



Dysproteinemia: An Overview

Rathod PG^{1*}, Chaudhary SS¹ and Chauhan JM²

^{1*}Department of Veterinary Physiology and Biochemistry, College of Veterinary Science and Animal Husbandry, Kamdhenu University, Navsari, Gujarat, India

²Department of Veterinary Pathology, College of Veterinary Science and Animal Husbandry, Kamdhenu University, Junagadh, Gujarat, India

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Introduction

Dysproteinemia is a clinical state characterized by abnormal, often excessive, synthesis of immunoglobulin (Ig) molecules or subunits. Dysproteinemia results from clonal proliferation of plasma cells or B lymphocytes. The abnormal circulating Ig molecules or subunits (most commonly free light chains) reach the glomerulus via the systemic circulation and are associated with the development of a variety of pathologic lesions within the kidney. Free light chain molecules may pass through the glomerular basement membrane and form casts within distal tubular lumina (myeloma cast nephropathy) or form crystals within the cytoplasm of proximal tubules (light chain Fanconi syndrome). Alternatively, Ig molecules or subunits may form paraprotein tissue deposits and produce an array of pathologic lesions, most commonly amyloidosis and monoclonal Ig deposition disease. The pattern of renal parenchymal disease is determined by the unique properties of the Ig molecule or subunit. Each of the patterns of renal disease is in turn associated with unique, but frequently overlapping, clinical features and outcomes. Dysproteinemia is any disorder/abnormality of protein content of blood. The concentration of a protein in blood depends on the ratio between the rate of its synthesis and breakdown or excretion. If one or more fractions of globulins becomes more prominent, the ratio albumin-globulin - so called A/G coefficient changes.

General causes of dysproteinemia

- Congenital (mutation or loss of a gene) or acquired
- Loss of certain protein fractions:
 - Kidneys - proteinuria, damage to glomeruli
 - Skin - serious burns, extensive infections
 - Intestine - exudative enteropathy

- Disorders of proteosynthesis:
 - Liver - loss of function in cirrhosis, hepatitis - decreased synthesis of many serum proteins, e.g. albumin, factor II and I.
 - Insufficient dietary protein intake - kwashiorkor
- Hemoconcentration by loss of water, e.g., to interstice
- Changes of plasma cell numbers (synthesize immunoglobulins)

Dysproteinemia comprised of changes in more fractions or proteins

Hyperproteinemia

Increase in concentration of all serum proteins or (alternatively) increase in some proteins only which leads, however, to increase of protein concentration as a whole. If all the proteins are in increased concentration, then the increase is in fact relative - caused only by the loss of water which has concentrating effect on plasma. The resulting increase of oncotic pressure leads to movement of water from interstitial fluid to plasma. Hyperproteinemia (and paraproteinemia) can result in hyper viscosity syndrome (see lower).

Hypoproteinemia:

Decrease of the total concentration of serum proteins, particularly albumin. It is caused either by losses of proteins (to urine, to burned areas) or deficient protein production in liver. It results in decrease of oncotic pressure of plasma and oedemas.

Acute inflammation:

A typical change is so called acute phase reaction, which is seen mainly as an increase in fractions of α_1 -globulins and α_2 -globulins.

Chronic inflammation:

A typical change is an increase of the γ -globulin fraction caused by magnified synthesis of IgG (or IgM). This in fact constitutes a *polyclonal hyperimmunoglobulinemia*, where the whole immune system is stimulated. It can be found in chronic infectious diseases, allergies, autoimmune disorders, malignancies. An increased level of Ig often represents more than a half of plasma proteins. Remark: *Monoclonal hyperimmunoglobulinemia* is the same thing as paraproteinemia.

Dysproteinemia comprised of changes in one fractions or proteins:

Changes in Albumin:

An albuminemia:

Rare genetic disorder, causing generalized or localized edemas. The oncotic pressure is decreased. Although albumin generally represents about 60% of serum proteins, it can be completely absent without causing serious complications. The level of globulins is elevated by compensatory reaction, the total protein concentration is, however, still below normal.



Changes in α_1 -globulins:

Lack of α_1 -antitrypsin:

Its level is decreased to about 10% of the norm. Large amounts of the protein are found in hepatocytes, apparently due to the defect in excretion mechanism, which can later result in cirrhosis. Increased levels of elastase, trypsin and other proteinases in blood. There is a damage to the pulmonary connective tissue, causing an obstructive disease (juvenile emphysema). The heredity is autosomal recessive. However, heterozygotes also have a slight decrease of serum levels.

Changes in α_2 -globulins:

Decrease in haptoglobin:

Primary decrease is a result of a rare genetic disorder. Secondary decrease is due to hemolysis, when all the haptoglobin is spent by binding hemoglobin and free haptoglobin is not detectable. Whatever the form is, there aren't any significant clinical consequences.

Lack of ceruloplasmin - Wilson's disease:

Ceruloplasmin is the most important copper binding protein in plasma. Its absence causes fast loss of copper into tissues or its excretion by kidneys. Subsequently is augmented the enteral absorption of copper, which keeps the positive balance of intake over losses. The copper is deposited mainly in brain, liver, proximal tubules of kidneys and cornea. For more information, you can visit regular Wikipedia.

Changes in β -globulins:

Lack of transferrin:

Defect of iron transport in plasma; insufficient supply of iron to the hematopoietic tissue. The result is an iron deficiency anemia and hemosiderosis. Heredity is autosomal dominant.

Changes in γ -globulins:

Agammaglobulinemia:

Hereditary form is X-linked. There is almost complete lack of γ -globulins in serum, their levels being around 100 mg/100ml (norm is 1600 mg/100 ml). Plasma cells are absent from the bone marrow, spleen and lymph nodes, apparently due to a defect in stem cell maturation. The onset takes place after weaning of the baby, when protection by mother's antibodies is lost. There is a low resistance to bacterial infections (pneumonias, sepsis). Treatment: i.m. injections of immunoglobulins. Acquired form is rare, manifestation takes place in adult men and women. The immunoglobulin levels are below 500 mg/ml. Plasma cells are absent from lymph nodes. The spleen and liver are enlarged. Symptoms: Frequent infections, susceptibility to autoimmune diseases.

Dys-gammaglobulinemia:

Some types of Ig are missing, others are in normal or increased concentration. Most commonly, IgG or IgA is missing and IgM is increased (as well as the number of plasma cells synthesizing IgM).



Symptoms: Susceptibility to infections, thrombocytopenia, autoimmune hemolytic anemia.

Hyperimmunoglobulinemia:

Increased level of γ -globulins caused by their elevated synthesis. Each clone of plasma cells produces just one immunoglobulin. Presence of elevated levels of Ig can be divided into monoclonal hyperimmunoglobulinemia (paraproteinemia) and polyclonal hyperimmunoglobulinemia.

References

<https://www.wikilectures.eu/w/Dysproteinaemia>

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