Correlations Between Cardiovascular/Cardiometabolic Risk and Standard Biochemical Investigations

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The metabolic syndrome is a pathologic constellation which brings negative effects on the heart, mainly by an atherosclerosis mechanism. Obesity, as a first rank component of the metabolic syndrome, leads to many imbalances of the cardiac function, respectively neurohormonal activation with hypervolemia, apoptosis, fibrosis, and hypertrophy, triggered by the proinflammatory adipocytokines, associated with the lypotoxic effect of the fats of myocardial cells. Arterial hypertension can lead to left ventricular hypertrophy, but it can also occur in obese people, independently from arterial hypertension. Initially concentric, it evolves into non-concentric, being associated with diastolic dysfunction, left atrial enlargement, right ventricular enlargement and hypertrophy, etc. There have been attempts to define the relation between obesity, cardiovascular diseases and standard biochemical investigations, observing the direct relation between these clinical – pathological variables and the changes of paraclinical parameters, frequently used and studied in medical practice. The retrospective randomized double-blind study was conducted on a 2 years' period of time, between 2013 and 2014, and included 2 individualized groups, one that included patients with metabolic syndrome, clinically and functionally investigated, and a control group, subject to the same evaluations. Thus, it was useful to re-introduce a basic package of routine evaluation investigations. The purpose of this biochemical evaluation is the medium- and long-term prophylaxis of MS, respectively of the four components, HTN, dyslipidemia syndrome, sugar diabetes, and obesity.

Keywords: atherosclerosis mechanism, metabolic syndrome, hypervolemia, apoptosis, fibrosis, hypertrophy

In this paper was studied the possibility to re-introduce a *basic package* of bio-chemical investigation to population, with economic and social advantages (low costs and with the involvement of general medical staff, already present), with a significant role in determining the cardiometabolic and cardiovascular risk.

Experimental part

Materials and methods

Our study was conducted in the Fifth Medical Geriatrics and Gerontology Clinic, between 2013 and 2014, with the approval of the ethics commission of C.F. Hospital in Iasi, and with patients' informed consent.

We complied with the Law 46/2003 on personal data protection and free circulation. By this procedure, we have not studied an individual with precise identity, but a subject with certain demographic features, who accepted to be part of our study, by signing a free and informed consent.

Legislative stipulations on confidentiality of personal data of each individual have been complied, as well as the ones stipulating that during the entire period of study, the individual is not subject to techniques of treatment that affect the quality of life.

365 patients with MS have been selected, who have been clinically and paraclinically evaluated. MS diagnosis was set based on the association of HTN with sugar diabetes, dyslipidemia, respectively, enlargement of abdominal girth.

These patients were subject to the following biochemical investigations: glycemia, total cholesterol, HDL cholesterol, LDL cholesterol, GOT, ALT, CBC, and C-reactive protein. The need for each analysis was justified in the context of associated cardiovascular risk factors.

We should mention the fact that conditions that grant the accuracy of determining the values of lipid profile have been obeyed. Thus, all subjects that have been enrolled in this study were clinically stable, and the evaluation of lipid status took place prior to individual instructions on conditions that must be met on blood sampling.

Sampling was done on peripheral blood à jeun, after at least 10-12 h from the last mean and no alcohol consumption during 24-48 h, in order to prevent unconcludent results. Both the values of total cholesterol, and LDL cholesterol were valid only after two determination performed at one-week interval. If the value of the two parameters varied with more 30 mg/dL, the mean of two values was considered.

Taking into consideration the particularities of the risk factors depending on gender and age, we divided the patients into two subgroups: subgroup I – adults, and subgroup II – elderly.

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Age	Group I – Adults	Group II - Elderly
18-30 years	23 (6.3%)	0
31-54 years	104 (28.5%)	0
54-64 years	118 (32.3%)	0
65-74 years	0	67 (18.4%)
75-84 years	0	34 (9.3%)
≥85 years	0	19 (5.2%)
TOTAL	245 (67.1%)	120 (32.9%)

Table I
DISTRIBUTION OF PATIENTS WITH MS, HOSPITALIZED IN THE FIFTH MEDICAL GERIATRICS - GERONTOLOGY CLINIC, ON A TWO YEARS' PERIOD OF TIME (JANUARY 2013 – DECEMBER 2014), ON AGE GROUPS

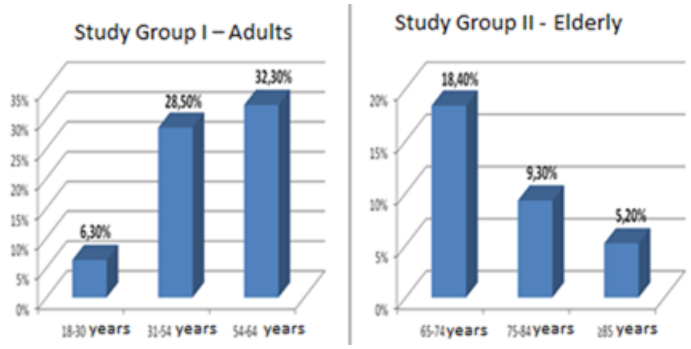


Fig. 1. Distribution of hospitalized patients in the Fifth Medical Geriatrics and Gerontology Clinic, on age

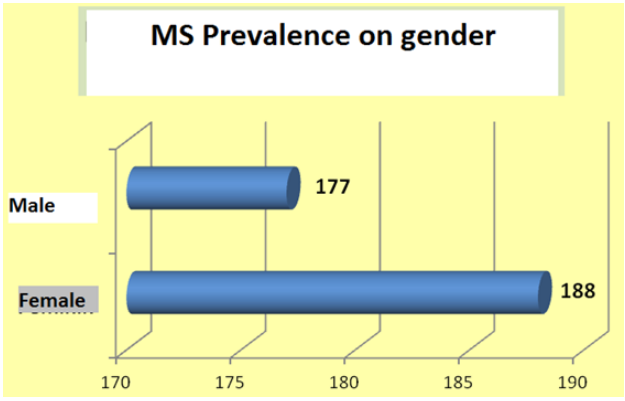


Fig. 2 Distribution of patients with MS, depending on gender

Results and discussions

The study was focused on the analysis of the 365 patients with MS, hospitalized for a period of two years in an Internal Medicine Clinic, whom we analyzed depending on two study groups, adults and elderly, on: gender, environmental origin, level of education, smoking, alcohol consumption, and weight. Further on, we studied the incidence of essential arterial hypertension and of sugar diabetes, completing our research with determinations of lipid imbalance, proinflammatory state, hepatic and renal damage.

The patients of both study groups have been studied depending on age groups, namely: Study Group I – adults: 18-30 years old, 31-54 years old, 55-64 years old; Study Group II - elderly: 65-74 years old, 75-84 years oldand e" 85 years old (table 1, fig 1).

In figure 1, one can see that within the group of adult patients with MS, the largest part consists of 54 – 64 age group, with 118 patients (32.30%). A small part of the patients of this group is under 30 years old – 23 patients (6.30%). There are 104 (28.50%) patients between 31 -54 years old. Within The Study Group II – elderly, the largest part of the cases is between 65 -74 years old, with 67 cases (18.4%), while the group consisted of 35 patients (14.5%) over 75 years old.

The analysis of the 365 patients with Metabolic Syndrome showed a similar incidence between the two genders (53.5% female vs. 46.5% male, fig. 2), also visible by the statistical study realized on the total number of hospitalizations (13.60% vs. 14.50%).

Our results did not point out a significant statistical difference (p=0.552) on glycemia values in patients of the two study group (table 2).

Dyslipidemia is a notifiable risk factor with an important role in development of atherosclerosis and cardiovascular diseases. The disorders on the lipid metabolism can be genetically determined or progressively installed, depending on an inappropriate lifestyle, with excessive animal fats, stress or overstress.

To set the diagnosis of dyslipidemia, the following biochemical constants were determined: serum cholesterol, HDL cholesterol, LDL cholesterol, and serum triglycerides.

The biological reference interval for the normal values of cholesterol is 120-220 mg/dL. We calculated the mean values of cholesterol in our 365 patients, which afterwards

Table 2
STATISTICAL INDICATORS ON MEAN VALUES OF GLYCEMIA IN PATIENTS WITH METABOLIC SYNDROME, ON STUDY GROUPS

Study group	N	mean	Standard deviation	Standard error	Confidence interval		Min	Max	p
					- 95%CI	+95%CI			
Group I- adults	245	126.95	58.65	3.75	119.57	134.33	78.00	509.30	
Group II - elderly	120	130.84	58.78	5.37	120.21	141.46	67.20	399.00	0.552
Total	365	128.23	58.64	3.07	122.19	134.26	67.20	509.30	

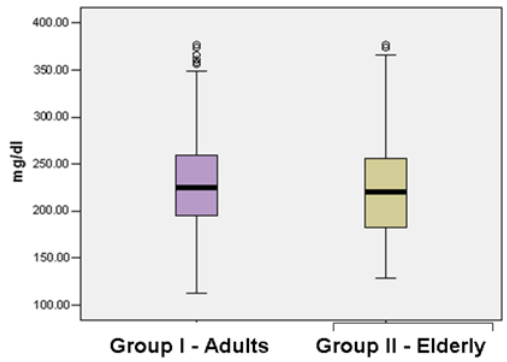


Fig. 3. Distribution of patients with MS on mean values of total serum cholesterol in the study groups

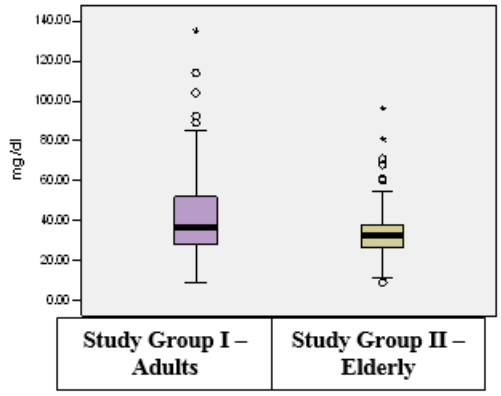


Fig. 4. Distribution of patients with MS on mean values of LDL cholesterol, on study groups

were distributed and analyzed on the two study groups, adults and elderly, specifying the statistical indicators.

Mean value of serum cholesterol in MS patients:

- study Group I – adults – mean value cholesterol: 230.68 mg/dl (DS=51.29);

- study Group II – elderly – mean value of cholesterol: 228.94 mg/dL (DS=57.05), (fig. 3).

Literature data indicate the fact that most of the patients with ischemic cardiopathy show moderate increases of the total cholesterol. So far, enough evidence has been collected to testify the relation between the anomalies of lipid metabolism and risk for coronary, cerebral or peripheral atherosclerosis.

Although high cholesterol levels in subjects with cardiovascular diseases have been noticed long before, only in 1984 results have been published, showing the reduction of risk for myocardial infarction as a result of lowering the value of serum cholesterol. Initially, most of the studies documented a close relation between the level of total cholesterol and ischemic cardiac disease, but afterward there has been noticed that in fact LDL cholesterol is the dominant causing agent with atherogenic properties, correlated with the increase of cardiovascular risk.

Determination of LDL cholesterol fraction is one of the essential elements of the lipid balance. Epidemiological and clinical studies showed that a reduction with 30 mg/dL of LDL plasma cholesterol is associated with a 30% decrease of the cardiovascular risk. That is why the evaluation of the level of LDL cholesterol is a key moment both in positive diagnosis of Metabolic Syndrome, and in determining the cardiovascular risk. Depending on its value, different intervention strategies are recommended, from changing the lifestyle, to drug therapy. The values of LDL cholesterol are defined in accordance with *ESC/EAS Guidelines for the Management of Dyslipidemia,* with the recommendation to gradually reduce it up to target values, depending on the starting value.

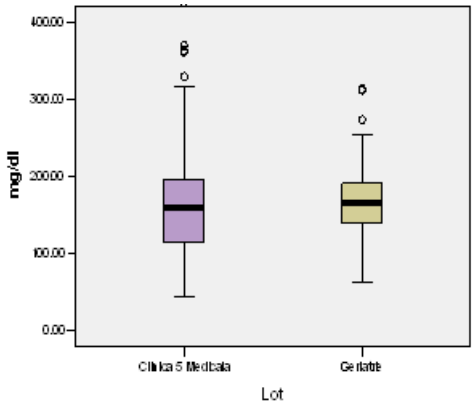


Fig. 5 Distribution of patients with MS on mean values of triglycerides, on study groups

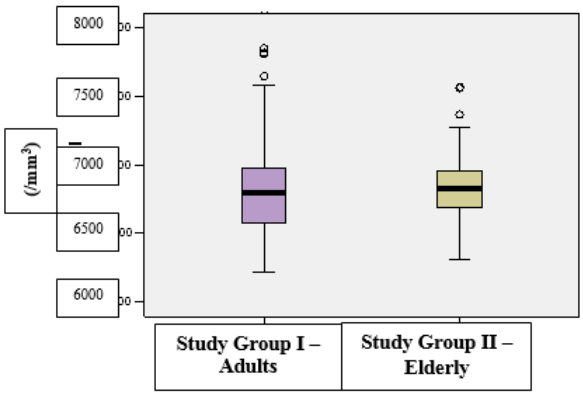


Fig. 6 Distribution of patients with SM on mean values of leukocytes

Mean value of LDL cholesterol in Metabolic Syndrome patients:

- s tudy Group I – adults – mean value of LDL cholesterol: 116.84 mg/dL (DS=35.82);

- study Group II – elderly – mean value of LDL cholesterol: 150.04 mg/dL (DS=37.82) (fig. 4).

The biological reference interval for serum triglycerides is 36mg/dL-165mg/dL. The mean value of triglycerides in MS patients:

- Study Group I – adults – mean value of triglycerides: 172.02 mg/dl (DS=111.01);

- Study Group II – elderly – mean value of triglycerides: 165.62 mg/dl (DS=45.98), (fig. 5).

Literature data indicate the fact that the cardiovascular risk is more associated with mild hyperglyceridemia than with severe hyperglyceridemia, probably due to the fact that mild hyperglyceridemia is caused by accumulation of IDL and small particles of VLDL, in plasma whereas the severe form is owed to the accumulation of chylomicrons and large particles of VLDL, which are not atherogenic.

Related to proinflammatory status, we analyzed the number of leukocytes and VSH, monitoring our patients with MS for any signs of proinflammatory status.

The mean value of leukocytes in SM patients was:

- Study Group I – adults – mean value of leukocytes: 6668 mm^3 (DS=1660);

- Study Group II – elderly – mean value of leukocytes: 6510/ mm^3 (DS=2079), (fig. 6).

Mean value of VSH in Metabolic Syndrome:

- Study Group I – adults - mean value of VSH: 11.84 mm/1h (DS=8.68); (fig. 7).

-la Study Group II – elderly – mean value of VSH 13.77 mm/1h (DS=12.83).

Out of the total of 365 patients with metabolic syndrome whom we studied, we noticed the proinflammatory status, objectivized by the increase of levels of VSH and leukocytes to 9.3% (34 patients) (34 patients) (fig. 8).

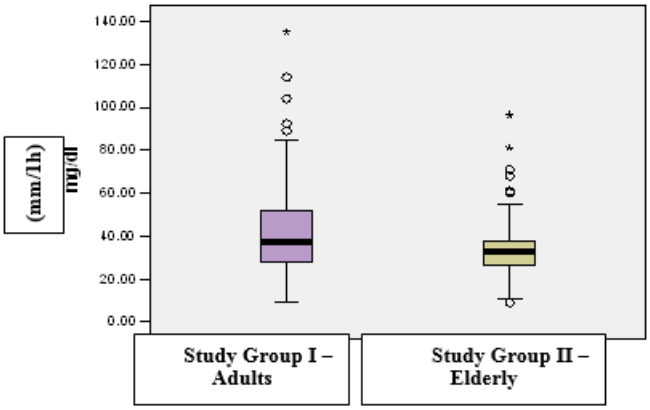


Fig. 7. Distribution of patients with Metabolic Syndrome on mean values of VSH

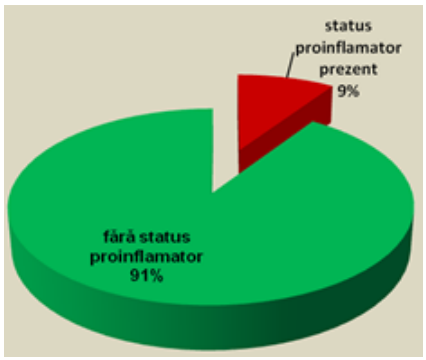
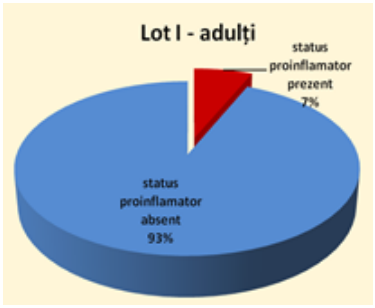


Fig. 8. Distribution of patients with proinflammatory status reported to number of patients with SM

Also, the evaluation in itself showed a lower percentage of proinflammatory status in patients with Metabolic Syndrome of the study group I – adults, comparatively with the study group II – elderly. Thus, 7% (16 patients) of adult patients with metabolic syndrome show metabolic syndrome, while 15% (18 patients) of the elderly with metabolic syndrome suffer from this change (fig. 9).

Statistic research showed changes of the proinflammatory status depending on the patients' gender; thus, in Study Group I – adults, the percentage of women with proinflammatory status was of 2.4% (6 patients), while in men the percentage was higher, respectively of 4.1% (10 patients). Analyzing Study Group II – elderly, we discovered that 9.2% of women (11 patients) presented proinflammatory status, while the percentage of men was lower, respectively 5.8% (7 patients), (fig. 10, table 3).

To study the liver damage, we determined the presence of hepatic cytolysis syndrome, measuring the level of serum transaminases: serum glutamate-oxaloacetate transaminase (SGOT), serum glutamate-pyruvate transaminase (SGPT), and gamma-glutamyl transpeptidase (GGT). We also added the echographic study of the liver, which revealed hepatic steatosis or signs of chronic hepatitis.



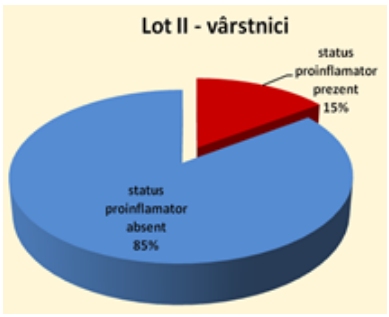


Fig. 9. Distribution of patients with metabolic syndrome and proinflammatory status on study groups (age parameter)

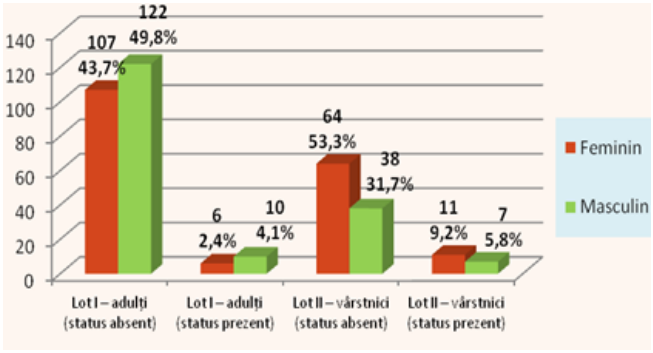


Fig. 10. Distribution of patients with metabolic syndrome on gender and study group (age parameter)

Out of the total of 365 patients with metabolic syndrome included in this study, we determined liver damage in 7% (27 patients) (fig. 11).

The comparative study revealed liver damage in a lower percentage of patients with metabolic syndrome of Study Group I – adults, comparing to Study Group II – elderly. Thus, 4% (11 patients) of the adult patients with metabolic syndrome have liver damage, and 13% (16 patients) of elderly with metabolic syndrome show this change (fig. 12).

Cardiovascular and cardiometabolic diseases have an explosive incidence both in our country, and abroad.

In this context, it is necessary to undergo a populational evaluation with prophylactic purpose, by means of sanitary education and adequate treatments. A few years ago a national programme of investigating the general health of

Study Group	N	Significance		RR	p
		χ^2	IC95%		
Study Group I – Adults					
Female	132	2.07	1.88÷1.20	1.83	
Male	113	2.52	2.25÷1.42	2.28	
Total	245	2.31	2.09÷1.35	2.10	
Study Group II – Elderly					**0.01**
Female	75	2.83	2.90÷1.78	2.98	
Male	45	2.65	2.57÷1.36	2.52	
Total	120	2.72	2.76÷1.52	2.71	
Total	365	2.54	2.44÷1.41	2.51	

Table 3
STATISTICAL INDICATORS CONCERNING DISTRIBUTION OF PATIENTS WITH METABOLIC SYNDROME AND PROINFLAMMATORY STATUS ON GENDER AND STUDY GROUP (AGE PARAMETER)

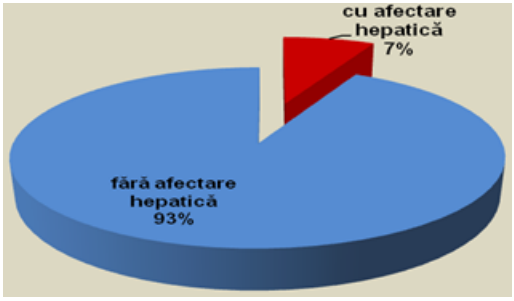


Fig. 11. Distribution of patients with liver damage reported to number of patients with metabolic syndrome

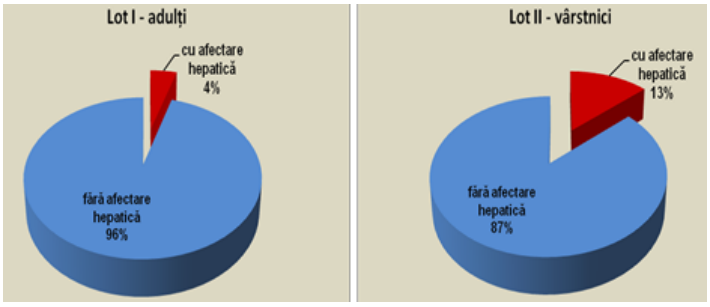


Fig. 12. Distribution of patients with metabolic syndrome and liver damage on study groups (age parameter)

patients was carried out thorough family doctors practice. The PhD thesis The Study of Metabolic Syndrome in Correlation with the Pathology of Depressive Disorder" that was carried out in our clinic for 4 years, using statistically significant groups of patients revealed the importance of the need to evaluate patients every year, as well as the role of the family doctor in the intervention plan of cardiovascular diseases, by detection and treatment of cardiovascular and metabolic risk factors.

Since the national programme was carried out for 1 year only, we believed it was useful to re-introduce a basic package regarding the necessary investigations for a routine evaluation. They would aim at Metabolic Syndrome prophylaxis, meaning its 4 components, namely arterial hypertension, dyslipidemia syndrome, sugar diabetes, and obesity. The clinical evaluations, associated with *the basic package* of biochemical and laboratory investigations, with no additional costs, could make the patients aware of the need to change their lifestyle, supplemented by adequate and individualized treatments.

Determining the cholesterol, HDL cholesterol and LDL cholesterol should be associated with determining the glycemia, while the elevated levels of serum transaminases (GOT and TGP) would indicate liver damage, especially when specialized literature reports that MS can be associated with hepatic steatosis. Also, it is necessary to determine the CBT, in order to detect the anemia syndrome in renal context.

We recommend to include C-reactive protein in *the basic package*, considering the role of inflammation in atherosclerosis, documented in recent years by Romanian and foreign studies.

Conclusions

Conclusions of this research, as well of the international studies, prove the explosive incidence of Metabolic Syndrome (27.6% *vs* 29.3%, adults /elderly) and contribute to a responsible approach, aiming at prevention and adequate treatment of cardiovascular diseases and depression disorders.

Age remains an unchangeable major risk factor, also for Metabolic Syndrome as our study proves, with a higher risk of onset in patients over 65 years (RR=5.8).

Increased frequency of *dyslipidemia,* showed in our study, confirms that fact that it is a treatable cardiovascular risk factor, both in adults and elderly, with a higher incidence in older women (p=0.002).

Considering numerous current studies on the implication of *proinflammatory* status and the *role of immunity* in etiopathology of atherosclerosis, our study focused on determining these parameters in metabolic syndrome, showing a higher incidence in elderly, comparing to adults, with statistically significant differences (p=0.001), older women being more prone to develop it (p=0.001).

Nonalcoholic steatohepatitis is a chronic hepatic condition, which can associate with metabolic syndrome, our study revealing a higher incidence in elderly comparatively with adults (13 vs 4%) and in men vs women (RR=1.18).

Our study, oriented towards pointing out the explosive incidence of Metabolic Syndrome, launches the idea of national programmes of "basic" biochemical investigation, with low costs and minimal human involvement (general medicine network, already existing), with an important effect on the prevention of cardiovascular risk factor, cardiovascular diseases and mental disorders as a consequence of dysmetabolic disorders, ultimately aiming at improving the quality of life and maintaining the public health.

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