UNIVERSITY OF MEDICINE AND PHARMACY CRAIOVA
FACULTY OF MEDICINE

Etiopathogenic and clinical correlations between chronic hepatitis and associated dermatologic diseases

-ABSTRACT-

Scientific coordinator,
Professor Tudorel Ciurea, MD, PhD, MSc

PhD Student,
Thomas Vasilakos

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Contents

Key words

- Chronic Hepatitis,
- Lichen Planus,
- Porphyria cutanea tarda,
- Autoimmune hepatitis,
- Pseudopellagroid syndrome,
- Photodermatosis

Background

Dysfunction in the body's second largest organ, the liver, often yields changes in the body's largest organ, the skin. If we can recognize these manifestations early, we are better able to promptly diagnose and treat the underlying liver disease, as well as the skin lesions. The liver has many jobs: synthesizing proteins such as clotting factors, complements, and albumin; neutralizing toxins; and metabolizing lipids and carbohydrates. Insults to the liver can compromise any of these functions, affecting visceral organs, joints, gastrointestinal tissues, and the skin. Dermatologic signs of specific liver diseases include alopecia and vitiligo associated with autoimmune hepatitis, and xanthelasma in chronic cholestatic liver disease.

Jaundice and Hyperbilirubinemia

Jaundice, the cardinal sign of hyperbilirubinemia, is usually recognizable when serum bilirubin levels exceed 2.5 or 3.0 mg/dL. The color of the skin typically reflects the severity of the bilirubin elevation.Jaundice due to mild hyperbilirubinemia tends to be yellowish, while that due to severe hyperbilirubinemia tends to be brownish. Establishing whether the excess bilirubin is conjugated or unconjugated gives a clue as to whether the cause is prehepatic, intrahepatic, or posthepatic. Prehepatic causes of jaundice include hemolysis and ineffective erythropoiesis, both of which lead to higher levels of circulating unconjugated bilirubin. Intrahepatic causes of jaundice can lead to both unconjugated and conjugated hyperbilirubinemia. Posthepatic causes such as bile duct obstruction primarily result in conjugated hyperbilirubinemia.

Pruritus and prurigo nodularis

Pruritus can be multifactorial or the result of a specific dermatologic or systemic condition. A thorough history and physical examination are warranted to rule out hepatic or systemic causes of itching. The liver neutralizes toxins and filters bile salts. If its function is impaired, these materials can accumulate in the body, and deposition in the skin causes irritation and itching. In cholestatic liver disorders such as primary sclerosing cholangitis and obstructive gallstone disease, pruritus tends to be generalized, but worse on the hands and feet. Although the severity of pruritus is not directly associated with the level of bile salts and toxic substances, lowering bile salt levels can mitigate symptoms.

Prurigo nodularis

Prurigo nodularis, distinguished by firm, crusty nodules, is associated with viral infections (eg, hepatitis C, human immunodeficiency virus), bacterial infections, and kidney dysfunction. The lesions are intensely pruritic and often lead to persistent scratching, excoriation, and, ultimately, diffuse scarring.

SUPERFICIAL VASCULAR SIGNS

Spider angiomas

Spider angiomas, or spider nevi, are collections of dilated blood vessels near the surface of the skin. They appear as slightly raised, small, reddish spots from which fine lines radiate outward, giving them a spider-like appearance. Spider angiomas can occur anywhere on the body, but they occur most often on the face and the trunk. A key feature is that disappear when pressure is applied and reappear when pressure is removed. Biopsy is rarely necessary for diagnosis.

These lesions occur with elevated estrogen levels, such as in cirrhosis, during estrogen therapy, or during pregnancy. Although spider angiomas are common in pregnant women and in children, adults with spider angiomas deserve a workup for liver dysfunction. Given their innocuous nature and asymptomatic course, spider angiomas themselves require no medical treatment.

Bier spots

Bier spots are small, irregularly shaped, hypopigmented atches on the arms and legs. They are likely due to venous stasis associated with functional damage to the small vessels of the skin. Since Bier spots are a sign of liver disease, they must be distinguished from true pigmentation disorders. A key distinguishing feature is that Bier spots disappear when pressure is applied. Also, raising the affected limb from a dependent position causes the hypopigmented macules of Bier spots to disappear, which is not the case in true pigmentation disorders.

Paper-money skin

Paper-money skin (or “dollar-paper” markings) describes the condition in which the upper trunk is covered with many randomly scattered, needle-thin superficial capillaries. It often occurs in association with spider angiomas. The name comes from the resemblance the thread-like capillaries have to the finely chopped silk threads in American dollar bills. The condition is commonly seen in patients with alcoholic cirrhosis and may improve with hemodialysis.

Palmar erythema

Palmar erythema is a florid, crimson coloration of the palms of the hands and the fingertips. It can occur anywhere on the palm and fingers but is most common on the hypothenar eminence. It can occur in a number of liver conditions but most often with cirrhosis. Hepatic compromise, as seen in alcoholic liver disease, disrupts the body's androgen balance, causing local vasodilation and erythema. Although the exact mechanism remains unknown, research suggests that prostacyclins and nitric oxide play a role, as both are increased in liver disease.

Xanthelasma

Xanthelasma - a localized cholesterol deposit beneath the skin and especially beneath the eyelids - is a common manifestation of hypercholesterolemia. Xanthelasma often presents as a painless, yellowish, soft plaque with welldefined borders, which may enlarge over the course of weeks.

Several liver diseases can lead to various forms of secondary dyslipoproteinemia. The most common dyslipoproteinemias in liver disease are hypertriglyceridemia and low levels of high-density lipoprotein cholesterol, and both of these often accompany fatty liver disease. Hypercholesterolemia is a common feature of primary biliary cirrhosis and other forms of cholestatic liver disease. Studies suggest that the total plasma cholesterol level is elevated in as many as 50% of patients with compromised liver function.

OTHER CUTANEOUS FINDINGS IN LIVER DISEASE

Bleeding and bruising. Liver disease can cause hypersplenism and thrombocytopenia, in addition to a decrease in clotting factors. These may present with a myriad of cutaneous symptoms, including purpura, bleeding gums, and easy bruising and bleeding, even from minor trauma.

Hyperpigmentation of the skin may accompany hemochromatosis, alcoholic liver disease, and cirrhosis.

Hair and nail loss. Patients with hepatocellular dysfunction may develop hair-thinning or hair loss and nail changes such as clubbing, leukonychia (whitening), or onycholysis, affecting the nails of the hands and feet.

"Terry's nails," in which the proximal two-thirds of the nail plate turns powdery white with a ground-glass opacity, may develop in patients with advanced cirrhosis.

ALCOHOLIC CIRRHOSIS AND THE SKIN

The cutaneous changes associated with alcoholic cirrhosis are more widely recognized than those due to other forms of liver dysfunction. In the United States, approximately 3 million people have alcoholic cirrhosis, the secondleading reason for liver transplantation. As the body's main site of alcohol metabolism, the liver is the organ most affected by excessive alcohol intake, which can lead to end-stage liver disease secondary to alcoholic cirrhosis. The characteristic feature of cirrhosis is advanced fibrous scarring of parenchymal tissue and the formation of regenerative nodules with increased resistance to blood flow throughout the organ. The insufficient blood flow damages vital structures in the liver and compromises liver function. For example, liver cirrhosis leads to defective hepatic synthesis of clotting factors and results in bleeding disorders. Cutaneous lesions often accompany alcoholic cirrhosis and have been detected in up to 43% of people with chronic alcoholism. Skin changes in alcoholic cirrhosis can be of great diagnostic value. The combined prevalence of spider angiomas, palmar erythema, and Dupuytren contracture in alcoholic cirrhosis was found to be 72%. Paper-money skin and Dupuytren contracture are more distinct lesions for alcoholic cirrhosis. Recognizing these skin changes contributes to the diagnosis and staging of liver cirrhosis.

Dupuytren contracture

Dupuytren contracture is characterized by progressive fibrosis and thickening of tendons in the palmar fascia, the connective tissue that lies beneath the skin of the palms. Over time, as fibrotic involvement expands across the fascia, rampant stiffness of the joints ensues, sometimes to a point where the fingers cannot fully flex or extend. Although the exact cause of Dupuytren contracture is unknown, it appears to be associated with excess alcohol consumption and can be found in patients with alcoholic cirrhosis. These patients often present with painless stiffness of the fingers, curling of fingers, and loss of motion in involved fingers.
Surgery in the form of limited fasciectomy has been curative in such patients.54

Disseminated superficial porokeratosis

Porokeratosis is a keratinization disorder of clonal origin that presents as a linear configuration of white scaly papules that coalesce into plaques throughout the body. Although it most

commonly afflicts fair-skinned people, patients with alcoholic cirrhosis have a much greater susceptibility than the general population.

A recent study documented that the lesions completely resolved when liver function improved, thus underlining the relationship between the two conditions. Since immunosuppression has been linked to eruption of the lesion, the fact that both humoral and cell-mediated immune responses are impaired in alcoholic liver disease provides another dimension to the association between porokeratosis and alcoholic cirrhosis. These lesions can transform into squamous cell carcinoma. The risk of widespread metastases in squamous cell carcinoma highlights the importance of dermatologic consultation in such patients.

HEPATITIS AND THE SKIN

Extrahepatic manifestations have been documented in up to 74% of people with hepatitis C virus infection. In addition to parasthesias, arthralgias, and myalgias, hepatitis C has a significant association with porphyria cutanea tarda, lichen planus, vitiligo, sialadenitis, urticarial vasculitis, corneal ulcers, xerosis, pruritus, and prurigo nodularis. Although the primary causative agents of sialadenitis are bacteria, viruses such as hepatitis C have been implicated as a cause of chronic sialadenitis with associated xerostomia. Patients with hepatitis C being treated with interferons also present with cutaneous manifestations such as hyperkeratosis and vasculitis.

Porphyria cutanea tarda

Porphyria cutanea tarda is the most common of the porphyrias, disorders distinguished by deficiencies or defects in one or more of the enzymes responsible for hepatic production of heme. If these enzymes are impaired, heme precursors such as porphyrins accumulate. Porphyria cutanea tarda results from a deficiency of the hepatic enzyme uroporphyrin decarboxylase. In the absence of this enzyme, shortwave visible light activates uroporphyrin deposited in the skin, resulting in a photochemicalreaction that generates reactive oxygen species that lead to the characteristic skin blistering.

Although porphyria cutanea tarda is associated with liver disease in general, recent studies confirm that patients with hepatitis C are at particularly high risk. Those with the disorder often present with skin photosensitivity. Many develop blisters on sun-exposed skin, including the dorsal aspects of the hands and forearms and on the neck and face. Chronic porphyria cutanea tarda can lead to scarring,

alopecia, and skin ulceration. As the blisters heal, keratin-filled milial cysts may develop in the areas of ulceration. The condition is also commonly associated with melasma-like hyperpigmentation and hypertrichosis in sun-exposed areas of the head and neck. People of Northern European ancestry may be more at risk than the general population because of a presumed genetic susceptibility.

Lichen planus

Lichen planus is a chronic pruritic, popular condition that often presents clinically with the “five P’s”: pruritic, planar, polygonal, purple papules. It can occur throughout the body but typically affects the wrists and ankles, causing mild to severe itching in most affected people. In about 50% of patients, the lesions resolve within 6 months, and in 85% they subside within 18 months. Lichen planopilaris is a subset of lichen planus that causes scaling and atrophy of the scalp and permanent hair loss.

Interferon-induced vitiligo

Vitiligo is an autoimmune disease in which melanocytes in the skin are destroyed, with resulting depigmentation in affected areas. Although it has no specific association with liver disease, it has been linked to treatments for hepatitis C such as interferons. Interferon-induced vitiligo often completely resolves when interferon is stopped. Typical findings include aggregations of irregularly shaped white patches in a focal or segmental pattern. The diagnosis is based on the medical history, physical examination,
and sometimes skin biopsy.

HEMOCHROMATOSIS

Hemochromatosis or *“bronze diabetes”* is a devastating multisystem disease with a relentless course. It is among the most common genetic disorders of metabolism, and results in deposition of iron in tissues and organs throughout the body, including the liver, usually in patients ages 30 to 40. As iron stores increase in tissues and organs, multiorgan failure and associated complications may ensue. In addition, surplus iron stores can also result in widespread bronze discoloration of skin exposed to the sun. Hemochromatosis also results in loss of body hair, ichthyosiform alterations, and koilonychia.

Objectives

The research theme is of great actuality because it explores and brings important contributions in chronic hepatitis field and theirs associations with skin diseases, on the basis of clinical and serological assessment.

The existence in *Research Center of Gastroenterology and Hepatology Craiova* of high technology research infrastructure and qualified human resources created the premises of accomplishing the following main objectives:

- Clinical-statistical study:
  - Territorial distribution of the patients with these associated diseases
  - Distribution considering sex, age and profession
  - Fallow-up of the patients
- Etio-pathogenic study:
  - Identification of etiologic factors involved as triggers for hepatic or skin diseases
  - Study of biochemical and immunological alterations and their analysis in etiologic context of chronic hepatitis
- Clinical study:
  - The way of onset of the diseases
  - Evolution particularities and their correlations between clinical aspects and laboratory findings,
  - Skin affectivity in correlation with hepatic underling disease

Material and method

The study was performed in Medical I Clinic – Gastroenterology and Dermatology of University of Medicine and Pharmacy Craiova Romania between 2006 and 2010, on 95 admitted patients with chronic hepatitis and associated dermatological diseases: Lichen planus, Porphyria cutanea tarda, pellagroid syndrome and photodermatoses.

The patients were selected on clinical, laboratory and imagistic criteria; histological exam was performed in the majority of patients with chronic hepatitis analyzing the fragment obtained on liver biopsy.

The study of the etiological circumstances obtained by anamnesis, by determining serological viral infection markers and immunological disorders represented the modality of differentiate etiological chronic hepatitis forms.

In this way, out of the 95 patients with chronic hepatitis and dermatological associated diseases:

- 28 patients presented serological markers for chronic viral B hepatitis B
- 43 patients presented serological markers for chronic viral C hepatitis
- 18 patients did not present epidemiological or serological arguments for viral infection and did present specific autoimmune hepatitis immunological markers
- 6 patients with chronic hepatitis presented pharmacological etiology (after Metil Dopa, Sulfasalazine and Amiodarone prolonged administration)

After thoroughgoing study of the hepatic disease for each studied case, an individual complete dermatological diagnostic plug was attained for each patient, containing, beside the personal data, a number of different observations concerning:

- Cutaneous organ estate;
- The existence of precursory or simultaneously diseases, facilitating disease development ;
- The way of onset
- The evolution in time until the examination;
- The present estate;
- Clinical diagnostic;
- Usual exploration results;
- Hospital treatment;

The studied casuistry in this scientific paper is represented by a number of 95 patients hospitalized in the Medical Clinic I and in the Dermatology Clinic of the Emergency Clinic Hospital Craiova with chronic hepatitis and dermatological associated diseases as follows:

- Lichen planus – 45.26 % (n=43)
- Porphiria cutanea tarda – 16.84% (n=16)
- Pseudopellagroid syndrome and photodermatosis – 37.89 % (n=36)

Conclusions

- Taking into account the general exposed data and the one obtained from the undertaken study on the selected group, few conclusions with both theoretical and practical importance can be formulated.
- The results of the study underline the biochemical and immunological modifications and also their significance in the pathogenesis of chronic hepatitis at patients with dermatological associated diseases. By our observations we brought arguments to support the immunological mechanisms correlated with chronic hepatitis etiology. Immunoreactivity study was considered important for chronic hepatitis differential diagnostic, prognosis and treatment.
- The etiological circumstances showed by the anamnesis, by determining viral infection markers in the serum and immunological disorder are necessary for the differentiation of chronic hepatitis etiological forms, in order to prevent the evolution toward cirrhosis and also to assure a proper treatment. The presence of extra hepatic symptoms was noticed in all etiological forms of chronic hepatitis associated with dermatological disease, the incidence being higher in autoimmune hepatitis than in viral hepatitis.
- Lichen planus is a chronic mucocutaneous dermatosis of the adult age, with an unknown cause, clinically manifested by a typical monomorphic eruption characteristically located.

Known eversince Hipocrate, lichen planus remained permanently in actuality due to its unsolved etiopathogeny, despite the existence of numerous etiopathogenical theories.

- As we examined a number of 43 cases of lichen planus associated with chronic hepatitis we noticed that the disease affect both sexes, but with a greater incidence in women (69.8 %) than in men (30.2%). The distribution on groups of ages illustrates a high level of morbidity that maintains its value at the groups aged 40-49 and 50-59, the majority of the patients coming from urban areas.
- Lesions topography and their clinical aspects are able to objectify the cutaneous pathological phenomenon and to provide data for the disease evolution surveillance.
  The most common clinical form in 56.8% of the cases consisted in a typical cutaneous
  eruption made of red-purple polygonal papules, indirect light shining, covered by a discreet scaling, placed on the anterior side of the forearms, calfs, presacral and paravertebral, accompanied by an excruciating pruritus. The disease has a chronic evolution with longer or shorter periods of lull, depending on the applied treatment, the psycho-emotional status and also on the eventual morbid associated entities.
- Porphiria cutanea tarda usually appears in over 50 years old male adults. The average age of disease occurrence was 50.4 years old and males/females ratio was 6.72. Porphiria cutanea tarda of the adult has a chronic evolution, with quiet (asymptomatic) periods and
  relapses with major cutaneous eruption, in the sunny months (July - September). The additional risk factors to interfere in starting the disease, identified on the group of patients we studied are, in order of frequency: chronic alcohol consuming, prolonged solar light exposure trough the nature of the patients' professions and industrial toxic.
- By studying clinical manifestations and by correlating them with some clinical and biological parameters, we noticed that the gravity of clinical manifestations lineary depends on the alcohol input, the value of serum iron and on the total quantity of urinary eliminated porphyrins, moreover palpable hepatomegaly presence constitutes a clinical sign of disease gravity.
- Photodermatosis associated with autoimmune hepatitis are cutaneous diseases started or aggravated by solar radiation,

that can act alone or in competition with some photoreactiv endogenous or exogenous substance. Photodermatosis frequently occur in persons exercising their profession outdoors (farmers, machine operators, fishermen). The disease is seasonal, occurring in spring months (March - June). At the same time relapses occur. The determining factor in pseudopellagroid syndrome is repeated exposure to the sun of uncovered skin surfaces. A high morbidity level with a lineary maintenance was noticed on groups of ages especially in the groups aged 41-50 and 51-60, for both sexes. The most frequently encountered clinical form was the one with entemato - edemato – flictenular plaques, well defined and covered by scales and hematic crusts, followed by postlesional hyperpigmentation.

- From the data of scientific literature and the one we obtained, photodermatosis can be considered true “iatrogenic diseases”, some of them with a professional character, others with an indubitable malign potential. The medical, economical and social implications that arise from the last years’ increase in the number of pseudopellagroid syndrome, constitute the premises that should be the foundation of medical and educational methods for preventing this syndrome.

References

- **Hazin R, Abu-Rajab Tamimi TI, Abuzetun JY, Zein NN.** Recognizing and treating cutaneous signs of liver disease. Cleve Clin J Med. 2009 Oct;76(10):599-606. Review.
- **Morioka D, Togo S, Kumamoto T, et al**. Six consecutive cases of successful adult ABO-incompatible living donor liver transplantation: a proposal for grading the severity of antibody-mediated rejection. Transplantation 2008; 85:171–178.
- **Bertini G, Rubaltelli FF**. Non-invasive bilirubinometry in neonatal jaundice. Semin Neonatol 2002; 7:129–133.
- **Polat M, Oztas P, Ilhan MN, Yalçin B, Alli N**. Generalized pruritus: a prospective study concerning etiology. Am J Clin Dermatol 2008; 9:39–44.
- **G aspari R, Avolio AW, Zileri Dal Verme L, et al**. Molecular adsorbent recirculating system in liver transplantation: safety and efficacy. Transplant Proc 2006; 38:3544–3551.
- **Dasgupta R, Saha I, Pal S, et al**. Immunosuppression, hepatotoxicity and depression of antioxidant status by arecoline in albino mice. Toxicology 2006; 227:94–104.
- **Neri S, Raciti C, D'Angelo G, Ierna D, Bruno CM**. Hyde's prurigo nodularis and chronic HCV hepatitis. J Hepatol 1998; 28:161–164.
- **Brown MA, George CR, Dunstan CR, Kalowski S, Corrigan AB**. Prurigo nodularis and aluminium overload in maintenance haemodialysis. Lancet 1992; 340:48.
- **Stander S, Luger T, Metze D**. Treatment of prurigo nodularis with topical capsaicin. J Am Acad Dermatol 2001; 44:471–478.
- **Requena L, Sangueza OP**. Cutaneous vascular anomalies. Part I. Hamartomas, malformations, and dilation of preexisting vessels. J Am Acad Dermatol 1997; 37:523–549.
- **Khasnis A, Gokula RM.** Spider nevus. J Postgrad Med 2002;48:307-9.
- **Sood A, Midha V.** Spider angiomas in the gastrointestinal tract. Trop Gastroenterol 2000;21:77.
- **Jaqueti G, Gonzalez-Lopez P, Ballesteros N**. Cutaneous hepatic porphyria and associated skin calcinosis. Actas Dermosifiliogr 1964; 55:513-20.
- **Li CP, Lee FY, Hwang SJ, et al**. Spider angiomas in patients with liver cirrhosis: role of vascular endothelial growth factor and basic fibroblast growth factor. World J Gastroenterolfs 2003;9:2832-5.
- **Gu JW, Elam J, Sartin A, Li W, Roach R, Adair TH**. Moderate levels of ethanol induce expression of vascular endothelial growth factor and stimulate angiogenesis. Am J Physiol Regul Integr Comp Physiol 2001; 281:R365-72.
- **Li CP, Lee FY, Hwang SJ, et al.** Role of substance P in the pathogenesis of spider angiomas in patients with nonalcoholic liver cirrhosis. Am J Gastroenterol 1999;94:502-7.

CURRICULUM VITAE

Personal Information

Name: Vasilakos Thomas

Address: Iezekiil 29, Karditsa, P.C. 43 100, Greece

Telephone: 00306974666702

E-mail: vasilakosuth@yahoo.gr

Nationality: Greek

Birth date: 25.06.1971

Professional experience

- **08.01.2009 - present,** doctor in Dermatology-Aphrodisiology with private cabinet
- **24.11.2008 – 24.11.2009**, doctor in Dermatology - Aphrodisiology at the Social Services Foundation at the compartment of Karditsa, Greece
- **24.12.2009 – 23.12.2010**, doctor in Dermatology - Aphrodisiology at the Social Services Foundation at the compartment of Karditsa, Greece
- **21.10.2004 - 28.10.2007,** trainee doctor at the clinic of Dermatology - Aphrodisiology at the University Hospital of Rio, Patras, Greece
- **19.02.2002 – 16.08.2003,** trainee doctor at the clinic of Pathology at St. Andrews General State Hospital of Patras, Greece

- **17.08.2003 – 17.08.2004**, training in the Nephrology clinic at St. Andrews General State Hospital of Patras, Greece
- **2002** Educational and Training Seminar organized by the Gastroenterology Clinic of the University of Florence with the title "Programmes of Alcohol Prevention", Patras, Greece
- **07.09.1999 - 11.06.2001,** doctor in rural medical service

Education and others

- **01.11.1989 - 15.07.1990,** learning Romanian language at the University of Bucharest, Faculty of Literature
- **30.09.1996,** graduated from the University of Bucharest, Faculty of Medicine
- **07.06.1989,** graduated from High School of Aliartos-Greece
- **21.09.1998 – 21.03.2000,** Military service, Greece

Personal skills and competences

- **Foreign Languages:** Greek, Romanian (very good), English (good)
- **Skills and professional competences:** PC user (Internet Explorer, Microsoft Word, Microsoft Power Point), driving license

Presentations (in international conferences)

1. Implicari imunologice in boala lupica. Silosi, I., Rogoz, S., Silosi, C., Drackoulogona, O., Avramescu, C., Romanescu, F., & Vasilakos, T. (2007). Simpozion de Morfologie Microscopica, Craiova, Universitatea de Medicina si Farmacie, 16-20 Mai, 2007.

2. Mecanisme Imune Implicate in Dezvoltarea Candidozei. Silosi, I., Silosi, C., Rogoz S., Avramescu, C., Vasilakos, T., & Drakoulogona, O. (2007). Manifestari Strintifice, Craiova, Universitatea de Medicina si Farmacie, 08-09 Iunie, 2007.

3. Evaluation of increased cholesterol in patients with CRV. Vasilakos, T., Gioka, M., Karavoulia, S., Zigouris, N., Devves, I., Georgiadis, Belas, A., Kanelopoulos, K., Desinioti, K., Hristopoulos, I. & Giannoulaki, E., 5th Pampeloponnesian Medical Conference, Patras, Greece, 18-20 October, 2002.

4. SD2 Complications in hyper-aged patients. Gioka, M., Karavoulia, S., Zigouris, N., Devves, I., Georgiadis, D., Vasilakos, T., Belas, A., Kanelopoulos, K., Desinioti, K., Hristopoulos, I. & Giannoulaki, E., 5th Pampeloponnesian Medical Conference, Patras, Greece, 18-20 October, 2002.

5. CRP Levels of Ascitic Accumulations. Devves, I., Gioka, M., Karavoulia, S., Zigouris, N., Georgiadis, D., Vasilakos, T., Belas, A., Kanelopoulos, K., Desinioti, K., Hristopoulos, I. & Giannoulaki, E., 5th Pampeloponnesian Medical Conference, Patras, Greece, 18-20 October, 2002.

6. Conscience Disorders in hyper-aged patients. Belas, A., Devves, I., Gioka, M., Karavoulia, S., Zigouris, N., Georgiadis, D., Vasilakos, T., Kanelopoulos, K., Desinioti, K., Hristopoulos, I. & Giannoulaki, E., 5th Pampeloponnesian Medical Conference, Patras, Greece, 18-20 October, 2002.

7. SD2 Complications Correlated with BMI in hyper-aged patients. Kanelopoulos, K., Gioka, M., Karavoulia, S., Zigouris, N., Devves, I., Georgiadis, D., Vasilakos, T., Belas, A., Desinioti, K., Hristopoulos, I. & Giannoulaki, E., 5th Pampeloponnesian Medical Conference,

Patras, Greece, 18-20 October, 2002.

8. Anaemia Investigations in hyper-aged patients. Desinioti, K., Belas, A., Devves, I., Gioka, M., Karavoulia, S., Zigouris, N., Georgiadis, D., Vasilakos, T., Kanelopoulos, K., Hristopoulos, I. & Giannoulaki, E., 5th Pampeloponnesian Medical Conference, Patras, Greece, 18-20 October, 2002.
