Studii și Cercetări Științifice. Biologie
Scientific Study & Research. Biology
Print ISSN 1224-919X Online ISSN 2457-5178
2024, 33 (1), 75-80

PROTEINOGRAM CHANGES IN MULTIPLE MYELOMA

Daniela TIȚĂ[1], Tatiana CIUREA[2], Ionuț STOICA[3*], Dumitra RĂDUCANU[3*], Diana Ioana TIȚĂ[4]

[1]County Emergency Hospital, 2-4 Spiru Haret Street, Bacau, Romania
[2]"Titu Maiorescu" University, Faculty of Medicine, Bucharest, Romania
[3]"Vasile Alecsandri" University of Bacău, Faculty of Science, Department of Biology, Ecology and Environmental Protection, 157 Calea Mărăşeşti Street, 600115, Bacău, Romania
[4]Colțea Clinical Hospital, Bucharest, Romania

KEYWORDS

M component
Monoclonal proliferation
Multiple myeloma
Plasma cells

ABSTRACT

Multiple myeloma is the third most common type of blood cancer, after leukemia and non-Hodgkin's lymphoma. It represents a complex medical challenge, and early diagnosis and appropriate treatment can improve the patient's prognosis and quality of life. The diagnosis of multiple myeloma is made with the help of serum protein electrophoresis, which shows the excess of a certain type of antibodies that is highlighted by a peak, called "monoclonal peak". The proteinogram changes in multiple myeloma are strongly expressed and characteristic, having diagnostic value, and, for greater certainty of the diagnosis, blood tests will be corroborated with bone radiography, computed tomography and marrow biopsy.

INTRODUCTION

Multiple myeloma is a rare form of cancer, with a low incidence before the age of 40, the average age at which the disease is diagnosed is 67 years. Multiple myeloma (plasmocytoma) or Kahler's disease, is a type of cancer specific to the bone marrow, characterized by the malignant degeneration of plasma cells. Plasmocytes are the most important component of the immune system, they help in the fight against infections by generating antibodies.
Monoclonal proliferation, in the condition of multiple myeloma, leads to the overproduction of specific antibodies (one of the types of monoclonal immunoglobulin) or of a segment of the structure of these antibodies (eg: their light chains). Multiple myeloma is characterized by the following basic conditions: the production of homogeneous paraproteins (which are called the M component, which has a monospecific character), bone marrow failure syndrome and destructive bone alteration. The most recent studies have not clearly identified the cause that would underlie the appearance of multiple myeloma, but it is assumed that there are certain factors that trigger the disease, among which we list: male sex, adults over 65 years old, obesity, exposure to insecticides, contact with organic solvents, woodworking, exposure to radiation, alcohol consumption, African-American race, contact with chemicals used in rubber manufacturing, firefighting, family member suffering from this condition, some inflammatory conditions such as rheumatoid arthritis or diabetes, personal history of monoclonal gammopathy of undetermined significance (MGUS).
The latest research would explain, however, the onset of this disease due to the presence of abnormalities in the genetic code of plasma cells at the level of chromosome 14. The symptoms of multiple myeloma vary from person to person. The first warning sign is bone pain, but multiple myeloma can present a variety of symptoms such as: anemia that causes a feeling of constant weakness, permanent fatigue, vomiting, dehydration, loss of appetite, dizziness and confusion, unexplained weight loss, numbness, nausea, fever and spontaneous bleeding. Bones and kidneys are negatively affected by the presence of this disease, ultimately leading to complications such as kidney problems and fractures.
The blood analyses, which contribute to the classic diagnosis given by the laboratory, are: calcium, ionogram, VSH, urea, serum creatinine, hemogram, peripheral blood smear, LDH, serum protein electrophoresis, electrophoresis with immunofixation of urinary proteins. All these blood analyses, to which we add the imaging ones (MRI, CT) and those that investigate and evaluate the structure and function of the hematogenous marrow (osteo-medullary biopsy, cytogenetic examination, medullary puncture), will ultimately contribute to the clear diagnosis of the disease.

* Corresponding authors: Stoica I., Răducanu D.
E-mail address: ionut_stoica23@yahoo.com, dora.raducanu@ub.ro
https://doi.org/10.29081/scsb.2024.33.1.09

The present study aims to evaluate the protein fractions in patients who had monoclonal diproteinemia in order to confirm or deny the diagnosis of myeloma.

MATERIALS AND METHODS

The biological material used for serum protein electrophoresis is venous blood (hemolyzed samples are not tested), which is collected in a vacutainer without anticoagulant with/without separating gel.
The vacutainers were centrifuged after expressing the clot at 3500-4000 rpm for 15 minutes. If not used immediately, the serum can be stored for a period of time (4 days at 20-25°C, 2 weeks at 2 – 8°C and one month at temperatures ≤ - 20°C).
Old primary samples will be avoided because the proteins may undergo enzymatic degradation or those containing plasma (fibrinogen gives a false monoclonal band, increasing the percentage value of the area).
The dosage of total serum proteins was carried out by the spectophotometric method, and the separation of the protein fractions was carried out on the automatic analyzer, EASY INTERLAB G26.

RESULTS AND DISCUSSION

The present study is a retrospective one and aims to identify the variation of serum proteins in multiple myeloma on a group of 75 patients between the ages of 31 and 90, hospitalized in the departments of internal medicine and gastroenterology, between 2019 and 2022.
Of the 75 patients taken into the study, 29 patients are female, representing 39% and 46 male patients, representing 61%, of the total number of patients, the gender ratio being F/B = 0.63 (Figure 1)

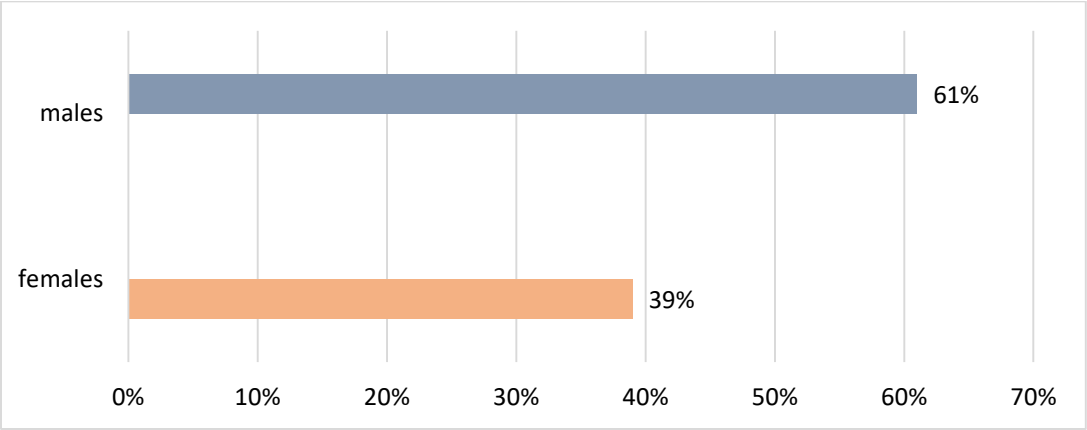

Figure 1. Gender distribution of investigated patients

From the gender distribution of the investigated patients, it can be seen that the number of male patients investigated was higher than the number of female patients.
The investigated female patients were divided into the following age groups (Figure 2):

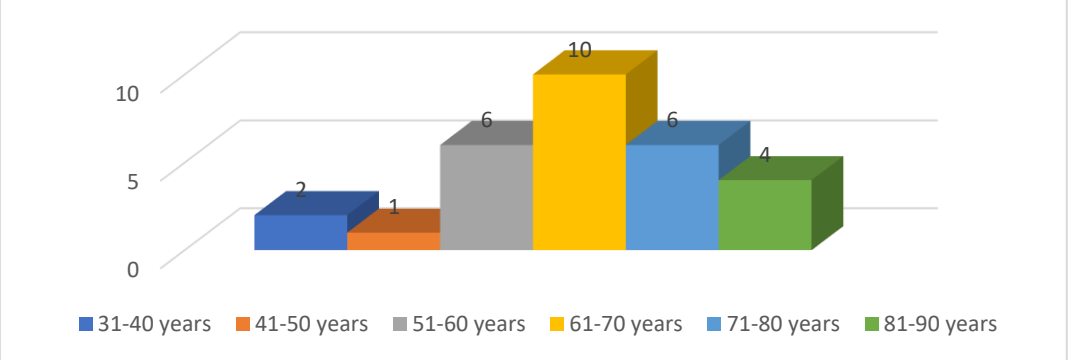

Figure 2. Distribution by age groups of female patients

From the analysis of Figure 2, it can be seen that the largest number of cases for female patients was in the age group 61-70 years, followed by the age groups 51-60 years, respectively 71-80 years.

The breakdown by age group of male patients was as follows:

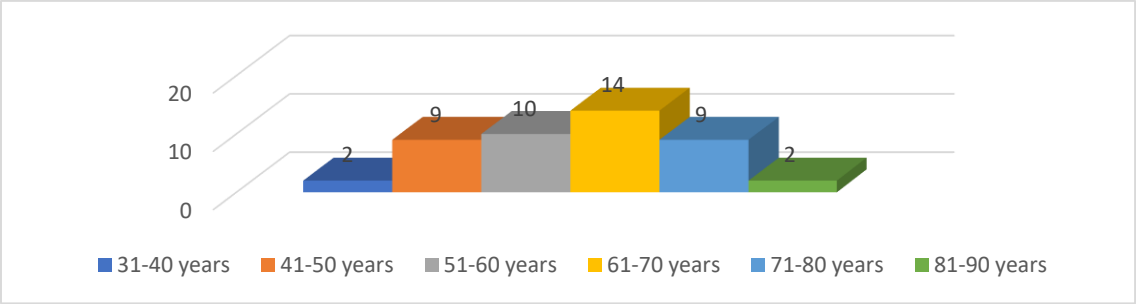

Figure 3. Distribution by age groups of male patients

Analyzing Figure 3, it can be seen that in male patients, the largest number of cases was also registered in the 61-70 age group. During the serum protein electrophoresis, the following results were obtained:

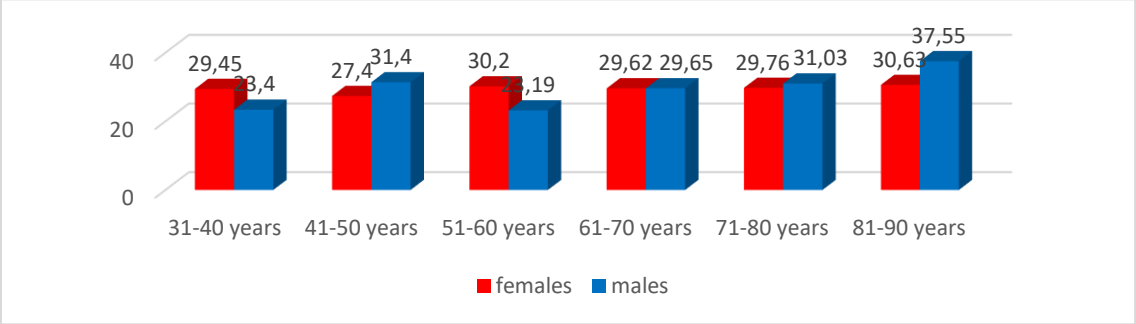

Figure 4. Comparative representation of the percentage value of the albumin fraction in the investigated patients

From the comparative analysis (Figure 4) of the average values of albumin, the following aspects can be seen: in the age groups 31 – 40 and 51 – 60, male patients show a more pronounced decrease in albumin, and in the groups 41 – 50 and 81 - 90, the decrease in albumin values is more pronounced in female patients, the decrease remains in the range of 27.4 - 30.63%.

Electrophoresis of total proteins is definitely the starting point in the biochemical investigation of any pathological area and can provide global information on the biochemical status of the respective patient, highlighting the affected segments, other than the incriminated ones.

In our study, in patients with a presumptive diagnosis of multiple myeloma, serum albumin values were outside the reference range (54 – 66%) and varied in female patients between 21.7% and 39.4%, and for male patients they varied between 10.2% and 41.8%.

According to specialized literature, hypoalbuminemia occurs as a result of an imbalance between the processes of synthesis and destruction or loss of albumins. As albumin binds approximately 40% of circulating calcium, a substantial decrease in albumin will cause, in turn, a decrease in calcium in the body (patients diagnosed with multiple myeloma will also complain of bone pain).

If for female patients values of alpha1 globulins (Figure 5) outside the reference range were recorded in the groups 81-90 years, 51-60 years, for male patients the recorded values fell within the range reference. Acute inflammatory diseases and chronic liver diseases are manifested when alpha1 globulins do not fall within the reference range, a fact highlighted by the values obtained in patients of both sexes.

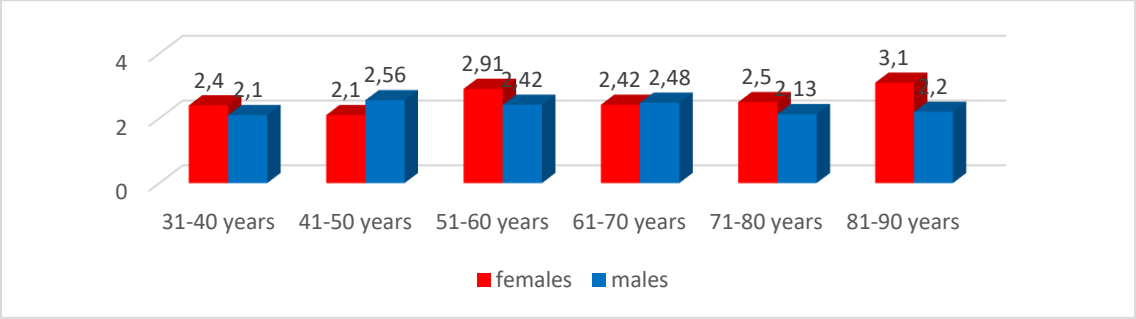

Figure 5. Comparative representation of the percentage value of the alpha1 globulin fraction in the investigated patients

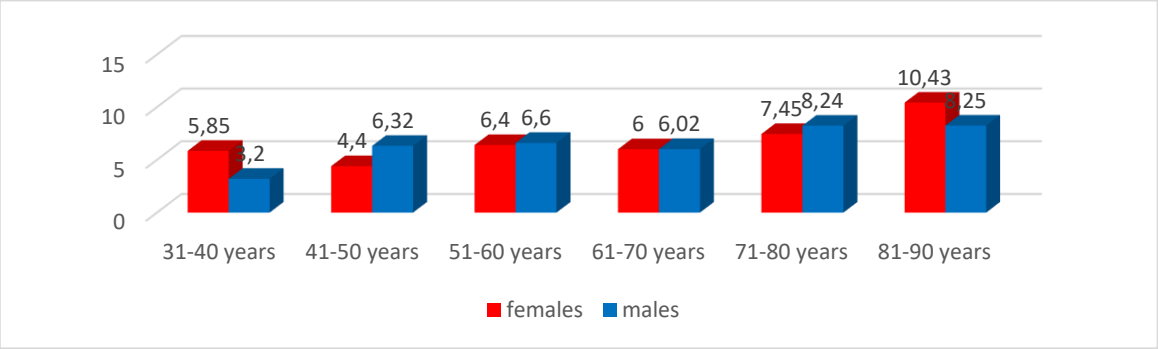

Figure 6. Comparative representation of the percentage value of the alpha2 globulin fraction in the investigated patients

In the age groups between 31 - 40 years and 81 - 90 years, we observe that female patients have a higher average value for alpha2 globulins than male patients, and in the age groups 41 - 50 and 71 - 80, the values are much higher lower, compared to male patients (6.32% and 8.24%).
Clinical studies have highlighted the fact that patients with a deficiency of alpha 2 globulins can develop severe liver failure, acute pancreatitis, sepsis, and those with elevated values have nephrotic syndrome.

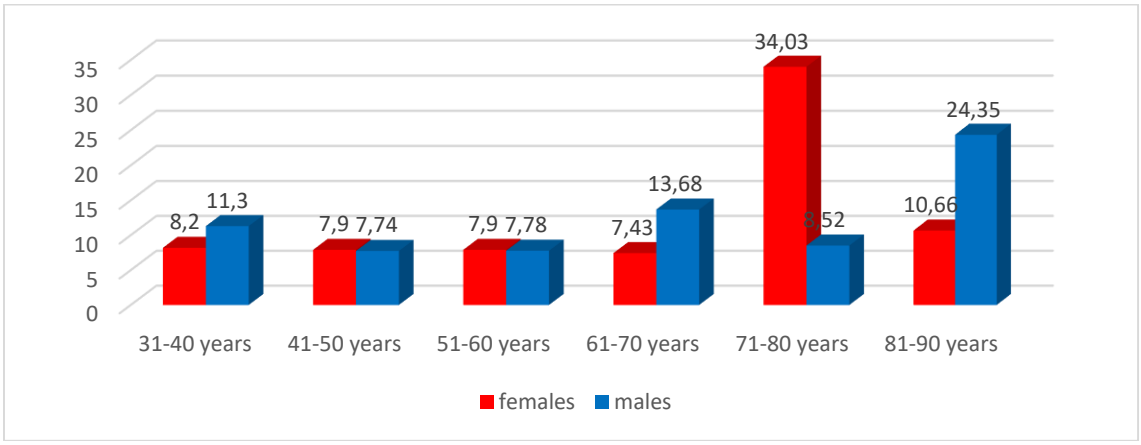

Figure 7. Comparative representation of the percentage value of beta globulins in the investigated patients

From the analysis of Figure 7, it is observed that the values of this parameter were low in both female and male patients for the groups: 41-50 years, respectively 51-60 years, while for the groups: 71-80 years and 81-90 years, female patients have the highest average value of beta globulins.
According to specialized literature, female and male patients over 70 years of age are the most likely to be diagnosed with multiple myeloma, the monoclonal component being on the beta fraction. The values for beta globulins varied between 3.1% and 51.3%, and in male patients the values of this parameter varied between 3.2% and 42.4%. For subjects studied with very high beta globulin values (42.4%, 51.3%, 66%) outside the reference range (8.7 – 14.4), the M component appears at the level of this fraction on the electrophorogram .

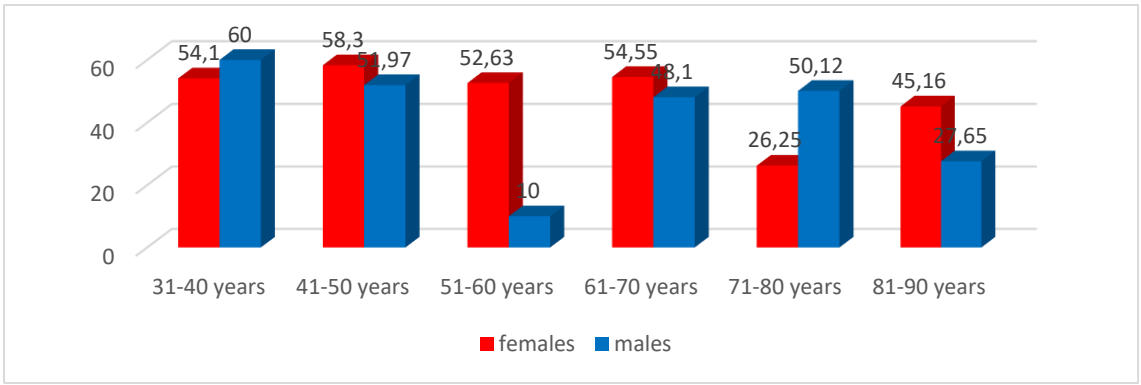

Figure 8. Comparative representation of the percentage value of gamma globulins in the investigated patients

The values of gamma globulins, for female and male patients, are close for patients aged between 31-40 years, 41-50 years and 61-70 years, the values varying between 54.1 and 54.55% for female patients and 48.1 and 60% for male patients. For the age groups 51 – 60 years, 71 – 80 years and 81 – 90 years, it is observed that the value of globulins for female patients varies between 26.25 – 52.63% compared to male patients whose values are between 10 – 50.12% (fig. 8). The lowest value of gamma globulins was recorded in a 75-year-old female patient (2.3%) in whom the value of beta globulins is high (64.5%), and for male patients, the lowest value was recorded at a 65-year-old subject (1.45%) in whom the value of beta globulins registered a value of 54.9%.

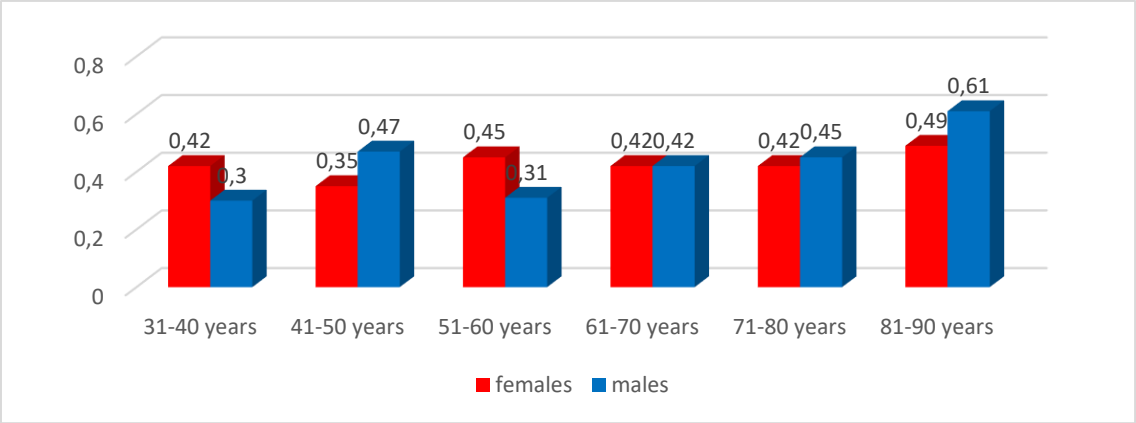

Figure 9. Comparative representation of the albumin/globulin ratio in the investigated patients

From Figure 9 it is observed that, regardless of age, the albumin/globulin ratio is subunit both in female and male patients. In female patients, the ratio varies between 0.42 - 0.49 and in male patients it varies between 0.30 - 0.61.
The reference interval of the albumin/globulin ratio for a healthy patient is 1.2 - 1.5, therefore, all patients have values below the minimum limit of the interval, which denotes a pathological condition found in cirrhosis, nephrotic syndromes, autoimmune diseases and in multiple myeloma, according to the specialized literature. Albumins recorded a very low value, while gamma globulins have a much higher value compared to the upper limit of the reference range. The specialized literature specifies that a low value of albumins and a very high one of globulins can be found in nutritional disorders, kidney diseases, hyperthyroidism, heart failure, diabetes, Hodgkin's disease, in the chronic evolution of some autoimmune diseases, leukemias, lymphomas, multiple myeloma.
The albumin and globulin values were outside the reference range for all patients included in the study. The albumin/globulin ratio showed low values for all subjects studied, values that varied between 0.11 and 0.89. Dysproteinemia in multiple myeloma achieves different aspects depending on etiology and evolutionary stage.
The proteinogram changes in multiple myeloma are strongly expressed and characteristic with diagnostic value, but for greater certainty of the diagnosis, blood tests will be corroborated with bone x-ray, computed tomography and marrow biopsy.

CONCLUSION

Multiple myeloma represents a complex medical challenge, and early diagnosis and appropriate treatment can improve the patient's prognosis and quality of life.
The diagnosis of multiple myeloma is made with the help of serum protein electrophoresis, highlighting the excess of a certain type of antibodies that will be highlighted by a peak called "monoclonal peak".
Both for female patients and for male patients, the weight of age regarding the susceptibility of the incidence of the disease is relatively the same, age over 65 years.
The value for: alpha1, alpha2 and beta globulins represents a sensitive indicator regarding the prognosis and the evolution of the disease.
The value of gamma globulins, for most of the patients, with the presumptive diagnosis of multiple myeloma were increased above the upper limit of the reference interval.
Multiple myeloma can manifest itself through the excessive production of antibodies in the kidney, eventually leading to renal failure.
Dysproteinemia in multiple myeloma achieves different aspects depending on etiology and evolutionary stage.The proteinogram changes in multiple myeloma are strongly expressed and characteristic, having diagnostic value.
It is essential to pay attention to the symptoms and seek specialized medical assistance in a timely manner for the effective management of this condition.

REFERENCES

1. Ashley B., Irish B., Rajalingam S. *Dysproteinemias of lightchain diseases*. Nephrology secrets Publishing House, USA, 2021.
2. Atanasiu V., Mohora M. et al. *Biochimie medicală*. Editura Universității Carol Davila, Bucureşti, 2023.
3. Busher J.T. *Serum Albumin and Globulin*. Chapter 101, In: Walker H.K., Hall W.D., Hurst J.W., editors. Clinical Methods: The History, Physical, and Laboratory Examinations. 3rd ed. Butterworth Publishers, Boston, MA, USA, 1990.
4. Chiva A. *Actualităţi în diagnosticul electroforetic de laborator*. Editura Universității Carol Davila, Bucureşti, 2011.
5. Cucuianu M., Crâsnic I., Pleşca-Manea L. *Biochimie clinică, fundamentare fiziopatologică*. Editura Dacia, Cluj Napoca, 1998.
6. Fisch F. *Immunodiagnostic studies in a manual of laboratory and diagnostic tests*. Lippincott Williams & Wilkins Publishing House, USA, 2004.
7. Geng C. *What are the risk factors for multiple myeloma.* Medical news today Publishing House, USA, 2021.
8. Harrison C. *Bioseparations science and engineering*. Oxford University Press, New York, 2003.
9. Kyle R., Katzmann A. *Monoclonal gammopathies of undetermined significance and Bence – Jones myloma. In monoclonal gammopathies and the kidney.* Springer Publishing House, Dordrecht, 2012.
10. Krupp M.A., Chatton M.J. *Curent medical. Diagnosis, treatment.* Lang medical publications Publishing House, USA, 1983.
11. Mihele D. *Biochimie clinică – Metode de laborator*. Editura Medicală, București, 2000.
12. O´Connel T. *Understanding and interpreting the serum protein electrophoresis*. American family physician, 2005, 71 (1): 105-112.
13. Popa C. *Catalogul Analizelor Medicale din compartimentele de Biochimie, Hematologie, Hemostaza si Imunologie*. 2016.
14. Popescu O.V. *Electroforeza proteinelor în geluri de poliacrilamidă*. Editura Tehnică, Bucureşti, 1990.
15. Tierney L., Mcphee S., Papadakis M. *Diagnostic și tratament în practica medicală*. McGraw Hill, 2001.
16. Tietz N. *General clinical tests in clinical guide to laboratory tests*. W. B. Saunders, USA, 1995.
17. Vasudevan D., M., Sreekumari S., Kannan V. *Manual de biochimie pentru studenţii la medicină*. Jaipee Medical Publishers, USA, 2010.
18. Wallach J. *Interpretarea testelor de diagnostic*. *Ed. a VII-a.* Editura Științelor Medicale, 2009.

Web sources:

19. https://www.medlife.romielommultiplu
20. https://www.nhs.uk<multiple myeloma>
21. https://www.webmed.com
22. https://www.mayocliniclabs.com
23. https://www.donnamedical center.ro <proteine totale serice>
24. https://www.reginamaria.ro<electroforeza proteinelor serice>
25. https://bioclinica.ro<proteine totale serice>
26. https://apitherapy.ro<proteinemia, proteinele totale şi disproteinemia>
27. https://www.hcgoncology.com<Kahler´s diseaseormultiple myeloma-blood cancer where plasma cells in the blood grow uncontrolled-HCG oncology
28. https://www.healthline.com<what is multiple myeloma>
29. https://www.sciencedirect.com<turbidimetria-o privire de ansam
30. https://powerfulpatients.org/ro/11/06/multiple-myeloma-bone-marrow
31. https://www.wikipedia.org<protein.precipitation>