.
- Evaluation of the impact of proteomic techniques on routine diagnosis and their integration with the traditional proteinogram.

The future of plasma protein analysis is marked by proteomics. While traditional electrophoresis separates proteins into a few fractions, mass spectrometry techniques have the ability to identify and quantify hundreds of specific proteins simultaneously [50]. This allows the discovery of new biomarkers with specificity and sensitivity far superior to classic patterns. The possibility of performing a complete proteomic "scan" of plasma, as mentioned in recent literature, promises a medicine with a greater degree of personalization and predictive

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capacity [51]. Nevertheless, the cost and complexity of these techniques still limit their use to research laboratories and very specialized clinical settings, maintaining electrophoresis as the screening technique par excellence in daily routine.

CONCLUSIONS

Plasma proteins are a complex set of molecules essential for homeostasis, with critical functions in transport, immunity, coagulation, and maintenance of oncotic pressure. Their synthesis is mostly hepatic, except for immunoglobulins. The proteinogram, obtained mainly by electrophoresis, is a diagnostic tool of great value. The separation of proteins into albumin and globulin fractions (α1, α2, β, and γ) allows the identification of characteristic patterns associated with various diseases. Interpretation of the proteinogram should take into account the physiological variations that occur throughout life, such as altered levels in newborns, the effect of hemodilution in pregnancy, and possible changes in the elderly. The identification of specific patterns such as the inflammatory, nephrotic, and hepatic patterns, and, above all, the detection of a monoclonal gammopathy, are findings that decisively guide the patient's diagnosis and management. New proteomic technologies are notably expanding the diagnostic potential of plasma protein analysis, although electrophoresis remains the fundamental pillar for screening in the routine clinical laboratory

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AUTHOR CONTRIBUTIONS

ARR: conceptualization, formal analysis, methodology, project administration, writing – original draft, writing – review and editing.

LMH: conceptualization, data curation, investigation, supervision, writing – original draft.

MARC: conceptualization, methodology, supervision, writing – review and editing.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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USE OF ARTIFICIAL INTELLIGENCE

The authors declare that artificial intelligence was not used in the writing of this manuscript.

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