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content

A New Faculty with European Standards and Mentality

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«I have a dream», said Martin Luther King. „Trust your dreams. Have the courage to go after them, „another wise man had said. „Do not allow small minds to convince you that your dreams are too great," advised another wise man.

It was considered a big dream the idea of creating a new Albanian non-public faculty in the field of medicine and health.

In fact it was a dream that was born in the mind of Henri Çili and preserved for many years in his heart. He is one of the most passionate innovators in the field of

higher education and our social liberalization in general. He together with three other open-minded inovators created the European University of Tirana (UET), which in the last ten years marked impressive stories of success.

Those prominent professionals, elite scientists and elite academics of Albanian medicine who believed in that dream, who contributed and pursued with persistence and hope the initiator, without calling it either great or unachievable or even impossible as many skeptics claimed, deserve the same acknowledgment.

So, the Faculty Of Medical Technical Sciences was created and licensed. It is going to open its' doors today to start the activity at UET. It is a joyous day of success as a first step, but also a prelude to a new challenge, as seductive as the step towards the extension to a full nonpublic Albanian medical faculty (or why not to a new medical university) with all branches even the specialties that our population needs and the free market of health services demands.

This faculty was born due to the logical consequence of the growing needs of our population for nursing, physiotherapy, imaging services and professionals, while their number in relation to our population is the lowest not only in Europe but also in the region. It was born when a part of such professionals are emigrating each year more and more to the huge demand Europe has for them, and also the aging of our population is growing unbreakably in percentage, along with the specific needs they have for such services.

Actually, It did not spring up in the emptiness. Other courses, one or two year schools and up to state and private universities have contributed over the years to the education and training of such health professionals. They also deserve our deep appreciation and gratitude. Thanks to their recent achievements and the identification of shortcomings, we have learned the lessons, especially in the ambition to create a more advanced model and quality of their education and training: that of skilled, competent and professional health workers but even with empathy, with the smile, eye and eye contact and listening attentively to patients and citizens; the demands that „in today's industry" such services have become necessary standards for implementation.

There are some existing UET advantages that allow such goals. The new Faculty Of Technical Medical Sciences had the fate that was born in UET, now a „grizzly" university in pedagogical, with a scientific and managerial experience „with renewed teaching and learning concepts, with new pedagogical interactive methods based on the concept of „adult-adult" dialogue that allows students not only to gain knowledge but also to give their own opinions and have the feeling that they are not just UET's customers, but also an active partner in the process of continuous perfection and the assurance of appropriate European standards for accreditation. Our goal is not „business as usual" or to produce „more of the same existing", but to educate and train medical professionals of a new type, the type that the population, the market and the time we live demands of.

Nurses will not acquire in UET just another paperboard diploma, as an aide or „secondhand worker", not to say „maidservant" of the superiors, but will be trained as professional partners with competences for specific activities independent of the doctor. Such nurses could create a „nursing sector" which our system and health market lacks nowadays. This will gibe them the possibility that after graduation, instead of seeking jobs somewhere in existing public or private institutions centers, they will be able to create the workplace themselves, even employ others by creating a free „market independent nursing centers" with certified competence for specific standardized medical service facilities, which they will be able to add to and expand upon their own initiative according to their ability and client requirements.

Ten years of UET's success have given it a modern European mentality and functionality. An innovation of interest in creating a multidimensional and multifactorial „mini universe", which gives the appropriate meaning to the university term but which our higher education lacked . This „universe" as a bouquet of programs, offers its students not only theoretical knowledge in auditoriums or how to put those in practice, but also cultural and intellectual erudition in the fields of sociology, psychology, economics and management, pedagogy, justice, ethics, arts, communication and information sciences; irradiated by the respective faculties in the UET atmosphere.

UET, beside being a higher education institution, it is an „environment which encourages freedom and intellectualism" condensed with knowledge, science, ideas, and alternatives that are developed with a reciprocal representation. It offers free debates and forums with renowned local and international scholars, artists and intellectuals, young writers, avant-garde art exhibitions, where the Albanian Academy of Arts and Science holds its meetings, where honoris causa titles, grants and donations are awarded to prominent personalities and to excellent students and also to those in need.

All this constitute a precious asset for the overall ethical and cultural formation of the new medical professionals, which are crucial today because medical sciences have surpassed the previous biological boundaries focused on organs and the physical body and extended to sociological, psychological, ethical and economical aspects, of sick people and citizens in general. A new type of medical professionals can not be fully shqped, nor can he/she perform successfully if he/she has only received a paperboard certificate for the knowledge but they will still remain spiritually dry.

With the potential of UET and its many faculties, in non-medical fields and profiles, will strongly radiate. So, new faculty students, after finishing their studies will not leave with the white coat, not just with a paperboard diploma but also with erudition, ethics and civil culture as humanists and dignified intellectuals. And of course with a white heart.

Let's congratulate together the new faculty and this first edition magazine.

The Challenge of Quality Improvement in Our Health System

Prof. Dr. Isuf Kalo

Quality in health as a concept, as a demand and as a measurable indicator of success has long been forgotten or underestimated. Just a few decades ago, it has entered in its dictionary and programs. Yet it is still perceived as an optional innovation, but not as a necessity and priority to it.

The same thing happens in our health system. The challenge of structured quality improvement, security and performance started too late, in 2006 with the establishment of QKCSA-ISH. Thereafter, it began to be mentioned more often in political, managerial and professional rhetoric; but mainly as a sermon and desire, not in a concrete way and not in a consistent manner with the major objective of the health reform.

In fact, health systems are not perfect nowadays. They have impressive achievements but also serious defects and serious deficiencies. And there is a need for quality review and improvement. They almost do not differ from each other by the universal principles and their guiding values. But they differ from the architecture of functionality and especially from their performance and quality. And this from one country to another, and also strangely between countries of the same community as those of EU.

Interest for the quality was added to health sector when its unjustified variations emerged in services of the same type. And even differences between analogue institutions within the same state and even within the same city. The comparison, for example, carried out by QKCSA for the quality of the same services in the two maternity hospitals of Tirana, having the same mission and the same resources resulted in some of the best quality in one maternity and some others to the other maternity.

This proved the existence of subjective factors and the unequal utilization of available resources and potentials. The improvement of quality in health was due to

the need to recognize and eliminate such barriers and at the same time to maximize the use of resources at the institutional and system level.

The philosophy of improvement is based on a progressive positivist paradigm: not merely correction of defects and blaming for the consequences the ones who caused it, but the identification and promotion of the demonstrated and certified practice as the best. And its reward. First of all, the "champion" examples of quality should be identified, discovering their success secrets and then spreading them to other institutions in and out of the country. The same paradigm is proposed recently in the Security field, where the "Safety 1" method focusing on identifying and correcting mistakes and failures is being replaced by "Safety 2", which instead utilizes, disseminates and promotes proven and successful practices that are actually many times larger than the first one.

This is not an original method of health system. It is borrowed by the industry, which has implemented it many years before it. In a simplified form, healthcare quality means "doing what it takes properly, to the right patients, at the right time and price". Applied in different fields and populations, this philosophy created in itself great aspects and great research methodology. Currently, quality improvement in healthcare sector has gained scientific character as a new field of study in terms of health systems with architecture and different opportunities.

Trust or measurement?

It is a fact that quality has traditionally been somewhat a naïve approach based on access a priori to white coats professionals. Trust based on the diploma they possess and a code of ethics known as the Hippocratic Oath, in which the doctors vow to do the best for the patients. So they left the "best possible" thing in their hands neither measured nor verified. The quality of services was judged based on opinions, rumors, or advertisements.

Meanwhile, the unified metering tools ("meters", "scales") were both missing (as unnecessary) as for quality and performance, which made it impossible to evaluate and compare objectively the quality among analogue institutions. As a consequence of the reckless, unrecognized and unpublished, good quality and bad quality services of analogue institutions, are still treated and rewarded equally in public healthcare sector.

Parameters that were measured, reported and rewarded in health system generally referred only to the quantity, volume and spectrum of health activity, but not to their quality. One of the reasons was that the measurement and evaluation of the quality was not liked neither by the professional elite nor by the leadership and managerial elite. A priori trust was by itself more preferred than measurement.

They could put the real results of the qualitaty in front of the mirror in relation to expectations by the population.

The situation was changed by the free health market. In its demand-offerings apart from the quantitative side, consumers also rightly ask for the "label" of the quality, cost and security of the services they pay. The unmeasured "good" it is not a without fail good thing. In our healthcare market the quality is still unverified and its "label" is generally absent. This leaves room for abusive advertising which lead to the disorientation of consumers. Establishing them and regulating new free market relations with quality and real cost remains for us a heavy burden like Sifiz.

Illusion and resistance

It should be said that one of the most widespread illusions regarding the goodness of the general health is that money is the only way forward. It is not quite so. The best quality is mainly given by people themselves, as passionate and motivated individuals, or more often in programmed interaction with partners and other interested parties. Medical care is the human product that is created and offered mostly by man to man. Undoubtedly, quality improvement, both at institutional and system level, requires an initial financial investment. It is necessary to create the concepts, the strategy, tools, methods and culture of measurement and improvement. But this investment returns a few years later by reducing unnecessary excessive expenditures, lost from incorrect quality practices and not effective. Health systems, including ours, are like a container with many holes, from where too much money flows in vain. The most frequent current barriers to quality improvement in our health come from: conservative thinking, indifference, lack of recognition, arise from resistance, inertia of the inherited routine, wrong subjective decision making and unfounded in scientifically evidence. They also come from discouragement and disbelief for success. They appear whenever it is attempted to move from a lower quality level A to the highest quality B.

Regardless of how they disguise it, such resistance is encountered both at local and central policy and decision-makers, elite health professionals, managers, hospital and ambulatory medical staff, health insurance agencies, patients and our passive citizens. While in principle and rhetoric they are all in favor of quality, they virtually expect it as a gift from someone else and not as one of their own duties.

The best quality efforts in our healthcare context were not limited to making it possible to measure and verify. Measurement only gives figures. The goal of quality movement is not just photography but continuous improvement, not just one episode. Improvement is created only if it is acted upon. It begins with the creation

of the first good quality embryos and examples. Not acting like it will fall from the sky; either wait to be imported or donated by someone.

The first action step is consensus with all stakeholders and partners of the "good quality" definition according to our understanding and expectation. What will be the targeted values and parameters ?

According to the American Institute of Medicine, "good quality" consists of 6 basic features or values: **Health Care** safety (minimizing mistakes and risks during medical practice), clinical effectiveness (in diagnosis and treatment), patients at the center (respect their rights), efficiency (maximizing results with the available resources) and equality (non-discrimination, unbiased) in the provision of services. No health system can accomplish those at once and should therefore be selected and focused on those selected as priority.

Standardization without implementation

In this context in 2005, thanks to the cooperation with WHO and the World Bank, a consensual strategic document for quality development in our healthcare was produced. The focus was on three main features selected: safety, effectiveness, and center-based patients. Based on this strategy, the QKCSA-ISH (National Center for Quality, Safety and Accreditation of Health Institutions) was established as a new structure that would lead the process, provide concepts, vision and create quality measurement tools and at the same time improve its methods. At the same time, they would encourage, coordinate and support the expertise of their institution-building activity under the leadership and executive authority of the Ministry of Health.

The QKCSA activity has been successful in the strategic conceptual aspects and the creation of tools and methods for improving quality and its progress is evident.

It is worth mentioning here apart from the national strategy, that for the first time (even the first in the region) of a set of standards, for measuring the quality and institutional performance necessary for licensing and accreditation of hospitals and primary centers, dental services, pharmaceutical and laboratory services. Also, the establishment of the first network of specifically trained institutional coordinators and the drafting of a methodological strategy for designing UPK and PPK best clinical practice. CBSA-ISH has produced and distributed a considerable number of materials, methodological documents, books and toolkits, rights charts and methodologies, instructive documents and structures to promote its concepts to healthcare staff and empower patients and citizens as the best quality active partner. It has organized national and international conferences every year with recent issues regarding quality of our health and beyond, where achievements and problems are presented, also challenges for the future.

Unfortunately, the implementation process from healthcare institutions, in terms of using and implementing these methods and concepts, tools and materials has been sluggish and deceptive. QKCSA-ISH has promoted, trained and produced but had no executive and enforcement powers in the center and or institution level. The Ministry of Health has them.

Lack of Quality Mechanisms and Culture

The inactivity in the implementation of available tools and methods highlighted the need to develop a culture of quality and responsibility and motivational mechanisms for its development, both in white coat professionals and our local institutional leaders and managers. The culture of quality means the disagreement with the bad quality and the conscious commitment to improving it within everyone's reach in the daily practice of healthcare links.

It has already been proven that measuring and evaluating quality in healthcare institutions can be technically correct from the outside, but its substantial and continuous improvement can only be accomplished and achieved by inside actions from the dedicated and motivated staff.

The European Association of Physicians in 1994, in its resolution, recognized the responsibility and protagonism of white coat professionals towards "quality" as the leader of the movement towards the best. "Providing health care with the highest possible quality,- it is said in it,- constitutes an obligation of the health profession ". Whereas WHO, in 1998, proclaimed the continued assurance of the best possible quality as a "healthcare obligation to a legitimate right of the sick people".

But quality improvement also requires innovative methods and specific tactics, which should be recognized and applied scientifically and creatively under the specific conditions of each institution. One of the essential principles is stop sporadic actions and say no to propagandistic campaigning with the quality as a façade, but with a plan and seriousness, with stages in order to achieve the best targets. The next condition is the creation of a favorable, intra-institutional climate with a motivation for better quality. Prior to the preparation of the terrain, the lack of the necessary devotion to quality towards excellence in institutions, it shows that numerous attempts do not yield fruits. QKCSA is offered to help with expertise in them but unfortunately institutional receptivity is not in its best place. The ringer of the quality clock has still not ringed to them. And not only to them.

Experiences prove that good quality is achieved not by decrees or by dictates, nor by preaching or by fear and punishment. Commitment for it arises first in the mind, in the heart and in the professional and institutional attitudes, mainly

as an ethical and cultural element. Then It is furtherly developed through the example of the best practices, demonstrated as "champions", which inspires and then encourages imitation and race to overcome qualitative levels among them.

The father of quality in healthcare A. Donabedian insisted that "Quality is Love". According to him nothing qualitative cannot be realized unwillingly, without love and passion and without feeling inwardly the need for it. But the success or failure of quality programs is also determined by a pragmatic element such as the existence of correct or incorrect use of incentives, motivating and rewarding to "militant" and enthusiastic individuals, be they ethical incentives, honorific, career promoters, or why not even financial.

From the network of first volunteer quality coordinators formed by QKCSA-ISH through special trainings in hospitals and health centers of our country, unfortunately only in very few places, they kept the enthusiasm still heated. Most of them were "extinguished" in the ice of the indifference of the leaders of the institutions, who changed one after the other without being acquainted neither with the dictionary of the quality, nor with the merits, efforts, achievements and precious values of these first admirable pioneers.

Still far away from the desired quality

However, it has come the time that our quality health should be seen not as a luxury or as a secondary issue, but as an unfulfilled debt and obligation to our patients and our citizens. Unfortunately, it has not been rated as such. Out of the three strategic objectives of quality, **safety, efficiency and patient satisfaction**, selected since 2006: none has been achieved. Even though there have been taken some steps forward, our health system remains far from the objectives of a qualitative system.

One of the causes has been that the cause of quality has generally been misunderstood, sometimes even misused. Variations and all-around activities often serve as quality enhancing equivalents. Under the name and with the cause of quality, projects and initiatives without real connection with quality have been fabricated. Quality means moving towards the verified best. Not every "change" turns out to be such. Some of them concede towards regression.

Obstacles to a long-term process of inconsistent continuity such as quality improvement have been also the politicization or more precisely the "politically lead" of our health system expressed by the heavy circulation of heterogeneous leaders with unusually subjective and nihilistic attitudes, among them that turn everything useful at reaching the zero point of resumption. The shine in our health looks like it has walked on the tango forward and backward like the knit – unknit process of Penelope's fabric...

Some recommendations aimed for improvement would be:

- Our current healthcare steps towards the best quality should be preserved without drawbacks.
- Tracking the predetermined milestones in the strategic document. Walking slowly is more justified than hurrying and changing the direction of the new wrong paths.
- The focus of improvement should be on the processes of internal "soft" aspects of the activity and not in the structure, in the drugs and in the technology acquired as it has been so far.
- The direction needs to be decentralized and based on multi-partnership. Systematic accountability and institutional autonomy should be installed. Participation and contribution of patients and citizens should be strengthened. And the provision of medical care and "decision making technology" at all levels of the system should not be based on subjective "expert" or administrative and political opinions, but on scientific evidence.
- Today's health system is offers multiple risks for patients. Minimizing risks, mistakes and damaging is urgent in order to avoid unsafe medical practices.
- Accreditation of quality in institutions, especially of hospitals, should not be done with campaign, without the preparation of its success in achieving the required standards. The culture of quality and security in our institutions is still very low. Leaders and staffs are not motivated.
- Accreditation should not produce fictitious certificates, but true, verified, deserved quality level. The Ministry of Health should not interfere and patronize the accreditation process. The Accreditation Council should be autonomous in decision-making and not under the tutelage of the Minister of Health. Otherwise, the QKCSA will have to become independent, as a self-financing public good.
- Actually, our public health institutions, as well as private ones, need to be urgently and compulsorily subject to the licensing process, meeting minimum mandatory standards to be allowed to function. Their condition makes them ineffective and risky, therefore unsafe for the life and health of citizens.
- The "Quality Label" (Accreditation) should be transformed into the key instrument of our healthcare market, in serving citizens' (customers) to give them the possibility to select and perform the best, safest, most cost-effective healthcare purchases for them.

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Focus On Health Or Illness?

Promotion and Prophylaxis Reports with Diagnostics and Measurement

Prof. Dr. Eduard Kakarriqi

The two "kingdoms" of medicine are **community medicine (or public health or preventive medicine**) and **clinical medicine**. While in **clinical medicine** the actor is the clinician and his client is an individual-patient, in the community medicine, he is an epidemiologist and his client is the community, that is - the population, *understood not as a numerator of only individuals-patients, but as the plural of all individuals community or population components.*

Clinical and community medicine differ essentially between them. While clinical medicine decides the diagnosis through anamnesis and physical examination of the individual, community medicine determines the diagnosis through estimation of population patterns. On the other hand, while clinical medicine treats (cures) the individual, community medicine uses programs for the treatment of specific population groups. These differences dictate the undertaking of efforts to achieve the equiliber (balance) between the community and the individual.

The basic question "The focus should be on health or the disease?" of this talk is a question, the answer to which would essentially embody questions such as "What is health and what does healthy mean " and "what is the disease and what does 'sick' mean related to the 'natural history of the disease'? "; "What is community medicine (or public health) and clinical medicine, and what is the relationship between them: controversy or interaction?"; "What is the 'gnosis' process in public health (community medicine) and clinical medicine related to etiology or causality ('diagnosis'), and prognosis?"; as well as "What is the prevention of the" natural history of the disease "and what is its relation to public health (community medicine) and clinical medicine?". These questions, which actually express the reports of health promotion and prophylaxis of community medicine, i.e public health, diagnosis and treatment (cure, treatment) of clinical medicine, and vice versa.

And it is precisely the concept of the term "disease" in the sense of '*sickness*', '*disease*' and '*illness*' (a single term in Albanian and in Neolithic languages versus three meaningful Anglo-Saxon terms), the concept of 'natural history of the disease ', the concept of' *continuum* 'of' '*disease*' 'disease in nature, and the concept of epidemiology and epidemiology ', those that would constitute the scientific foundation of the response to the baseline question and the underlying questions above.

Based on the **'natural history of the disease', disease '*sickness*'** represents the widest time span in my timing axis, which includes **'predicament or preface'** of 'sickness' plus '**disease**', which in turn includes **illness'**. "Disease" are anatomical (morphological), biochemical, physiological, and / or psychological disorders that are installed and developed in the human organism as a result of the action of the respective cause, i.e the ensemble of the respective risk factors (determinants) at a time $\mathbf{t_0}$ of 'natural disease history' in the time progression **t**, the realization of which was enabled by the 'social, psychological and economic predication' of placing the individual-patient in his or her surrounding environment. It is precisely 'disease' or 'marked targeting' (the most accurate term), which, in relation to etiology, pathogenesis, clinical picture or presentation, therapeutic management and prognosis, is included in the textbooks in clear-cut way. Meanwhile, disease '**illness**', a constituent part of 'disease' **t1** in the 'natural history of disease' is nothing but a clinical manifestation of the anatomic-biochemical-physiological-psychological "*marked disorder*" 'disease' at a time $\mathbf{t_1}$, with the cluster of clinical symptoms and clinical signs that, together with the relevant laboratory tests, reflect the 'case definition' of 'disease', on which is based the clinical '*diagnosis*', namely ' 'the modus operandi of the clinician.

But, we must always have in mind that, in nature, there is no 'sick' / 'not sick' division associated with every *'disease'*. **In nature, '*disease*' is displayed with a continuum of its severity**. The categorical dichotomic (binomial) division of the 'sick' and 'not sick' with the '*disease*' of interest has been done with convention (agreement) precisely by clinical medicine because without such division it could not operate. And, consequently, **'case definition'**, that is, the set of symptoms and clinical signs and relevant diagnostic tests for any 'disease' of the [*International Classification of Diseases* - **ICD**] is totally conventional. Without the **definition of a case**, **the diagnosis** at the $\mathbf{t_1}$ stage of the natural history of the disease can not be realized (= disease *'illness*' is clinically manifested). It is a crucial moment in clinical medicine, but of the same importance in the epidemiological perspective, because its quantitative deficiencies and its quality shortcomings directly affect the epidemiological surveillance data.

The most prominent illustration can be found **in the field of infectious diseases**, where the postulated "infection is different from the disease" i.e. "not

every infected gets sick". Specifically, the infection/disease ratio for any *'disease'* is never 1/1 (with the exception of measles only), but at least 2/1, to reach 5/1 or 20 / 1 (eg rubella), 100/1 (e.g cholera) or 1000/1 (e.g, paralytic polio), which means that for clinical medicine, an individual with the *'disease'* but without disease '*illness*' is not [ill], while for nature he is sick with the '*disease*'.

The situation is the same in chronic non-infectious diseases, neoplasmic diseases, mental illnesses, i.e. in all *'disease'*. Myocardial infarction has coronary heart disease on its substrate, but coronary heart disease itself does not necessarily end with myocardial infarction. Neoplasmic diseases (cancer) have on their substrate initial changes at the subcirculation level, but only in a proportion of cases these changes escalate at the cellular level. At each individual there is a dose of psychopathy, but he can never be labeled as a mentally ill person.

We emphasize that the most accurate term from scientific and generalization prespective would be **'health events'** (including 'health status') versus the **'disease'**. Accident, trauma or poisoning is a 'health event' and not a 'disease'. Death is absolutely a 'health event'. Which means that any 'disease' is essentially a 'health event', but not all 'health events' are 'diseases'. However, it is the term 'disease' that has virtually acquired the ownership use of "scientific divulgation".

'Gnosis' (= recognition) is essential in both the kingdoms of medicine, clinical medicine and community medicine or public health. It is **a category of probability** because it is based on an incomplete set of facts. And, when we talk about '*gnosis*', we mean all three of them - **'etiognosis', 'diagnosis', and 'prognosis'.** 'Diagnosis' is precisely the diagnosis (based on the definition of the case) of 'disease' at the moment of its 'disease' clinical manifestation at the moment t1 of the 'natural history of the disease'.We repeat the importance of its accuracy at the same moment for clinical medicine (accurate diagnosis for the individual who is a patient) and for community medicine (accurate epidemiological determination of the specific importance of the disease in interest of the population). **'Prognosis'** relates to the advancement of the disease from t1 to its end (recovery as the best option and death as the worst) at the right next moment so-called t2 of the 'natural history of the disease'. In clinical medicine, prognosis (prognosis) relates to treatment (ie medication), ie the quality of medical care, while in community medicine or public health, the spectrum of prognosis extends much more, because it implies the future advancement of the disease of interest in the community / population , a prediction that epidemiological research achieves. Meanwhile, **'etiognosis'** is almost the "property" of community medicine: one of the main directions of epidemiology is the study of causality, *the determination of the connection between cause and the interest about the disease, with the ultimate goal of intervention for control and prevention.*

The individual lives and develops his/ her own life activity in the micro, and macro-physical, chemical, biological, and social environment that surrounds him/her. This environment carries a vast and varied range of physical, chemical, biological, and social factors that act upon the individual by defining (determining) the risk of the installation of sickness (illness) in him/her. Meanwhile, even the individual carries his/her own specifics in the way of behaving, acting and living in the surrounding environment, which can also act as a determinant risk of the disease. We have the environmental or individual **risk factors or determinants,** as well as the person on which they operate. We also have the **medical implication** of this action, which is characterized by relevant organic (pat-morphologic), physiological (physical-pathological) and / or psychological (psychological) damages that at one time (hours, days, months or years) then become or are not (apparently) apparent, accessible through relevant clinical signs and symptoms.

Epidemiology, (biostatistics is implied as its inherent component), is the basic science of public health. Consequently, **as a community medicine science, epidemiology focuses precisely on the group-community-population** ignoring the peculiarities of the individual. It is based firstly on the fact that population sickness does not happen by chance, and secondly, that the disease has causal factors and preventive factors (precautionary) that can and should be identified through systematic research of different populations or groups of individuals within a population in different countries or at different times. Focused on the population and based on these two concepts, **epidemiology studies the disease (overall health outcomes) in the population regarding distribution, frequency and its risk determinants, and applies this study to control and prevent the disease.**

It is totally understandable the crucial role of epidemiology in community medicine, i.e. in the public health process, where it constitutes the scientific axis. But what is the role of epidemiology in clinical medicine?

In his clinical practice, the clinician faces the diagnosis and tries to manage the patient, and he historically thought that he basically practices **"the art and science of clinical medicine"**; ("Art" is based on such elements as our conviction, judgment, and intuition, which are unexplainable to us, while "science" in knowledge [*'gnosis'*], our logic and experience, as explainable elements). However, events and requirements in clinical practice, encountered at different times and in different situations, made the clinician aware of the need to apply in clinical practice of "**clinical oriented epidemiology"** or "**clinical epidemiology**", as a scientific basis for the interpretation of clinical phenomena, until the necessity of combining the clinical medicine with clinical epidemiology was finally fully understood. The recognition by the clinicians of the principles of epidemiology and the application of their beliefs, judgments and intuitions that make up the "art" of medicine, helps

the clinician realise in his clinical practice with the individual who is a patient essential improvement of the accuracy and efficiency of diagnosis and prognosis, as well as effectiveness of management. **The thesis that epidemiology constitutes the basic science of medical prevention was also extended to clinical medicine (curative) by arguing conclusively that epidemiology is "the art of medicine".**

Our natural condition is good health. But, "sickness" is felt, while good health is not felt at all", says an ancient Chinese proverb**.** Consequently, health has received less philosophical attention than the disease**.** The conceptual terrain in the case of health is a bit more complex than that of the disease. It is with this field that the current definition of health is related. **The World Health Organization** defines health as **"a state of complete physical, mental and social wellbeing, and not just a lack of disease, being a fundamental right of everyone (health equity)".** Although this WHO definition has been criticized because of the difficulty in defining and measuring the "full" quality of the "welfare", it essentially implies that **"health is a condition characterized by anatomical, physiological and psychological integrity of the individual; the ability of the individual to perform (to act in practice) values, moral norms and the role of family, community and society; the ability of the individual to cope with physical, biological, psychological and social stress; a sense of well-being; and, lastly, the freedom from the risk of the '*disease*' and premature death. "**

So health is a complex concept. It means that the same complexity represents the field of Public Health: Public Health is combined with various disciplines such as *biology, sociology, psychology, economy, agriculture and veterinary, education, culture, environmental protection,* etc., having as a basic method of operation *epidemiology* (where biostatistics is understood as an integral part of epidemiology). It means that the **medical model of health** cannot be understood disconnected from **the social model of health**: they intertwine rather than contrast.

Specifically, **the medical model of health** consists in: (i) the focus is that '*disease*' is considered the opposite of health; (ii) clinical medicine or the diagnosis and treatment of the sick individual is what implies tertiary prevention, ie quality of health care; and (iii) public health or community medicine is the one that carries out the community diagnosis and primary and secondary prevention, having in its essence the study of the cause (cause and effect connection) on the basis of cause (ensemble of factors or risk determinants) proximal in the sense of connection due to proximal-related disease. Whereas **the social model of health** consists in: (i) health is the result of the effects of all factors affecting the individual, the family or the community, through different ways; (ii) ie the study of causation extends to the the concept of causality chain ' - or in general a chain of causes now distal (each cause always considered as an ensemble of factors or risk determinants), where the outcome is the proximal cause directly related to illness or ill health.

The basic purposes of medicine are (i) to promot health, (ii) to maintain health, (iii) to restore (renewing) health when it is impaired, and (iv) to minimize bodily and/or mental suffering. These basic purposes are embedded (included) in the **term 'prevention'**. Prevention represents the essential moment of medical philosophy, synthetically expressed in the "**better prevent than treat**" postulate. The breadth of the concept of 'prevention' and directions of intervention for its realization, explains the variety of models, approaches and strategies of this process. Except that his scientific understanding requires as a condition *sine qua non:* (i) the founding of the prevention in the concept of 'natural disease history'; (ii) the founding of prevention in the broad concept of *causation*; and (iii) the founding of prevention in the concept of inclusiveness (individual-community-and the whole society as actors), guided by the philosophical dostojevskian principle "We are all responsible for everything" (Dostoyevsky).

Prevention would be defined as the actions/interventions undertaken to eradicate, eliminate or minimize the disease`s impact and disability, or if none of these would be possible, then the aim would be to delay the progress of the disease and disability. The concept of prevention is defined or best defined in the context of its traditional, primary, secondary, tertiary (and / or four-level) levels, as well as their predecessors - primordial prevention.

Primordial prevention consists on interventions, actions, measures taken to stop the appearance or development of risk factors (determinants), component of the consequential ensemble, these environmental (biological, physical, chemical) factors, economic, social, behaviour and lifestyle, etc. So, it is to be undertaken before the installation of the 'predicament' or 'preamble' phase (the initial part of the disease in the 'natural history of the disease'), represented by individual and community education and **is the sole object of public health or community medicine operation.**

Primary prevention would be defined as the action or intervention that is undertaken before the outbreak of the disease, ie prior to the onset of specific morphological, biological, physiological or psychological changes associated with the linked disease, and implies intervention in the stage of its pre-pathogenesis, with the aim of preventing the disease totally or to prevent the onset of the disease. **This operation is primarily a public health or community medicine operation, but does not exclude, in certain cases, clinical medicine,** and consists in "health promotion", namely in the health education, environmental modification, nutrition or nutrition interventions, changes of behaviour and lifestyle, as well as in "specific protection", namely, vaccination , chemoprophylaxis, use of nutrients and specific supplements, protection against occupational injuries, food safety, environmental pest control (air pollution, etc.).

Secondary prevention is defined as the action/intervention undertaken to stop the progression of disease to its development in clinical manifestation (= 'disease') with relevant clinical signs and symptoms and the relevant laboratory tests / tests (= 'random definition '). It consists on early diagnosis (screening tests) and adequate treatment and **is a operation subject to both public health or community medicine and clinical medicine interaction, in interaction between them.**

Tertiary prevention is carried out at that stage of the 'disease history' of the 'disease' when it has already become clinically manifest (= 'illness') and consists precisely in the quality of medical care to cure and to avoid or minimize disability, **by being presented only as a operation for clinical medicine.**

Regarding the **causality**, it's a complex matter that should always be considered: (i) biological and behaviour factors, (ii) environmental factors; (iii) immunological factors, (iv) nutritional factors (nutrition), (v) genetic factors, (vi) social, economic, and spiritual factors, and (vi) factors related to health and /or social services (availability, access, quality, etc.). Or, according to another kind of classification: (i) predisposing factors (such as age, gender, previous disease), (ii) enabling factors (such as income, nutrition, housing, availability of medical care), (iii) precipitating factors (such as exposure to a particular disease or to a certain toxic agent), and (iv) amplifier factors (such as repeated exposure, type of work, deprivation). Detailed elaboration on causality shows that: (i) it is never a single cause (= single causal component, determinant/risk factor alone) that, even if necessary, be capable of causing it alone the effect of the interest; (ii) the necessary cause is part of sufficient cause; (iii) sufficient cause is **a mist of causal necessary and unnecessary components,, that act together in the ensemble (= as a whole) and in interaction with one another.** But it's not just interaction. **Interaction is just a form.** While **the content is the concept of causation chain** mentioned above.

Public health or community medicine and clinical medicine are often seen as two completely different disciplinary frameworks, a misconception because the individual's health and community health are interrelated and interdependent. Which implies that these two different disciplinary frameworks are such only in a first and superficial view, while fundamentally they are but two compartments of the same disciplinary framework - the kingdom of medicine, which are interrelated between them and mutually interdependent . Public health and clinical approach prove this statement.

The public health approach, in its ideal concept, deals with communities - community health. This approach emphasizes primordial, primary, and secondary prevention. At community level, the difference between prevention and treatment may not be clear. The scope of public health is much broader than that of a clinical approach, because it involves the research of 'etiognosis/aetiology', the research

of causality, which is unlikely to be accomplished at the level of an independent patient in clinical medicine.

Meanwhile, **clinical approach** deals with individuals, families. The service provider's mission (= clinician) is to do the best for the patient. Although criticized for an insufficient attention to prevention, clinical medicine is not only inherently related to the treatment (treatment, cure) of the patient, but also to the prevention. In fact, in recent decades, time and resources devoted to prevention of the 'disease' have been significantly increased, especially in the area of secondary prevention (screening). At times, clinicians have emphasise the importance of the primary prevention. On the other hand, it is true that the inner, intrinsic of clinical approach is the focus on the individual, or sometimes even the family, regarding the diagnosis and therapeutic intervention, with the aim of realizing tertiary prevention, ie healing (though essentially without restitutio ad integrum) but meanwhile, education and health promotion to the patient and also to his/her family environment remains the other side of the medal of modus operandi of every clinician.

In conclusion, let's hope that all of the above elaboration, with the emphasis in the last part of it, has answered the basic question of this paper "Focus on health or illness?".

Diagnoses and Surgical Management. (Personal Case)

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Congenital posterior urethral-perinal fistula is a rare anomaly of which there have been reported only one case to date. This report outline the simple clinical presentation, diagnosis and simple technique surgical management. Congenital posterior urethral-perineal fistula is a rare anomaly. This is a rare case in the world literature. There are reported only six cases since 1964. Dr. William C. Brown, Dillon, Heusele has reported one case (diagnosis and new surgical technique). Other authors have reported rare cases: Le Duc has reported one instance ofan urethral-rectal fistula in the absence of any anorectal abnormality. Out of the 7 cases previously reported one is actually an urethral scrotal fistula but it is included since it has a similar embrylogic origin to the rest of the series.

The embrylogic basis for these anomalies is unclear. However two main theories have been proposed. Olbourne believes that if delay occurs in the descent of the anorectal septum at four weeks of gestation, then a fistula could result between the inferioraspect of the rectum and the primitive urogenital sinus. This may occur along the distance between entrance of the mesonephricduct which is the area of the prostatic urethrea and the urogenital ostium which will be the future area of the bulbons urethrae. Later dissolution of the anal membrane leaves the fistula at the site of the anal rectal junction. If the urethral folds start their fusion too far forward then a fistula may result.

In contrast to this I believe that the lateral ridges of the urorectal septum grow. into the cloaca and divide it as they meet in the midline. A defect in this midline joining would certainly account for fistula.

The anal plate which forms separately forces the opening to develop outside the anal sphincter and anus. This is important for surgical management. Woodhead

attempted of the fistula by endoscopically fulgurating the opening in the urethra; Elder's technique for correction was a combination of open excision and technique of fulguration which has provided outcome at six months.

A six year old boy from Southern part of Albania visited at Clinic of Urology in Tirana. His father explained that his child has dribbling urine from perineum with voiding. Physical examination in the clinic revealed no anorectal malformations. His urinary stream was normal in force and calibre. (The child's long miction was points-points urinefrom perineal fistula). The biochemical analysis were normal. The patent's urinalysis and urine culture were within the normal limits.

U.I.V. The kidneys were normally functioning and so were the ureter and bladder. Avoiding cystourethrogram revealed a prominent posterior urethral between prostate and bladden neck was fistula. At this study it was not yet know whether the fistula opened into the rectum or opened into the perineum. For this reason the child was scheduled for uretroscopy and cystoscopy-chomocystoskopy. This examination is conducted under anaesthesia with ketamini. Before the operation we put in fistula meatus a cutaneopennealis catheter uretheral Nr. 4Ch.

During urethroscopy urethre at two o'clock we observed in the posterior urethral wall above veromontary, on the left side position and the catheter uretheral looked inside in urether. The diagnosis is clear. Fistula urethro-perineal-cutanea.

The position Trendelenburg with incision median suprapubic prepareted blodder looked one cordon fibrous 2 cm with catheter uretheral inside. This cordon was coming between left lob prostate in apex and bladden neck.

We made excision and put 2 suture with vicrol 3,0 in the uretrae outside. In the urethare and bladder put one Foley catheter Nr. 12 ch and removed it after seven days. The child' went home after nine days. After six months or one year the child was in a good health. The congenital urethrae perianal is closed. The congenital urethral-cutaneo-perianal is a rare case. The approach to repair of posterior urethral-cutaneo-peranal congenital fistula with incision suprapubik median in Tredelenburg position with sunture and excision ligation cordon fibrotic is very well for me. (this is good result).

In view of the success of this procedure we believe that endoscopy (1) for defining the diagnosis and operation is very efficient. The child stays 10 days in hospital and enjoys good health.

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Preeclampsia: The importance in our country

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Preeclampsia (PE) continues to be a serious complication of pregnancy, full of unknown things. It remains a pathology with unpredictable beginning and performance for both the mother and her child. However, significant advances have been made regarding the management and treatment of this disease. Due to the fact that the ultimate treatment of preeclampsia is the termination of pregnancy, the most important step in managing this disease remains the progress of the last twenty years in treating prematurely born neonates. In this context, the treatment of preeclampsia has the future in front of it, so with the improvement of results in the perinatal service, even in countries that are now somewhat behind.

In order to judge what weight preeclampsia has in the perinatal service we may mention: 10 to 15% of mother's deaths occur due to the preeclampsia;

This means that every year around the world, because of this intercourse, they lose 50,000 to 60,000 patients. As time passes, the preeclampsia frequency remains the same, complicating 5-7% of pregnant women. On the other hand, one in ten pregnant women passes a hypertensive episode during the pregnancy.

Preeclampsia is a medical cause for premature infants, a part of these children are also inappropriately-fed during pregnancy and show a retardation of physical development. In international literature, preeclampsia causes 10 to 25% of premature births. The trend over the years shows an increase of this figure, because prenatal service tends to protect the mother more, relying on the increased survival potential of newborns.

Preeclampsia is a high-risk disease, mainly related to the necessary examination and the cost of service to the newborn. However, investments made are less likely to prevent this disease or mitigate its progress. Prevention is still an investment of the future.

Preeclampsia is "changing its face" over the years. We do not see classic forms, like high albuminuria or exemplary edema, but the implications now affect more and more the melanoma, hemopoetic or coagulation system.

The preeclampsia definition remains more closely related to high blood pressure figures. The diagnosis for this disease is 140 systolic and 90 diastolic. We should pay attention to measurement techniques, because the patient should be in a state of well-being. The voltage should be measured 2 times every 4 hours. Proteinuria is assessed in favor of the diagnosis for quantities greater than 300 grams / 24 hours. It is accepted in favor of diagnosis also the fast weight gain: 300 mg / 24 hours.

It remains acceptable that preeclampsia is considered to be of severe form when it affects the function of the larynx, hepatic, pulmonary, cerebral and ultimately neuronal convulsions. Today in international literature it is acknowledged, that lack of albuminuria does not persist in diagnosis. In 10 patients with preeclampsia, there are no traces of albuminuria.

The level of proteinuria over 5-6 grams / 24 hours is no longer a criterion to distinguish between severe and light preeclampsia forms. Treatment of preeclampsia with magnesium sulphate is not recommended in any case. This drug should be used in specific cases such as: patients with history of several preeclampsia activity or those with symptomatology of the central nervous system. Preeclampsia often affects patients that have a certain risk factor. Among other things, when the mother is over 40 years old, the first pregnancy, the pregnancy from a new partner or the family preeclampsia history. Preeclampsia often occurs in patients who have given birth to low wight children, who have become fetomorous or who have become dyslexic in the placenta. Thrombophilia and more burdens are also included in the mother's dangers. Diabetes is a metabolic disease that is often associated with this complication. This happens more often in patients suffering from diabetic vasculopathy, as shown in the table below:

Piable classification according to white and preeclampsia

Class DM	% e Preeclamptic risks
Class B	1 1%
Class C	22%
Class D	21%
Class R	36%

From this table, we assess that the risk for preeclampsia triples for patients who are in the R class of the White classification.

In the international literature, attention is drawn to the risk that preeclampsia is repeated in the second pregnancy. This is related to the age when preeclampsia

has started the first time. If preeclampsia has started before the 27th week then 50% of patients will repeat these complications. Conversely, when preeclampsia begins after the week 37 in the first pregnancy, only one in five of the patients will be affected in the next pregnancy. These figures should be taken into account for preventative treatment or near follow-up of the risk-taking pregnancies.

Some of the traditional forms of preeclampsia treatment are now considered ineffective. For example, limiting salt does not lessen the risk. Bed regime offers possible, particularly thrombolytic, effects without affecting the softening of preeclampsia. The prescription of antioxidants does not reduce the risk of preeclampsia. The decision on when to stop pregnancy is the cornerstone of success or in dealing with this complication. There are a wide-ranging debates between the risk of premature mortality in terms of quality of life and risk of death. Because of this, they are more important than other motherhood complications, such as severe hyper blood pressure, placenta or "HELLP" syndrome.

Neonatal care should be included in the fetal health assessment. The more approaching system for fetal health is the biophysical profile. The mother should be aware of her situation by self-assessing the fetal movements.

The biophysical profile will be carefully evaluated in all its components, in order to have the result as closely as possible to the reality of fetal health. The fifth or sixth biophysical profile components can be used for:

a. Acute fetal condition (NST, fetal respiratory movements);
b. Long-term chronic fetal condition (amount of amnial fluid, placental maturation rate).

Fetal growth evaluation should be taken in consideration as follows:

A. It is recommended that the ultrasound be performed by the same physician and ultrasound apparatus.
B. Retardation in fetal growth should be evaluated symmetrically, asymmetrically or mixed;
C. Early retardation in fetal growth, the more likely it is its genetic origin. With the growth of pregnancy, genetic origin is almost excluded and emerge in the foreground of causes such as preeclampsia or infection;
D. Must be differentiated between SGA and IUGR. Both of these forms of lack of fetal growth will provide babies with small or premature weight. SGA is a constant growth baby, but describes the trajectory at the end of the normal fetal growth area. IUGR is a normal growth baby up to a certain period of pregnancy and subsequently decreases growth, while also inhibiting it and consequently emerging from the normal fetal growth

area. This happens when there are complications and the first place for this incurrence is occupied by preeclampsia. Many advanced obstetric services, recommend that the growth area of the fetal population be renewed once a year or two years. This due to the evidence that fetal growth can change significantly in a few years. Fetal growth over the norm may be due to a complication of pregnancy, where in the first place is diabetes, mainly that induced by pregnancy. Regular measurement of arterial pressure is a non-invasive, classical and easily feasible form of observation of the preeclampsia performance.

Assessment through proteinuria of renal glomerulus damage can be done in some forms. What is considered most useful is the amount of urine for 24 hours and the protein eliminated for the same period. The patient is advised that the diet and especially the amount of fluids taken should not change 24 hours before the diuretic evaluation. The amount of urine along with the weight of the patient is the traditional way, but still valid as a precursor to the possible deterioration of mother and child health. The advice is:

- weigh the patient every day,
- measure the amount of urine,
- measure the protuberance of the kidney every 24 hours and the arterial blood pressure 2-4 times per day.

Preeclampsia in most cases can be treated ambulatory. Patients need no absolute bed regime, should not stop the salt and you shouldn't recommend medications for arterial blood pressure up to 160/90 figures. Medication treatment should be started at figures above this level and can be continued out patiently.

In medicament treatment should be present the fact that:

a. Treatment should be started with a medication. If for some days we do not accomplish the goal, another should be added;
b. Blood pressure should not be reduced immediately, but gradually;
c. Blood pressure should be maintained between the figures 130-140 for the systolic. Adhering to these principles primarily protects the health and the fetal life, from a major risk of placental hypovolemia and fetal hypoxia.

In cases where arterial tension is rebellious or manifests pre-stroke complications, patients should be hospitalized. Magnesium should be chosen the prevention and treatment of the eclipse crisis. The first time usage was done in 1906 and over the

years this drug carries the country deserving of this pathology. Magnesium should not be used in all preeclampsia patients, but only in complicated cases, especially for patients with cerebral symptoms such as headache, appearance, dizziness, vomiting and vomiting. Magnesium is the first line medication selected for the treatment of preeclampsia, from the beginning up to 24 hours postpartum.

The confrontation with preeclampsia requires a group work of health care workers from the family doctor, midwife, and obstetrician and in some cases nephrologists, cardiologists, neurologists and others.

Preeclampsia In SUOGJ Mbreteresha Geraldine Hospital– Observation

Every year there are hospitalized 120-370 cases of preeclampsia in the SUOGJ "Mbreteresha Geraldine" hospital. Almost half of these cases are from the city of Tirana, although the city's population is bigger than the village. It's been around 20 years that in every three patients, one comes from outside Tirana and among them are the most complicated patients.

TABLE I. Preeclampsia distribution Tirana / village / town.

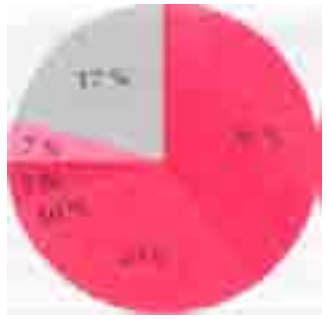
Year	Total	Tirana	%	Rural	%	District	%
1995	277	164	59	76	27	37	13
							8
1997	219	78	36	85	39	56	26
1998	164	71	43	53	32	40	24
1999	130	58	45	45	35	27	21
2000	123	63	51	34	28	26	21
2001	103	62	60	28	27	13	13
2002	132	44	33	43	33	45	34
2003	173	56	32	56	32	61	35
2004	129	42	33	56	43	31	24
2005	369	130	35	116	31	123	33
2006	195	69	35	74	38	52	27
2007	216	95	44	83	38	38	18
						49	21
2009	192	72	38	82	43	38	20
2010	227	83	37	77	34	67	30

2011	234	92	39	73	31	69	29
2012	206	75	36	57	28	74	36
			29				

National mortality in the SUOGJ "Mbreteresha Geraldine" hospital in the last 20 years it has had constant decrease. From 1995-2014 we have lost 30 patients in this hospital, of whom 1/3 because of the preeclampsia and in the second place is hemorrhage.

GRAF 1. Local mortality (1995 – 2014)

- Preeclampsia Hemorrhage
- Heart disease
- IRA
- Other Leucosis



GRAF 2. Local mortality (where do this patients come from)

It's been years since we started involving the patient and spouse in decision-making. This desire and obligation of doctors in our hospital is also improved because of the following reasons:

- cultural growth of the population;
- the ability of the population to be informed,
- the opportunity to choose the doctor and service he wants, public or private healthcare system.

In the future, this trend will have the necessary ground to be furtherly improved.

Preeclampsia remains a disease which requires many actresses and factors to improve the results in its treatment. At the local level, it would also be beneficial for the treatment of the preeclampsia to organize a reference system.

In this way, they would find a more accurate and more relevant response to any obstetric service, in the following questions:

A. Which type of patients do we have to treat? (Every service should be determined based on the results and the possibilities it has, to what extent a patient should be treated by him. This assessment should be made for the mother, but mainly for the future of fetal maternity.
B. Each service should determine what level of complications a pregnant patient should be transferred.
C. The third step in the referral system is where to transfer a patient. Generally, transference is performed in a parallel or higher level service.
D. Finally, how should transportation be performed and whose responsibility is it. This transfer is related to the selection of the staff that will accompany the patient and the means of transport. In a preliminary agreement, transportation may be the responsibility of the hospital where the patient or the hospital he/she will go to. Here is not excluded the possibility of personal car transports.

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Coexistence of Psychiatric Symptoms and Chiari Type I Malformation - A Case Report

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Abstract

Introduction: *Chiari type I malformation has been described infrequently in association with defined psychiatric syndromes.* ***Method:*** *There is a limited literature about obsessions in comorbidity with Chiari malformation. It is described a case of an adolescent with obsessive compulsive disorder and Chiari I malformation and it is reviewed the literature regarding Chiari I malformation and psychiatric disorders. The child came to the attention of child psychiatrist at the age of 7 years old when he manifested developmental delay and various kinds of behavioral symptoms. He was followed up at the age of fifteen when he developed obsessions and upon MRI was identified a Chiari malformation type I.* ***Discussion:*** *This paper discusses the likely under recognized co-occurrence of Chiari malformation and psychiatric symptoms. Currently available data from case reports associate Chiari I malformation with a variability of psychiatric symptoms: autism spectrum disorder, bipolar disorder, seizures, developmental delay, generalized anxiety disorder, panic attacks, Tourette's syndrome, OCD, ADHD, cognitive disorder NOS and psychosis. It is concluded that mixed psychiatric symptoms and developmental delay might be a more common finding in comorbidity with Arnold Chiari type I malformation.*

Keywords*: case report; obsessions; Arnold Chiari type I malformation; coexistence*

Introduction

Various types of congenital lesion are associated with neuropsychological impairments and behavioral changes (Riva et al., 2011). Chiari I malformations are poorly understood and in need of much greater systematic investigation that has been the case up until now. The brain regions involved in this condition are highly sensitive and can easily contribute to deficits in the development of self-regulation or executive function (Koziol et al., 2013).

This paper discusses the co-occurrence of Chiari type I malformation and psychiatric symptoms. Arnold Chiari malformation is characterized by four subtypes with different degrees of herniation of the cerebellar structures through the foramen magnum. The Chiari I malformation is defined as herniation of the cerebellar tonsils through the foramen magnum (at least 3 to 5 mm). In the type I malformation there is a caudal descent of the cerebellar tonsils only, while in type II the cerebellar vermis and possibly the fourth ventricle and pons are involved (Chisholm et al., 1993). Chiari III and IV malformations are rare. Type III is characterized by an encephalocele, the descent of both cerebellum and brainstem into the spine and internal sac and type IV is associated with cerebellar atrophy. Although Chiari I malformation is considered to derive from a mesodermal disorder resulting in underdevelopment of the posterior fossa relative to its content, evidence for a possible heterogeneous etiology also has been reported (Grosso et al., 2001).

The cerebellum was once believed to be almost exclusively involved in coordinated voluntary movement. Currently the role of cerebellum in the modulation of the higher cognitive functions is becoming increasingly clear. Numerous studies on adults have confirmed that the cerebellum has a role in processing higher brain functions as intelligence; language; higher social functions; perceptual, language-related; visual-spatial and cognitive & affective functions, procedural and declarative memory and evidence of this role has emerged more recently in developmental age as well. In Chiari malformation, the cerebellar structures are squeezed and crowded inside the posterior fossa and along the time this could generate various kinds of cognitive and behavioral disorders (Riva et al. 2011). Therefore it is hypothesized that the compression of the structure in the posterior fossa could negatively affect how these cerebellar structures function. Chiari malformation can also cause cortical deficit. Chiari malformations cause obstruction to cerebrospinal fluid flow in the posterior fossa and foramen magnum that elevates cranial pressure and this can cause hydrocephaly. It can damage neural tissue by ischemic and mechanical forces. Gonzales and Campa-Santamarina (2018) provided evidence of possible deficits or anomalies in the cognitive executive functions of patients with Chiari type I. They were affected in the processes of inhibition and self-control as well as in attention

capacity and maintaining a course of thought and action. According to Koziol and Barker (2013) patients with Chiari I have behavioral disorders with impairments in executive functions, verbal fluency, abstract thinking and working memory.

Method

There is a limited literature about psychiatric symptoms with Chiari malformation, and to my knowledge two cases have been reported of obsessions in association with this brain anomaly (Tubbs et al., 2003; Zayman and Erbay, 2016). This paper discusses the likely under recognized co-occurrence of Chiari I malformation and psychiatric symptoms. It is described the case of a child who has obsessions and Chiari I malformation and the review of the literature regarding Chiari I malformation & other psychiatric disorders.

Case Description

M. is a fifteen years old male who lives with both parents. He is the only child in the family. Pregnancy and birth were unremarkable, except a subcutaneous head hematoma.

Mother recalled that during infancy M. had sleep disturbances (late falling asleep, 1-2 a.m. during the first three years of life). When M. started walking he was a hyperactive toddler, running without direction. As a toddler he was inpatient and sometimes aggressive in kindergarten. He also had language delay and started to talk at about 5 years old.

The child came to the attention of child psychiatrist at the age of seven years old, when he manifested developmental delay and various kinds of behavioral symptoms. The teacher at primary school noted that M. was easily distracted by noises and showed academic difficulties. He spoked clearly, except some pronunciation difficulties related to specific consonants. He could read, but had difficulty to retell, which might suggest memory problems. He showed poor math abilities. M. was consulted by the school psychologist. It was administered Son-R test which reported mental retardation (chronological age of 7 years and 8 months, mental age 6 years old). M. displayed some autistic features. In respect to social interaction he interacted with peers, but became easily nervous and sometimes was aggressive toward them. M. didn't obey to the rules of play and insisted that other children should met his rules, so he couldn't enjoy the play and as the consequence it was easily interrupted. M. worn shoes on the opposite foot until he was 11 years old. He had short eye contact span and was often inpatient. M. was referred to the child psychiatrist who suspected hyperactivity. At that time M.

was also showing some unusual interest which could have been autistic traits or precursor of obsessive symptoms. He liked very much the topic war and soldiers, played with soldier figures and while having a conversation with children liked to switch inappropriately the topic of the conversation to war and soldiers. Parents attributed this unusual interest to the TV films with war themes he saw, despite they noticed it was incoherent.

Teenager years marked new and more severe symptoms. Obsessive compulsive disorder symptoms started when he was 12 years old and persisted six years later. The main type of obsessive thoughts were aggressive, followed by sexual ones which were hardly explored. M. at the age of fifteen had thoughts of harming with a knife the peers who bully him. He still was verbally aggressive to peers who bullied him. M. also had thoughts about harming his parents: with a knife, burning them or causing accidents (for example he had the urge to move the step while the father was climbing in the terrace, so he could fall). He felt bad about these ideas for his loved parents and tried to resist his thoughts – kept himself busy, when he was close to a knife he moved backwards or asked his mother to take it away. The mother described her son as childish, immature and had a feeling like she was talking with a child despite him being an adolescent.

The child was referred to several doctors following a care path from the school social worker and school psychologist at the age of 7 years old to the child psychiatrist. At the age of 13 years old was performed a brain Magnetic resonance imaging that identified a type I Chiari malformation (cerebellar tonsils were 7 mm under the foramen magnum).

Family history was positive for his maternal ancestry, with an anxiety disorder in his mother, a mood disorder in his maternal grandmother, his uncle has been hospitalized for schizophrenia and two cousins (uncle's daughter and aunt's son) also suffered mental problems.

M. received over more than 10 years several prescriptions of Concerta at the age of 7 years and a half, Atomoxetine and Risperidal with no improvement. At the age of 15 years old was prescribed sertraline and M. showed moderate improvement. His Obsessive compulsive disorder continued so far at the age of 18 years old. He did not underwent surgery for Chiari I malformation.

Literature review

Association of Chiari I malformation with psychiatric syndromes

Chiari type I malformation has been described infrequently in association with defined psychiatric syndromes. There are some case reports that highlight the

association of Arnold–Chiari malformation (ACM) with psychiatric symptoms. Bakim et al. (2013) assessed the association between Arnold Chiari malformation and psychiatric symptoms and risk factors in terms of psychiatric morbidity. They found out that about 43.8% of the patients had a psychiatric disorder. There are various reports of mental symptoms in children and adolescents associated with Chiari Malformation type I ranging from developmental delay to a more specific disorder, during the last 20 years (Figure 1).

FIGURE 1: Association of Arnold Chiari I malformation & psychiatric syndromes

Brill et al. (1997) reported on 11 children with Chiari I malformation who presented with seizures and developmental delay in motor or language function with or without autistic features. An association between Chiari I malformation and seizures or neurodevelopmental deficits or both had not been previously reported to their knowledge up to that time. They believed that Chiari I malformation should not be considered an incidental finding in these patients, but may be a marker for subtle cerebral dysgenesis. Chiari I and II malformations may constitute a complex but continuous spectrum, related to the timing and severity of a shared underlying embryologic mechanism. Autism cases were also bought into attention by Jayarao et al. (2015), who reported on 9 children with Autism spectrum disorder and Chiari

I malformation in a sample of 125 children. They stated that Chiari I malformation and Autism Spectrum Disorder may coexist and be under recognized.

Grosso et al. (2001) aimed to elucidate the relationship between Chiari I malformation and mental retardation, speech delay, and epilepsy to consider a possible specific pathogenetic background. They had a sample of 35 patients with Chiari type I malformation. Out of them nine patients (four boys and five girls) were affected by mental retardation, speech delay and epilepsy. They argued that the association of Chiari I malformation with epilepsy, speech delay, and mental retardation may not be a mere incidental finding but may be a marker for a different pathogenetic background.

Zeegers et al. (2006) evaluated the prevalence of brain abnormalities (MR study) in a group of 45 young children (mean age 43 months, SD=12, four females) with developmental disorders, specifically including children that came to the attention of a child psychiatrist before the age of 3 years. They found out about 50% intracranial abnormalities in this sample (22 children). One female was diagnosed with a Chiari I malformation. They argued that radiological findings do not contribute to the diagnosis of developmental disorders. However, young children with developmental disorders may not be able to express discomfort associated with brain abnormalities, such as a Chiari I malformation.

Riva et al. (2011) studied 35 children (mean age 6 and half years) of whom 20 children had associated conditions and symptoms and 15 children represented the control group. They had two cases with Chiari malformation and interestingly reported their behavioral changes after surgery. One case was that of a 5 year old boy with a history of language delay and behavioral issues. The child underwent surgery at the age of 3 and a 3 months. After surgery the child language improved, he showed increase in the verbal IQ measured by the Test of language assessment. On the other hand his behavioral issues which included behavioral difficulties, attentional and motor instability became worse than before surgery. The second case was that of a 15 year old girl who underwent surgery at 11 years. The girl's pattern of recovery took an opposite course. Before surgery her behavior had been characterized by mild hyperactivity and she was easily distracted, but after decompression she behaved normally. While her attentional instability improved considerably, her language skills became worse after surgery.

There are also several single case reports. For example Tubbs et al. (2003) described a 13 year old adolescent with Chiari I malformation and cutis marmorata telangiectatica congenita, who also showed Tourette's syndrome, obsessive-compulsive disorder, and seizures. Ciprero et al. (2005) reported three children with Kabuki syndrome who had Chiari I malformation. Kabuki (Niikawa-Kuroki) syndrome is associated with a characteristic facial appearance, cleft palate, congenital heart defects, and developmental delay. A more detailed

review of studies and cases with Chiari I malformation and psychiatric disorders is summarized in Table 1 as follows:

TABLE 1: Literature cases with Chiari I malformation and psychiatric disorders

Psychiatric disorders	Author	Year	Sample	Cases with co-occurrence of Chiari I and psychiatric disorders
Obsessive-compulsive disorder	Zayman and Erbay	2016		case report
Schizophrenia, obsessive ideas	Di Genova et al.	2015		case report
Autism spectrum disorder	Jayarao M. et al.	2015	n=125	n=9
Psychotic disorder, depersonalization/ derealization, major neurocognitive disorder	Hoederath L. et al.	2014		case report
Psychiatric disorder (various)	Bakim B. et al.	2013	n=16	n=7
Psychosis and panic attack disorder	Casale A. et al.	2012		case report
Language delay, mild hyperactivity and attentional instability	Riva D. et al.	2011	n=35	two case reports
Panic disorder and agoraphobia	Kuloglu M. et al.	2009		case report
ADHD, OCD and bipolar disorder	Koziol L. F. & Budding D. E.	2009		case report
Generalized anxiety disorder	Caykoylu A. et al.	2008		case report
Cognitive Disorder NOS	Pearce M. et al.	2006		case report
Developmental disorders	Zeegers M. et al.	2006	n=45	n=1
Psychotic events and epilepsy	Ilanković N. N. et al.	2006		case report
Kabuki syndrome (developmental delay)	Ciprero KL. et al.	2005		n=3
Tourette's syndrome, OCD and seizures	Tubbs RS et al.	2003		case report
Mental retardation, speech delay, and epilepsy	Grosso S. et al.	2001	n=35	n=9
Seizures and developmental delay in motor or language function with or without autistic features	Brill C. B. et al.	1997		n=11
Panic disorder with agarophobia	Chisholm et al.	1993		case report

Discussion And Conclusions

The literature review on co-occurrence of Chiari malformation and psychiatric symptoms shows that some studies report this association, but currently data

remain inconclusive. This case illustrates and support comorbidity of psychiatric symptoms and Chiari I malformation. However, prospective longitudinal studies on sizable series will be needed to ascertain whether and to what degree Chiari malformations may negatively affect mental functioning in developmental age.

The literature data shows a variability of psychiatric symptoms associated with Chiari I malformation, not merely a specific clinical picture. This case represent several psychiatric symptoms in a patient who has Arnold type I malformation, more prominent ones are obsessions, autistic features and developmental delay. The majority of cases show that Chiari malformation and anxiety disorder can exist together. To date, two case reports described the association with obsessions, but there were more cases reports which described the association with developmental delay and mixed psychiatric symptoms. It is concluded that mixed psychiatric symptoms and developmental delay as a common one might be a more common finding in comorbidity with Arnold Chiari type I malformation.

In the case described here it is reported the association, not the cause. It is possible that in this patient both conditions are separate unrelated pathological events. On the other hand, Chiari type I malformation could have made the patient susceptible to psychiatric symptoms. One might speculate that the neuroanatomical anomaly led to symptoms in a patient who was predisposed. A family history of psychiatric disorders suggests a genetic predisposition in this case. However none of the family members was investigated for brain anomalies. Increasing evidence suggests that in some families, there are strong genetic contributors to the development of Chiari malformation type I (Szewka et al., 2006). This case highlight the importance of not focusing only on psychiatric aspects, but considering a neuro-radiological investigation which can detect a lesion that might otherwise go undetected. It is important to consider an eventual organic etiology in a child while challenging a clinical picture with mixed symptomatology and developmental delay.

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Imatinib in Chronic myeloid leukemia in Albanian patients, overview

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Abstract

Imatinib was the first signal transduction inhibitor used in a clinical practice. Imatinib prevents the BCR-ABL protein from playing its role in the oncogenic pathway in chronic myeloid leukemia (CML). Imatinib directly inhibits tyrosine kinase activity. Imatinib binds to BCR-ABL kinase domain. As a result, the transmission of proliferative signals to the nucleus is blocked and leukemic cell apoptosis is induced. The FDA has approved imatinib as first-line treatment for newly diagnosed CML in December 2002 following an International Randomized Study (IRIS), who started in June 2000(1).Results from this study show the effectiveness of imatinib and its superiority with respect to the rates of complete hematological response (CHR), major and complete cytogenetic response (MCyR, CCyR). Patients randomized to imatinib arm at 8 – year data cut off continue to have a durable hematologic and cytogenetic responses, low progression to AP or BC, and remarkable survival outcomes. An overall survival (OS) rate is 85% for patients receiving imatinib (93% when only CML-related deaths and those prior to stem cell transplantation are considered).The very first patient treated with Imatinib for the first time was in 2002 in a 69 years old patient which is still alive and well today .

Introduction

Chronic myeloid leukemia accounts for 15% of all leukemia in adults. The incidence of this type of leukemia in adults in Albania is 0.6-1.1/100 000. On figure 3 we have a picture of the incidence of CML in Albania according to the cities.

Imatinib was the first signal transduction inhibitor (STI), used in a clinical practice. It prevents a BCR-ABL protein from playing its role in the oncogenic pathway in chronic myeloid leukemia (CML). Imatinib directly inhibits the tyrosine kinase activity, which results in the modification of the function of various genes involved in the control of the cell cycle, cell adhesion, cytoskeleton organization and finally in the apoptotic death of Ph(+) cells(2).

Imatinib binds to BCR-ABL kinase domain, which is in an inactive conformation in a pocket reserved for the ATP binding site, thus preventing the transfer of a phosphate group to tyrosine on the protein substrate and the subsequent activation of phosphorylated protein. As the result, the transmission of proliferative signals to the nucleus is blocked and leukemic cell apoptosis is induced (3). Imatinib exhibits high level of selectivity.

Imatinib in clinicals trials

The first phase I trial was initiated in June 1998 and enrolled patients diagnosed with CML in chronic phase (CP) who were resistant to or intolerant of interferon alpha (IFN alpha). Almost all patients (98%) treated with at least 300 mg imatinib per day achieved complete hematological response (CHR)(4).

All this results, made it possible to start phase two trial just one year later, three international multicenter phase II trials were initiated in 1999(5). The study population included patients with CML in myeloid BC, relapsed Ph+ALL, CML in AP, and patients who were resistant to IFN alpha. Ninety five percent of all patients achieved CHR; CCyR and MCyR were seen in 41% and 60% of patients respectively, and the progression-free survival rate at 18 months was 89%.

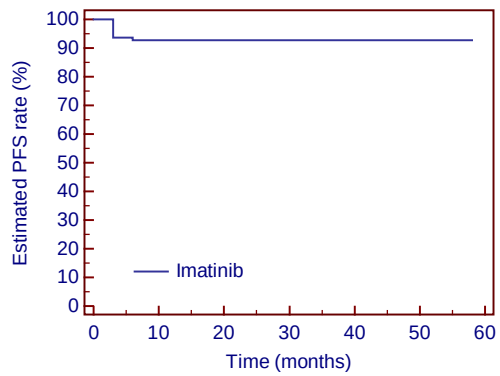
An International Randomized Study of Interferon and STI571 (IRIS) comparing imatinib at a single daily dose 400 mg to IFN alpha plus cytarabine in newly diagnosed patients with CML in CP was initiated in June 2000(6). Results from this study show the effectiveness of imatinib and its superiority with respect to the rates of CHR, MCyR and CCyR. Based on these results, the FDA has approved imatinib as first-line treatment for newly diagnosed CML in December 2002. The achievement of an MMR continued to be associated with an improved outcome at 5-year, with estimated rates without progression to AP/BC of 100%, 98%, and

87% for patients achieving CCyR and MMR, CCyR without MMR, and no CCyR, respectively. The best observed MMR rate with the 8-year follow-up of IRIS trial is 86%. The results of imatinib first line based on analysis of data derived from clinical trials and registries have been reported in the last three years by several groups (PETHEMA, SPIRIT, GIMEMA, CAMELIA, German Study Group IV, and others.). The rates of CCyR achieved after one year of therapy with imatinib at standard dose ranged from 49% to 77%, and the proportion of patients who achieved MMR after one year ranged between 18% and 58%.

Following this we made a retrospective study in our Albanian patients diagnosed with Chronic myeloid leukemia in chronic phase CP treated with Imatinib on first line (7).This is a comprehensive retrospective analysis of first-line CP CML pts treated with IM first-line 400 mg daily since diagnosis and followed in the Hematology clinic at the University Hospital Center 'Mother Teresa' between 2003 and 2008 a time that all our CML patients were introduced to Imatinib as the first line therapy. All the patients who are alive have given their agreement for participation in this retrospective analysis. Pts have been analyzed in intention-to-treat, CML was defined according to ELN criteria [CP, accelerated phase (AP) and blast crises (BC)], Sokal, Euro and EUTOS scores have been calculated at the diagnosis. Cytogenetic and molecular responses could not be monitored in our patients back at that time. Overall survival (OS) was calculated from the date of IM initiation until death at any time and for any reason; until progression to AP or BC at any time for progression-free survival (PFS); and until death, progression to AP or BC, failure on IM or IM treatment discontinuation for any cause including treatment-free remission (TFR).

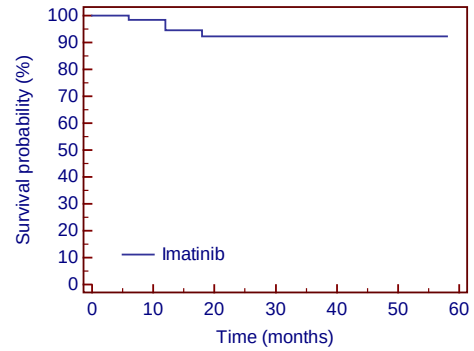
At time of analysis, 120 pts could be analyzed, with a median follow-up of 50 months (1-60) months, 70 (58%) were males, with a median age of 53 (11-85) at IM initiation. Eutos, Euro and Sokal scores had no impact on OS, PFS. The estimated PFS rate of patients treated with Imatinib is 92.8%. The overall survival OS of patients treated with Imatinib is 92.1%

FIG 1. PFS of patients treated with Imatinib



The estimated PFS rate of patients treated with Imatinib is 92.8%

FIG 2. Survival of patients treated with Imatinib



The survival of patients treated with Imatinib is 92.1%

FIG 3.

Conclusions

The usage of target therapy in this type of leukemia has made a lot of progress. Today, we have other kind of TKI like nilotinib, dasatinib, bosutinib some of which were better as far as molecular remission. Imatinib is still a good choice in the first line of therapy in patients with Chronic myeloid leukemia in chronic phase CP.

After a very long median follow-up of more than 60 months in our patients, imatinib still consistently provides high rates of remission and survival, without disease progression and severe long-term toxicities. In addition, this is the first data on our Albanian patients diagnosed with Chronic myeloid leukemia in chronic phase CP treated with Imatinib as first line therapy.

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The role of the private sector in developing the health system in Albania and governance

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Abstract

The private sector plays an increasingly important role in health systems in the countries with low and medium incomes. "Private health sector" includes a large variety of actors, including providers, financiers and physical and knowledge suppliers for the health sector. Boundaries between the public and private sector are often unclear, as many private actors act outside the framework health sector regulator on the basis of informality. Public sector institutions often have limited experience of engaging with the private sector due to lack of communication, concerns about sustainability, and complexity. This paper presents an analytical framework for conceptualizing the functioning of health care system governance and the role of government in the context of expanding private and public services its financing. Governance is increasingly recognized by the World Health Organization and other national and

global actors, to have an essencial role in the center of the health system, and central part of their healthcare sectors and strategies for development. Governance is a multi-dimensional concept, and there are norms, instruments, and pragmatic models of the administration. In our conceptual model, the government interacts with the private sector on three different levels: protecting the public interest, working with the private sector, and learning from each other. The possible roles of governance are identified in the context of a growth of the private sector. Progress indicators are also suggested. The framework recognizes many public and private sector actors, including individual consumers, civil society, and donors. These actors are in complex interconnections involving the exchange of funds, skills, inputs, services, information, influence and accountability. The framework is applied in the case of Albania illustrating how differences in context affect the nature of the administration function and approaches adopted for the governance of mixed health systems.

Key words: *Private Sector, Health system, Governance*

Introduction

The Albanian health system consists of two sectors, one focused on the health of the population, which is called the public health sector, or "Public Health", and a disease-focused sector called diagnostic-curative or otherwise "Medicine" sector.

Referring to the objectives of international organizations such as the World Health Organization, a health system should have key objectives such as continuous improvement of the health of it's population, high responsiveness to the needs and demands of citizens and patients, as well as fair funding, which includes support, the protection of citizens, especially the poorest from the financial burden of sickness costs. Medicine itself consists of the public and private sector, which compete the market, a different concept from that of the commercial market, to which the main goal is the profit.

The mompetition between the sectors of medicine is complementary and cooperative, with the aim of providing a better quality of service and responsiveness to the needs of the patient, in terms of the opportunities offered by each sector for quality, standards, cost, applied technology, attendance and respect.

Undoubtedly, the public sector remains irreplaceable and indispensable for hospitals and university hospital centers, as a clinical-diagnostic base, but also to the scientific, teaching, methodological centers, as well as for the continuing education and training of doctors and medical personnel.

Any health care system that does not pay attention to the elements that essentially constitute the objectives of its existence, such as equality in service delivery, justice,

economic efficiency, citizen information on health issues, high security of services medical care and choice, endangers the loss of public confidence in their health system and its leaders (Gudha, A. 2008)

The organization and functioning of the health system is initiated and supported by the Government at national, local and international level through legal acts, decrees, guidelines, etc. Different countries have drafted and adapted strategies for interventions in health policies. This is previously seen in the developed countries, and at last in the countries of the region, a similar pattern of political interaction, which on the one hand tries to maintain a stable balance between market-oriented mechanisms and, on the other hand, a mix of the decentralization of the public sector, with the tendency to increase the role of the private sector in the provision of health services and their financing.

Market elements are applied to healthcare providers (healthcare personnel) in the form of payment for work performed, as well as for healthcare providers (citizens, patients), through mechanisms such as cost sharing and increased options of choice. This is associated with the increasing role of patient-citizens in the development of strategies for development of the health system and their participation in clinical decision-making.

In Albania, the history of the health system is relatively new and closely related to political developments. The beginnings of a proper health system are found during the Zog leadership. Its strong influence was from the health system according to the Italian model of its organization. With the coming of the communist system that led the country during the years 1945-1990, significant changes occurred in the health system. Like any other aspect of the economic, political, social and cultural life, the Albanian health system was oriented and influenced by the model of the Soviet Union. The health system in Albania was essentially the implementation of the Semashko type, designed for the countries of the Soviet Union, the core element of which is the centralization of competencies. During the years of implementation of this system, we have important developments both in terms of infrastructure and achieved results for a better population health. This system of organization of the health system stopped the private initiative in the provision of health services, everything was state-owned and propagated that health was free. Despite developments, this system (as in any other country where it was implemented) left behind the development of health sector (pharmaceutical, medical, dental, and public health sectors) compared to Western countries whose health systems were based health insurance.

Among the weaknesses of the centralized health system we can mention low efficiency, low quality, slow pace of change, lack of response to external changes, and unsatisfied patients with the quality of services and overlooked decision making related to health issues.

Political changes in the early 1990 brought radical changes in the Albanian health system. In Albania was implemented the mix health system with dominant features of the German health system of organization, the Bismarck health system. It should be emphasized that private initiatives in health care were allowed in 1992 and the first steps of establishing a legal basis for allowing private initiatives and equal opportunities in the market were laid.

The importance of the private sector in health systems

The private sector plays an increasingly important role in low- and middle-income health systems. She has had insufficient attention due to lack of information about her role and importance. Public sector institutions often lack the skills and competences to engage with non-performing actors, without excluding motivation and interest in it (Balabanova, D. Oliveira-Cruz, V, Hanson K, (2008).

The World Bank, in the 1990s, has undertaken initiatives for the private sector as a partner in reforming the financing and delivery of healthcare, including the introduction of public access facilities in low and middle income countries, and finally re-evaluate the role of the private sector in relation to outsourcing, social reinsurance and the incorporation of public hospitals (Preker, A. & Harding, A. 2003).

The existence of a large private sector has many effects on the health care system. A high level of direct payments from the pocket for private health care is often the cause of catastrophic health spending (Das & Hammer 2007). When the public sector of the health systems are weak and poorly funded as in the case of Albania, patients and service providers may experience corrupt and informal payment phenomena (also a form of private sector unregulated practice) (Balabanova, McKee 2004). The use of the private sector can lead to irresistible and poor quality care, especially for the poorest groups, who have limited alternative options (Das and Hammer 2007).

The private sector, despite challenges, often undertakes initiatives that the public sector qualifies as unsuitable and ineffective by offering an inadequate service. In this regard, the pharmaceutical and dental sector has made an important contribution since 1992 to providing a quality service despite the risks.

Referring to a World Health Organization study (WHO 2007) in 39 low and middle income countries, healthcare services were available to citizens by 20% in the public sector and 56% in the private sector. This indicates not only the tendency of citizens for a better quality service but also the bureaucracy faced in the public sector, as well as the need for regulation through policies and other legal acts that regulate the activity of respective sectors, especially the public sector.

It is important to emphasize that the private sector can have interaction and relationship with different actors of the health system such as (Dina, B. Valeria, O. Kara, H. 2008) institutions that provide health services, health policy makers. The

role of this sector is complementary to the public system that fulfills the needs of the population for health services.

Objectives and Objectives

The purpose of this study is to identify the role of the private sector in the Albanian healthcare system in the development of specific health services, increase of the quality of health care system in the areas it operates, problems it faces during the development of its activity, opportunities and challenges for development of this sector while guaranteeing equity in the market.

The objectives of this study are:

- Analyzing the legal framework and other regulatory practices that imply the private health sector.
- Finding opportunities for this sector to interact with the public sector in favor of patients.
- The study should serve as an opportunity for Albanian healthcare policy makers to make appropriate interventions in the relevant legislation.
- Encouraging a debate between the actors of the Albanian healthcare system and the patient community.

Methodology

The study is qualitative, which is based on literature research, legal basis and data on organization, governance, management of the health system and aspects that imply it.

This paper presents an analytical framework for conceptualizing the functioning of the health system governance and the role of government in the context of the extended provision of private services and its financing. Governance has increasingly been recognized by the World Health Organization and other national and global actors, to be a core function in the health care center, and central to their health sectors and development strategies.

Results and Discussions

The first beginnings of the private sector in the Albanian health care system date back to changes in the political order of the early 1990s. The first sectors undergoing

their almost complete privatization were the pharmaceutical sector (excluding pharmacies of public hospitals) and the dental sector (emergency dentistry and dentistry in the schools). The performance of the pharmaceutical and dental sector compared to the health care and public health sector, which have been much more marked with regard to privatization, have been more effective both in terms of quality offered to patients and in terms of access the public and the patients have them.

Also in the early 1990's there was the opportunity to develop private initiatives for both primary care (family medicine) and hospital care.

The legal changes at that time were the most important steps through which the private sector developed rapidly and helped the development of the Albanian health system. In this regard, Law No. 7670, dated 13.10.1994 "On Health Insurance in the Republic of Albania" (www.shendetesia.gov.al) constitutes a real step by which the government not only accepts the private sector as complementary, but also contracts it to do a give health services. Pharmacists and pharmaceutical agencies that were then state-owned, are now being privatized and a large part of them that meet the pre-established conditions are contracted by the Health Insurance Institute to offer the reimbursable medicines to patients according to the respective definitions. This service has grown steadily from 1994 to 2018, as well as the number of pharmacies and contracted pharmaceutical agencies, as well as the number of medicines included in the list of reimbursable medicines. This scheme has proved efficient, flexible, and has increased the access of patients for the medications they receive.

Unlike the pharmaceutical sector, which was treated as an important partner by outsourcing its services to citizens, the dental sector did not pay such attention to the health policies that regulate its activity. Dental services remain over 90% of the games that they offer entirely private (with direct payment from citizen and patient) and less than 10% entirely state providers (emergency dentistry and school dentistry services). Despite this fact, the development of these two sectors of the health system, they had a very positive performance compared to that of medicine sector.

It is noticed an interruption of rapid development in the private sector during the years of political and social problems in the late 1990s.

In the beginning of the year 2000 there was an increasing tendency to increase the number of private medical clinics offering single services according to different specialties to patients, mainly concentrated in the large urban city.

After 2005, private hospitals started to operate in the Albanian medical market. There are currently 6 well-functioning hospital units as well as a number of clinics that are specialized in specific hospital services. These operators are concentrated in the Albanian capital city, and only one of them with several branches in other

cities. In all major cities of Albania there are clinics that offer services as primary and hospital care.

The role of private healthcare institutions that provide services to patients every day is with greater importance, both in the volume of procedures, medical visits, operations, examinations and laboratory analyzes, as well as in the enhancement of the quality of these services. Private sector not only has invested a lot of money in our health system but has brought advanced technologies, which have consequently increased the quality of health care. Law No. 10383, dated 24.2.2011 "On compulsory health insurance in the Republic of Albania", amended, created the possibility for private institutions providing health services to be contracted for certain needs by the compulsory health care fund .

Since 2014, a number of health services as in Table no 1 have been contracted for private hospitals for the provision of these services due to the overpopulation of public hospitals, increasing patient demand, and increasing the capacity of private hospitals to perform these services according to approved standards and protocols.

TABLE 1. Service packages covered 100% by Compulsory Health Insurance Fund (CHIF)

No	Type of service
1.	Dialysis
2.	Renal transplantation
3.	Therapy of Acute Renal Failure
4.	Pacemaker definitive
5.	Coronary Angiography
6.	Coronary angioplasty
7.	Valve interventions
8.	Congenital interevents
9.	Coronary By pass
10.	Cochlear implant for children with hearing problems

Source: Ministry of Health

The beneficiaries of these 10 packages, approved in June 2014, are covered 100% by the Compulsory Health Insurance Fund (CHIF), both in the case of receiving public and private hospitals that have already been contracted by Compulsory Health Care Fund (www.fsdksh.com.al).

The implementation of these packages can be considered as a major beginning of the application of public and private sector competition in the Albanian health system.

Another development over the last 5 years in public and private sector relations is the forms of cooperation initiated by the Albanian government. Concession and private public partnership in some health services, mainly medical, have been carried out over the years.

It is noticed a tendency of the government to organize tenders for 10 years, in some cases the subjects do not provide technical guarantees for achieving within the standards of the services for which they are contracted.

Dialysis case as a model of cooperation between private and public sector

TABLE 2. Number of patients treated with hemodialysis over the years

No	Year	Number of patients treated with hemodialysis
1.	2007	60
2.	2013	734
3.	2015	880
4.	2017	1050

Source: Ministry of Health

Its beginnings the Hemodialysis Service dates very late in 2007 to about 60 patients, based on the capacities the public sector provided at a time when the demand for this service was high and had no capacity for its coverage. From this moment and according to the needs, the private sector operates as a public sector planner in order to meet the growing needs for this service. Thanks to this initiative in 2013 this number reaches 734 patients treated with hemodialysis. Then in 2014 as a result of the initiatives of the Ministry of Health to concession to a part of the public health services, the Hemodialysis service was granted with a concession for a period of 10 years, thus increasing the capacity for the treatment of the patients, the number of beds, and dialysis centers in the cities of Tirana, Durres, Elbasan, Shkodra, Lezha, Berat, and Korça.

Increasing patient care capacities is a very good opportunity that should be encouraged also in other health services for which the public sector can not develop with the flexibility of the private sector.

The last five years in the Albanian healthcare system, services trusted to the private sector through concessions or public private partnerships are as follows:

TABLE 3. Hospital services provided with concession / PPP (private public partnership)

No	Private public partnership, type of service
1.	Check-Up
2.	Sterilization of medical and surgical equipment
3.	The hemodialysis service
4.	Treatment of hospital wastes
5.	Laboratory examinations in medical laboratories in public hospitals

The role of government in relation to the private sector

When describing relationships between different actors of the health system, the role of the government is understood as a Service Provider (WHO 2000) or the Health System Leader (WHO 2007) is considered to be a central role in guaranteeing a good governance of the system health care (Kaufman, Kraay 1999).

TABLE 4. Public and private sector cooperation tools

Public and private sector cooperation tools		
Protecting public interest	Cooperation with the private sector	Learning from each other's experience
Ensure good governance	Increase interventions in order to improve the quality	Dissolution of the best practices of the respective sectors in favor of the patient's interest
Ensure law enforcement	Reduce fragmentation and reach synergies	
To set the goals of health policies	To increase co-operation by creating a coalition between the two sectors	
To provide a healthcare service (access to the health system and its quality guaranteed)	Establish bodies that mediate and facilitate policy progress with common goals.	

TABLE 5. Forms of public and private sector engagement

Forms of public and private sector engagement		
Strengthen current legislation	Increase in the contribution of compulsory health insurance	Health system (public and private sector)
Applying quality standards for health services	Extending public money financing from the mandatory health insurance scheme to private operators	The private sector of the health system (dental sector, pharmaceutical sector, primary private health care sector, private hospital care operators)

Strengthening transparency and public information	Increasing the schemes that fund the healthcare infrastructure	Health system (public and private sector)
Strengthening the role of the patient and his rights	Application of the co-payment principle (to be recognized the right to use health insurances and to private operators)	Private healthcare providers
	Public-Private Partnership	Services by specification (those not provided by public operators, or in case of overload)
	Inclusion of other private and public health insurance funds	All public and private operators

Platform for an effective approach to private and public sector cooperation

1. Platform for effective public-private cooperation (annual meetings for problem-solving)
2. Joint initiatives (eg, trainings)
3. National strategic plants and technical policy documents
4. Health Information Management Systems
5. National System of Transparency regarding health
6. Annual performance reports
7. Improve and unify treatment protocols
8. Health insurance of patients from bad medical practices (insured physician)
9. Strengthen audit practices on insurance schemes for their private sector

Conclusions

The private sector has developed relatively recently compared to political, economic, and social development as a whole.

Health system sectors that have been subject to privatization since the early 1990s (whenever possible) have a much better performance than the public sector over the two decades of their activity.

The Ministry of Health has not responded during years to the velocity of development of the private health sector through legal or regulatory acts that regulate, specify, outline their activity not only as institutions providing health services, but also forms of cooperation with other public health institutions, as well as responding to patient requirements. Increase cooperation between public and private operators as well as create spaces for expanding the activity of healthcare providers for services that have high demand from patients, as well as specific services for which the state does not interest to develop them .

To increase the transparency of private healthcare providers to the public, in relation to their capacity as well as the quality of the service they provide.

Consider the possibility of increasing compulsory health contributions by expanding the mandatory health insurance scheme with other services that are not currently offered, but also extended to other private operators. It is also necessary to assess the possibility of entering into the health insurance market of funds, that imply other public health contributions, or even increase the cooperation with the private funds of health insurance. Parity in the financial treatment based on the health contribution of the public and private sector, based on indicators of the quality of the health service. The patient should choose which operator to spend his / her healthcare contribution for a particular service that has previously been costly.

To use the potentials of potential investors for the development of certain health services through possible forms of legal-financial cooperat

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Albanian Health Policy in Prevention of Chronic Kidney Disease

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Abstract

Nowadays Chronic Kidney Disease (CKD) has increasingly come and constitutes a public health problem of paramount importance. International institutions such as the "Center for Disease Control and Prevention" identify Chronic Kidney Disease as one of the main priorities in the era of the epidemiological transition. In Great Britain were articulated operational plans for identifying subjects with renal dysfunction or low-grade of renal failure . Refer to the data is estimated that in the adult population, about 1 adult individual in every 10 individuals has a moderate degree of renal failure, which means a renal function (expressed as glomerular filtrate) half or less than half of the normal rate. In Albania the problem is virtually unknown by the population, yet little-known and widely underestimated by doctors and by the policy makers , regional and / or national government public health authorities. What is proposed is intended to create the basis of data, knowledge and determine the functional organizational structure for the prevention of kidney disease (primary prevention), to slow down their development (Secondary prevention), and to prevent dangerous cardiovascular complications caused by renal insufficiency (tertiary prevention). The end result is intended to reduce morbidity and mortality from renal diseases, and improve the quality of health care provided to patients with kidney disease.

Key words: *Renal Chronic Disease, Prevenation, Public policy*

Introduction

Chronic kidney disease(CKD) is becoming recognized more and more as a global public health problem.

A health condition to be considered a public health issue, should complete four criteria: 1.) the issue / health condition should be expanded and constitute a heavy burden on society, a burden that is increasing despite existing control efforts; CKD burden of disease is high (ie, it is widespread in many people, has grown recently, and is likely to grow even more in the future). This burden of disease is translated in terms of mortality and morbidity, quality of life, cost, and perceived as a threat by the public, that it can get out of control.

2) The burden of disease should be distributed at random (ie, certain parts of the population are disproportionately affected); 3) there must be evidences that prevention strategies can significantly reduce the burden of issue / situation; and 4) such preventive strategies aren't yet well developed and implemented.

Now there is compelling evidence that CKD can be detected through a simple laboratori test , and that treatment can prevent or delay complications of the decreased function of the kidney, to slow the progression of kidney disease, and reduce the risk of cardiovascular disease complications (CVD) .

Since 2006 in the Conference of KDIGO on CKD were analyzed and were taken into consideration six main themes: (1) Classification of CKD, (2) screening and surveillance of CKD, (3) health policy for CKD, (4) Cardio-vascular diseases and their risk factors as risk factors for the development and progression of the CKD, (5) accompaniment of CKD with chronic infections, and (6) relation of cancer with CKD. In conclusion a report with recommendations was drafted, the implementation of which is going to be realized through cooperation with international organizations and national public health.

Screening and Surveillance

Screening is an activity where people of a given population who are not aware of suffering froma CKD , are tested to detect the presence of disease, and if present are treated to reduce the risk of progress of CKD and of its complications.

Surveillance refers to an activity to provide relevant information on CKD, such as time, location, size, and severity, in order to implement the guidelines for medical and public health measures to control the progress of CKD and its complications.

On the other side there is no evidence that the screening of the general population is going to be cost-effective.

Screening should be applied in those subgroups of the population that may have benefits from the detection of CKD. In developed countries and developing

countries, the risk for developing of CKD is increased in people with risk factors for CVD or CVD already installed, in which CKD multiplies the risk for negative outcomes of CVD. So , the CKD subgroup' of patients with CVD and risk factors for CVD is a high-risk group that require special attention.

As well as patients with contageos chronic diseases and cancer may have increased risk.

In these groups, screening for CKD can be implemented using the existing infrastructure for the detection of other chronic conditions.

Many countries such as Albania have registers for patients treated with hemodialysis and transplantation. However, these programs marginalize people with CKD of severe stages who die before starting treatment for renal failure with dialysis or renal transplantation.

In principle, the surveillance programs for CKD in stages 4 and 5 will helps the monitoring of the size and care for that populate with hight risk and high cost, and to reduce the progression of renal failure and the cost of renal dialysis and transplant .

While surveillance for patients in stage 3 of CKD will involve more people and can be an effective way to reduce the value of CVD and death, especially among older people with risk factors for CVD or CVD installed.

Health Policy

In some countries, the incidence of renal heart failure due to certain types of CKD is stabilizing or declining, reflecting the early detection and treatment.

Although the prevalence of renal failure varies substantially across the world, the number of patients and the cost of providing dialysis and transplantation continue to be increased.

Few countries have policies for the prevenation of CKD, although most of them are aware of the high prevalence of CKD, its impact on other diseases, and its large economic burden .

Prevention, early diagnosis and intervention are the most cost effective strategies for CKD.

At the same time, costs for other chronic diseases are increasing. In developed countries, the care for patients with hypertension, diabetes and cardiovascular disease consumes a large part of the income of health care.

Developing countries are now experiencing the burden of non-communicable diseases, although infectious diseases are still not under control. CKD are especially common in people with other chronic diseases and multiplies the risk for negative outcomes and higher costs. Thus, public health policy should be coordinated with CKD existing policies for other chronic diseases.

Methodology

The study is a quantitative one. It is realized through the research of literature, reports and periodicals reports of the Albanian Ministry of Health on health policy related to renal diseases.

Data from international health organizations are analyzed and compared with national ones. A detailed description is made on the other side and the 10-year screening program conducted through Albanian health policy . The data obtained help us in drafting clear conclusions, which highlight the necessary recommendations for the progress of the process.

Findings / Results

CKD prevalence in the United States in 2012 (excluding IRK) was estimated at 13.6%, and has been relatively stable over the last decade, but awareness and screening for the condition remains low in the general population. Claims data for patients with diabetes in the population indicate that testing for albuminuria is done in less than half of patients. Among all patients with diabetes, testing for albuminuria rate in 2008 was only 32%, and was increased to 40% in 2013.

In 2013 there were 117.162 new cases reported with End Stage Renal disease. However, adjusted incidence rate of End Stage Renal disease , which includes both patients on dialysis and those transplanted, remained unchanged from 2012 to 2013, to 352 million per year. A total of 671.851 people were treated for End Stage Renal disease, as the first quarter of 2014, a number that continues to grow due to the decline of mortality rates among those with the End Stage Renal disease.

CKD health related costs remain high. CKD costs for patients of age 65 and older exceeds $ 50 billion in 2013, representing 20% of all the expenditure in this age group. In 2013, costs for patients with End Stage Renal disease increased $ 31 billion, accounting for more than 7% of total spending.

The number of people on the waiting list for a kidney transplant was about 5 times greater than in 2013. Although 17,600 kidney transplants were performed in 2013, the list of pending kidney transplant increased by 3% compared with 2012, rising to 86.965 candidates.

By 2030, it is estimated that the annual number of people in the later stages of the CKD- End Stage Renal disease will exceed 450,000, and those receiving dialysis or who have performed kidney transplant will exceed 2 million.

Albania

Since 2007 patients with CKD in the last stages of the End Stage Renal disease are treated with hemodialysis in the public and private sector . In this period, the number of patients was 60.

TABLE 1. Number of patients who are treated with hemodialysis in years

No.	Year	Number of patients who are treated with hemodialysis
1.	2007	60
2.	2015	880

Source: Ministry of Health

During 2015 were implemented throughout the year, health packs, which are financed by the health insurance scheme. These packages are implemented by public hospitals as well as non-public health institutions, which are contracted due to the limited capacity of public hospitals, aiming to fulfill the needs of the population. Thus, during 2015 it has been provided hemodialysis for about 880 patients, 34 percent of them in public hospitals (Universitary hospital center-Mother Teresa, regional hospitals like Elbasan, Gjirokastra, Shkodra), and 66 per cent in 4 nonpublic(private) institutions.

TABLE 2. Presentation of the percentage by sector where patients are treated with hemodialysis

No	Private/Public sector	Percentage of the patients distributed by the sector
1.	Public	34%
2.	Private	66%

Source: Ministry of Health

Package of Basic Health Control

Albanian health policies have embraced an important initiative, the screening program "Check-up" application, a based control wide enough to ages 40-65 years old, with the help of public-private partnership for one period of 10 years. The package includes basic medical control:

Assessment, counseling, treatment and follow up on lifestyle factors:

- Nutrition;
- Smoking;
- Consume of Alcohol;
- The level of stress and depression.

Measurement, assessment, counseling, referral and monitoring of physiological parameters:

- Blood pressure;
- Body mass index;
- Heart activity (ECG).

Measurement, assessment, counseling, treatment, referral and monitoring of biochemical parameters:

- Blood formula;
- Hb, HCT, MCV, MCH, MCHC;
- Cholesterol Total, HDL cholesterol, LDL cholesterol, triglycerides;
- Glicemia;
- Faeces analize for occult blood;
- Albuminuria, presence of cells, cylinders, crystals in the urine, uremia and creatinemia;

Total and direct Bilirubine, transaminase (SGPT, SGOT)

Basic Health Control Program , are free (40-65year), Renal diseases, cardiovascular and diabetes have special attention, implemented these in 415 health centers in overall Albania.

This control, at the same time, has three main goals:

(I) to assess health risks;
(II) to communicate with citizens the health risk; and then,
(III) to build the bridge to manage this health risk, certainly for people in the age group 40-65.

The program attempts to address systematically the major causes of premature mortality (I) arterial hypertension; (II) obesity; (III) smoking; (IV) cholesterol; (V) poor diet; (VI) physical inactivity; and (VII) the use of alcohol.

During the control 6 basic component are assessed for basic health control: (I) cardiovascular diseases; (II) diabetes type 2; (III) mental health; (IV) lifestyle, including nutrition, smoking, alcohol, physical activity; (V) arterial hypertension; and (VI) laboratory tests to assess blood, urine, faeces for Ca colon / rectum, evaluation of heart and liver.

From data results with hypertension 37% of people who participated in control. About 18% do not know they are hypertensive, which means that we have a very high rate of disease in the population, initially, people did not know, and then, we did not have proper care for the disease. About 35% of the people know they are hypertensive, but on the day of control have the same results again of the state of the disease, which means, they are not treated properly.

Diabetes: 4% of people have resulting in diabetes control and do not know this fact. And if this 4% has come from the age group 40-65 years, means that the proportion is greater of people who have diabetes and do not know they have diabetes. Meanwhile, 12.5% of persons who have control, as assessed paradiabetic.

Minimally, results of controls that we have a high degree of obesity; which means that we have high degree of risk. Meanwhile, the patients we have today wich are diagnosed with diabetes, we note that 30% of patients with eye diseases are diabetic; 30% of those who have kidney disease and are treated with hemodialysis are diabetics; 30% of those who suffer from hypertension, have diabetes; that means we have in these cases of these diseases, some chronic diseases together.

All patients that have resulted with disorders of the urinary system indicators, including a complete analysis of urine or even creatinemia -azotemia through referral scheme have taken the necessary services through consultations by specialists of the field-Nephrology. On the other hand patients aware of the presence of nephropathy were evaluated and advised regarding risk factors and renal disease progression.

The burden of chronic kidney disease in the health system is great. The analysis in the statistical database service in Mother Teresa –University Hospital, in the nephrology service(not including hemodialysis services) results 4082 cases of hospitalization for the period 2012-2015, of which 3374 belong to chronic kidney disease. It is clear that about 82% of all cases of renal pathologies are chronic kidney disease of different stages and different origins.

The table below shows the distribution of these cases according to the basic pathology causes. Others involved in the field of diagnosis cause of CKD 's not above cited example skleroderima, Alport syndrome, unspecified nefroskleroza, transplant rejection, uric acid nephropathy and cases where the card was not recorded underlying disease that comprise approximately 1190 patients with CKD.

TABLE. 3 Distribution of cases by diagnosis based on chronic kidney disease

Glomerulonephritis	Pyelonephritis	Hipertension	Diabet	Renal Policitosis	Lupic Nephropatia	Other
186	1283	123	409	162	21	1190

Source: Database of statistics at the University Hospital Mother Teresa-Tirana

Referring to the results the highest number of cases of the disease causal basis of CKD 's hold pyelonephritis with 1283 cases. In second place with 409 cases diabetes ranks as the most rare cases occur in patients with Lupus nephropathy because the LES prevalence in the population which is low too.

TABLE. 5 Distribution by stage of disease

Stage of disease	Percentage
I	2.7
II	6.8
II	40.5
IV	14.9
V	35.1
Total	100.0

Source: Database of statistics at the University Hospital Center Mother Tereza- Tirana

Based on the distribution by stage of disease, patients with stage II-CKD represent the highest percentage of about 40.54%, accompanied by the fifth stage with 35.14%, the first stage is only 2,703%.

TABLE. 6 Diseases associating CKD

Diseases associating CKD	Percentage
Diabet Mellitus	24.5
Hipertension	63.4
KMP	37.2
Anemia	8.9

Source: Database of statistics at the University Hospital Center Mother Teresa-Tirana

The most common disease associated with CKD is Hipertension 63.4%, followed by 37.2% and KMP with less Anemia 8.9%.

Conclusions

CKD burden disease, in terms of human suffering and economic cost is steadily growing towards the 21st century, making it a major public health issue.

Approaches of different countries are different to those associated with incidence, prevalence or different forms of CKD to address effectively this serious health problem. The Albanian government has adopted a health policy regarding the CKD and further, supporting a program of screening and surveillance was associated with them, thanks to a public-private partnership. Albania has applied a broad screening program associated with chronic diseases associated with CKD in 40-65 age group, cardiovascular diseases, diabetes, etc. On the other hand the target group of patients of this age groups is addressed to these with the highest risk for this diseases. The tests include a complete urine analysis, proteinuria, and creatinemia, necessary for the calculation of glomerular filtration and evaluation of the renal function , detection of new cases, preventing chronization in time, slowing down the progress toward the terminal stage, and reducing complications and mortality.Tests above are applied once a year .

Recommendations

A. The expansion of the screening program in other age groups, in those younger than 40 years and especially over 65 years old, where risk factors are more present.
B. Organizational proposals to the Association of the Albanian Nephrologist

Prevention of chronic kidney diseases and their complications should be performed at three levels:

1. Primary Prevention

Primary prevention consists on informing and awareness on the population regarding the disease and risk factors, which in fact constitute a fundamental problem. This is achieved through information campaigns in the period who marks events, such as the International Day of the kidney, which are media campaign with educational character. These initiatives remain insufficient unless we put action plans and screening programs to better calibrated.

2. Secondary prevention

Secondary prevention consists in the identification and treatment of nephropathy and early, thus it is essential that integration between General Medicine / Family and Nephrology, enabling communication and the creation of diagnostic therapeutic pathways.

3. Tertiary prevention

Tertiary prevention and control consist essentially in search and control of factors of renal pathology progression and prevention of chronic renal complications of renal failure.Nephrologists play a key role in cooperation with other specialists to connect with them as such; diabetologists, cardiologists, but also imunologists, urologists, vascular surgeons etc.

Improve the quality of service delivery to patients with chronic nephropathy.

Improve quality of service for patients with cronic nephropathy includes:

a) Communication
b) the formation and ongoing education of nephrologists, consists in three main aspects:
   Adequate number of nephrologists
   Continuous formation of Nephrologist
   Ongoing Formation of family doctors
c) improvement of diagnostic-therapeutic protocols, seen especially in the direction of stabilization of one capillary proliferation program plan training for doctors in general medicine.
d) cooperation with other specialties, to encourage the exchange of ideas and dissemination of program tasks that final aims at preventing major causes of renal failure.
e) improving the functioning of the network of nephrologists etc.

In synthesis are necessary:
Integration -Programs Hospital-Territory
Adequate -Number of Nephrologist
- Ongoing formation programme especially for nephrologists and medical doctors in general medicine.
-Omogenisation of structural and accreditation criteria

C. Operative Proposals

Cooperation of central decision-making levels in scientific society for:

1) Use of existing tools for the detection of chronic diseases to determine cases, incidence, prevalence and trends for the future of CKD
2) Determining the epidemiological and social health importance of CKD.
3) Programming of an adequate number of nephrologists to deal effectively with CKD and inform the competent authorities, that they can adjust the number of training contracts with specialty in Nephrology.
4) Control of the costs and benefits of long-term prevention programs of CKD.
5) Promote the development of communication plans so that every citizen becomes aware of the condition of his kidney and the cardiovascular risk associated with and possible therapies.
6) Promotion periodically campaigns to promote the donation of organs, especially the kidney in this case.

Hospitals and hospitals enterprise

1. To help health institutions and public health institutions in the programming structures and strengthening the Network of Nephrology.
2. Alternative solutions assessment local programming already present, under the direction of the needs of the territory, in optics of efficiency and make full use of the competences of nephrologists.
3. E ntirely use of nephrologists competences, to avoid credulity treatment of patients with no nephrologists physicians , because it will reduce the quality of service and that of prevention.

Albanian Association of Nephrologist

Albanians Association of nephrologists, such us, represented by Nephrology experts, in their respective fields, should activate maneuvers prevention: to develop and update on a regular instructions to create website pages dedicated to patients, organizing events on World kidney day.

Also exist National register of dialysis and transplantation which are already used as a source of health information and planning for the terminal stage of CKD.

Also recommended the creation of a database for CKD in stage 4 and 5 and strengthening the existing Register of Dialysis and transplantation.

Data entry in this registers of the disease should be mandatory, as an element for accreditation and evaluation of the quality of services provided.

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New professionalism in the field of health

Dr. Shefqet Deliallisi

One hundred years ago, the application of the "Flexner" report introduced modern science to the foundations of the medical curriculum, created the academic model of doctors› education, created the conditions for the academic medical centers and decided to put scientific research in function to improve patient care and clinical training.

This model, which made a valuable contribution to health in the XXth century, is unable to prepare skilled health professionals for the challenges of the XXIst century. This due to the fact that we already live in a very different context, even in a very fast and uninterrupted change. We live in the conditions of a rapid demographic and epidemiological transition. We live in the time of the explosion of the flow of knowledge, technology, information and ease of access to it. We live in the time of the complexity and unstoppable growing cost of the health system. We live in times when other demands on health workers are being set. (2,3) When they are already facing chronic illnesses, different social states, with more knowledge, proactive and with other demands for their health (4,5,6)

What is "produced" today in the faculties of medicine?

"Today university hospitals - according to Knowles (9) - almost exclusively function as 'castles' of acute curative medicine .... Students are usually in contact with hospitalized patients, generally in severe condition, in most cases with acute problems. Current curricula do not provide a balanced vision for health care in general. According to them, the most important place where medicine is practiced is the hospital, which is considered a 'health repair service'. They report an underestimation for primary care, ambulatory patient, and those with minor

diseases. Negative habits are used to treat chronic diseases. They leave out of attention the prevention, community health or public health.... They leave out of attention the economic problems. The dominant model continues to be oriented to the disease, and not to the patient; there is a hospital basis, which means cure, not care. "

In most medical schools, the only formal learning that students receive for health insurance is the need for them to own it (10).

Shortly, educational strategies have stalled in the trap of the health conditions of the century we left behind. They produce doctors unprepared for the challenges of the time, which are primarily social and economic. Doctors prepare only 10% of what they will face in life, unable to keep in touch with the development of the health system.

Two surveys ...

1 - In the century we live, inadequate nutrition is the root of diseases that seriously threaten public health (obesity, diabetes, heart disease, cancer, etc.), and therefore science of nutrition is a basic discipline of health care. It improves the quality of life and saves the costs of health care. . In September 2011, the results of a survey with family doctors in Tirana were published by the Institute of Public Health. It turned out, among other things, that these doctors had insufficient knowledge of nutrition ... The result may have surprised the public, but not the physicians, who are aware that their dietary knowledge is extremely pervasive, and in many cases lacking at all. This is a defect in their formation at the Faculty of Medicine, where there is no nutrition department, where only a few are concerned about nutrition science, while they focus on the most "important" things, that they will have to deal with just a little or not at all during the exercise of the profession.

2- Whereas many talk about effective-costs, hospitalization, healthcare systems and other topics of this nature, the Medical Faculty considers this superficially. The fact that the health economy, which is indispensable in the conditions of a surge of spending on health care, is not being widely implemented, shows that doctors continue to lack the proper knowledge in this area. Not having an Albanian survey, I referred to a 2009 survey with a group of American students (11). The result: Less than half of the students believed they were properly educated on topics such as medical economics, healthcare systems, healthcare quality, healthcare, health policies, and legality. And all these shortcomings certainly have a direct impact on their later practice as doctors in cost-consciousness and facing everyday complex spending. These are all problems in the heart of contemporary health policies. (12.13)

Time for change...

Educational reforming of health professionals should start without wasting more time. A new vision is required. Informative and formal learning should leave the place to transformative learning. The old, fragmented and static curricula that produce poor leadership, incompetence in health policies and management, unprepared to improve the performance of the health system, unprepared for teamwork, prepared for persistent pursuit of chronicles patients, unprepared for primary care, unprepared for the challenges of public health and, most importantly, unprepared to successfully carry out health reform. On the other hand, it is necessary to set up interdisciplinary teams which should include health economists, medical sociologists, health policy analysts, people trained in different fields of social sciences, like business and organizational management, ethics and psychology. (14,15,16) Training in these areas is indispensable for young health professionals, prepared beyond the narrow field of medical care.

A paradox or a ? ...

In April 2012, Korean-American Jim Yong Kim was elected as the new World Bank director. The impression is that 52-year-old Kim, who will lead one of the world's most important financial institutions, is not an economist, but a doctor!!! Doctor in medicine and Ph.D. in anthropology. So, the World Bank won't be run by a finance expert, but by a graduate in medicine, who will lead 9 thousand economists and decide on billion credits...!!! Does Kim have enough knowledge on important topics related to development? In an interview in the New York Times magazine, Kim himself said: "Economic development and the fight against poverty are so complex that no single discipline can ever involve ... The World Bank has many experienced economists with whom I will cooperate ... Throughout my life as a physician I have tried to solve social problems across the world. So, for a new organization at the World Bank, Kim's experience in the health field as a development expert is required. And the doctor Kim has the required preparation of an expert in medicine, social medicine and human rights.

In conclusion…

As during a century ago, health education reform is a long and difficult process. Hard to design and slow to implement. Especially in countries with limited resources,

which are forced to channel funds into emergency projects. The Faculty of Medicine has made a valuable contribution to the preparation of health professionals, but in its new conditions its reform is indispensable (17). This reformation must at least go hand in hand with the health reform. If this does not happen, this reform can hardly be accomplished or will be poorly carried out. And this has consequences not only for doctors and patients....

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Malignant Hyperthermia

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Abstract

Malignant Hyperthermia (MH), is a rare emergency that happened during General Anesthesia. In Albania, during five last years have three cases diagnosed with Malignant Hyperthermia (MH), and two of them have been fatal finishing with death of two patients. Only one is saved. Malignant hyperthermia (MH), is disease passed down through families that causes a fast rise in body temperature (fever) and severe muscle contractions when the affected person gets general Anesthesia. Malignant hyperthermia's inheritance is Autosomal dominant. The defect is typically located on the long arm of chromosome 19 (19q13.1) involving the ryanodine receptor. More than 25 different mutations in this gene are linked with malignant hyperthermia. In this article I shall represents problems happened when during General Anesthesia, unexpected has e Malignant Hyperthermia. Malignant hyperthermia (MH), occurs in 1 in 5,000 to 50,000 instances (mainly in young people), in which people are given anesthetic gases. The most common triggering agents are volatile anesthetic gases, such as: Halothane, Sevoflurane, Desflurane, Isoflurane, Enflurane, Cyclopropane, Methoxyflurane; The depolarizing muscle relaxants suxamethonium and decamethonium, used primarily in general anesthesia. Other drugs that have been suspected of causing MH include catecholamines, phenothiazines, and monoamine oxidase inhibitors, caffeine. More frequent after ENT (ORL), squint or dental operation due to related with short anaesthetic procedures. -Researchers have described at least six forms of malignant hyperthermia susceptibility, which are caused by mutations in different genes. Variations of the CACNA1S and RYR1 genes increase the risk of developing malignant hyperthermia. Tests about discovering of MH are North American Protocol: Suspicous clinical history for MH, or The standard

procedure is the "caffeine-halothane contracture test", CHCT. Is an invasive test. The fresh biopsy (under local anesthesia), is bathed in solutions containing caffeine or halothane and observed for contraction; under good conditions, the sensitivity is 97%, and the specificity 78%; the use of the "calcium-induced calcium release" test -in addition to the CHCT to make the test more specific. Genetic testing is being performed in a limited fashion to determine susceptibility to MH. In people with a family history of MH, analysis for RYR1 mutations may be useful. Signs and symptoms are:Tachycardia : one of the earliest but a non specific sign,Tachypnea : in spontaneously ventilating patients. Increased sweating, During fulminant acute MH, body temperature may increase at a rate of 1.8–3.6°F (1–2°C) every 5 minutes, Cyanosis, flushing or blanching of skin, Cola coloured urine• masseter spasm or generalised muscle rigidity or both, Capnogram – Gradually increasing EtCO2 not related to other possible causes.. Biochemical parameters: Respiratory with or without metabolic acidosis, Hypercarbia, Hyperkalemia, Hyper calcemia, Hyper phosphatemia, Lacticacidemia, Myoglobinuria, Increase in creatinine kinase: neither a constant feature nor signifies increase muscle metabolism in intra operative period, Abnormal coagulation tests. Diagnostic Criteria are: Muscle rigidity (generalized rigidity including severe masseter muscle rigidity); Muscle breakdown (CK >20,000/L units, cola colored urine or excess myoglobin in urine or serum, potassium above 6 mmol/l); Temperature increase (rapidly increasing temperature, T >38.8°C); Other (rapid reversal of MH signs with dantrolene, elevated resting serum CK levels); Family history (autosomal dominant pattern). Differential Diagnosis ccan be made with: Pheochromocytoma,, Thyrotoxicosis (thyroid storm), Sepsis, Transfusion reactions (acute haemolytic and non haemolytic), Allergic reactions, Central nervous system dysfunction (pontine hge, hypoxic ischemic encephalopathy etc.), Neuroleptic malignant syndrome, Alcohol withdrawal,Drug interactions (MAOI and meperidine), some sort of cronic myopathy. For susceptible patients to MH, must be an special anesthetic procedures and must be ready with use of Dandrolene. Some anesthetic drugs are considered safe.These include local anesthetics (lidocaine, bupivacaine, mepivacaine), opiates (morphine, fentanyl), ketamine, barbiturates, propofol , etomidate, benzodiazepines. The nondepolarizing muscle relaxants pancuronium, cisatracurium, atracurium, mivacurium, vecuronium and rocuronium also do not cause MH. There is mounting evidence that some individuals with malignant hyperthermia susceptibility may develop MH with exercise and/or on exposure to hot environments, Local anaesthetics, Droperidol . Acute Management of MH crisis include:Stop exposure of triggering agents and give 100% O2, notify surgical team to abort intervention, administer 2.5mg/kg Dandrolene (or Azumolene) in repeated doses and 3 gr Mannitol, place the catheter Foley, monitor core temperatre, O2, CO2, urine output, Astrupograme, correct HperKalemi or other biochimic abnormality, correct cardiac problems. Conplications are plenty after Therapy as: Kidney failure,

rhabdomyolisis, KID, Respiratory failure, muscular dystrophy. Mortality was greater than 80% when do not put the right diagnosis, but with correct and fast diagnosis and the current management, however, mortality is now less than 5%.

***Key words**: MH- Malignant Hypertherima, CACNA1S - calcium voltage-gated channel subunit alpha1 S, RYR1 genes - ryanodine receptors 1, KID- disseminated intravascular coagulation.*

Objectives

- Describe the pathology- of Malignant Hyperthermia
- Problems of Inheritance and Genetics of Malignant Hyperthermia
- Principles of Treatment and Prevention of Malignant Hyperthermia

Goals

- Review Anesthetic problems during Malignant Hyperthermia
- Pathology-Physiology concepts of Malignant Hyperthermia
- Some characteristic feature of treatment of Malignant Hyperthermia

What is Malignant Hyperthermia

Malignant hyperthermia is disease passed down through families that causes a fast rise in body temperature (fever) and severe muscle contractions when the affected person gets general Anesthesia.

This condition is not the same medical emergencies e as hyperthermia that is due to such as heat Stroke or infection.

Malignant hyperthermia occurs in 1 in 5,000 to 50,000 instances in which people are given anesthetic gases.

Susceptibility to malignant hyperthermia is probably **more** frequent, because many people with an increased risk of this condition are never exposed to drugs that trigger a reaction.

Malignant hyperthermia susceptibility is inherited in an autosomal dominant manner (which means that one copy of the altered gene in each cell is sufficient to increase the risk of the condition).

Causes

The most common triggering agents are volatile anesthetic gases, such as:

Halothane, Sevoflurane, Desflurane, Isoflurane, Enflurane, Cyclopropane, Methoxyflurane

The depolarizing muscle relaxants suxamethonium and decamethonium, used primarily in general anesthesia.

Other drugs that have been suspected of causing MH include catecholamines, phenothiazines, and monoamine oxidase inhibitors, caffeine.

Epidemiology

Incidence is:

- 1:50,000 in adults , 1:15,000 in children incidence varies with triggering agent and geographic location.
- More prevalent in certain areas of a North America.
- Common in young children, but may occur in all age groups from infants in delivery room to 70 years of age.
- Male > female.
- More common in patients with large musculo-sceletal bulk and general anaesthesia after recent exercise.
- More frequent after ENT (ORL), squint or dental operation due to related short anaesthetic procedures.
- susceptible persons may have history of previous uneventful anaesthesia even with triggering agent.

Pathology-Physiology

- In MH susceptible patients the anaesthetic triggering agents cause prolonged opening of RYR1 channel (calcium release channel in muscle), overwhelming the reuptake process, resulting in excess accumulation of calcium intra cellularly.
- The muscle cell is damaged by the depletion of ATP and possibly the high temperatures, and cellular constituents “leak” into the circulation, including potassium, myoglobin, creatine, phosphate and creatine kinase.
- The sustained calcium overload stimulates several metabolic pathways.• Excess demand of ATP
- A hyper metabolic state. It should be remembered that ms mass constitute

30-40 % of body wt. so this hyper metabolic state leads to excess generation of heat.

- The sustained increase in [Ca2+]i leads to muscle contraction without relaxation, i.e. spasm, which, if prolonged, develops into severe contracture.
- The muscle contracture greatly increases the extra vascular resistance to muscle perfusion resulting in ischemia initially locally and eventually systemically.
- The excess oxygen need due to demand for production of extra ATP relative to diminished perfusion due to ischemia lead to metabolic exhaustion, muscle oedema and ultimately result in muscle breakdown.

Genetics

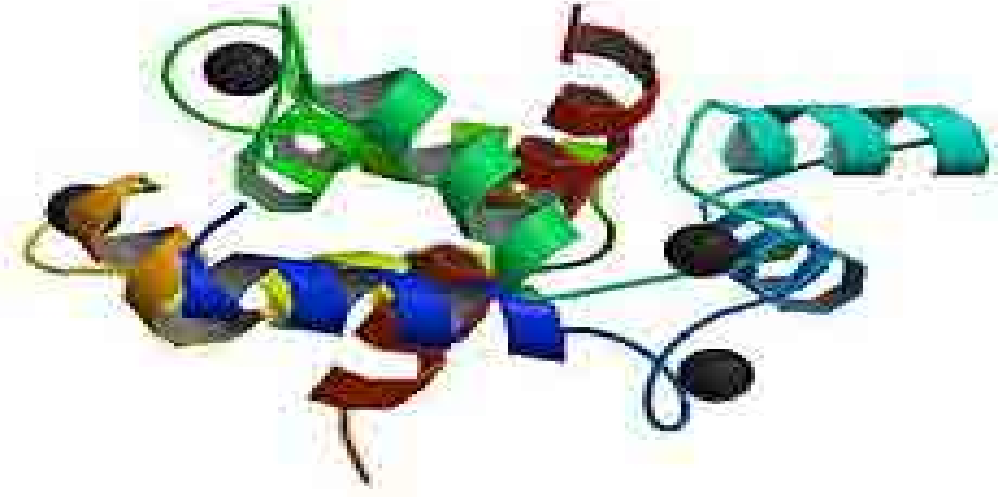
- Malignant hyperthermia's inheritance is Autosomal domiant.
- The defect is typically located on the long arm of chromosome 19 (19q13.1) involving the ryanodine receptor.
- More than 25 differen t mutations in this gene are linked with malignant hyperthermia.
- These mutations tend to cluster in one of three domains within the protein, designated MH1-3. MH1, MH2, are located in the N-terminus of the protein, which interacts with L-type calcium channels and Ca2+. MHS5
- MH3 is located in the transmembrane forming C-terminus.
- Chromosome 7q and chromosome 17 have also been implicated. It has also been postulated that MH and Central Core Disease may be allelic and thus can be co-inherited.
- Researchers have described at least six forms of malignant hyperthermia susceptibility, which are caused by mutations in different genes. Variations of the CACNA1S and RYR1 genes increase the risk of developing malignant hyperthermia.
- The genetic causes of several other types of malignant hyperthermia (MHS2, MHS4, and MHS6) are still under study.
- A form of the condition known as MHS3 has been linked to the CACNA2D1 gene.
- MHS5- An important gene associated with Malignant Hyperthermia Susceptibility Type 5 is CACNA1S.

(Note: CACNA1S-"calcium channel, voltage-dependent, L type, alpha 1S subunit", RYR1 - Ryanodine receptor 1 also known as skeletal muscle calcium release channel.)

Muscle contractions are triggered by the flow of certain charged atoms (ions) into muscle cells. The proteins produced from the *RYR1* and *CACNA1S* genes are involved in the movement of calcium ions within muscle cells.

- In response to certain signals, the CACNA1S protein helps activate the RYR1 channel, which releases stored calcium ions within muscle cells. The resulting increase in calcium ion concentration inside muscle cells stimulates muscle fibers to contract.
- An overabundance of available calcium ions causes skeletal muscles to contract abnormally, which leads to muscle rigidity in people with malignant hyperthermia.
- An increase in calcium ion concentration within muscle cells also activates processes that generate heat (leading to increased body temperature) and produce excess acid (leading to acidosis).

FOTO: Abnormalities in the Ryanodine receptor 1 gene are commonly detected in people with have experienced an episode of malignant hyperthermia, and may be used to determine the risk of episodes in their relatives



Susceptibility to MH is often inherited as an autosomal dominant disorder, for which there are at least 6 genetic loci of interest, most prominently the ryanodine receptor gene (*RYR1*).

MH susceptibility is phenotypically and genetically related to central core disease (CCD), an autosomal dominant disorder characterized both by MH symptoms and myopathy.

Suscebility Testing

The main candidates for testing are those with a close relative who has suffered an episode of MH or has been shown to be susceptible.

- The standard procedure is the "caffeine-halothane contracture test", CHCT. Is an invasive test.
- The fresh biopsy (under local anesthesia), is bathed in solutions containing caffeine or halothane and observed for contraction; under good conditions, the sensitivity is 97%, and the specificity 78%.
- The use of the "calcium-induced calcium release" test -in addition to the CHCT to make the test more specific.

Non invasive test is:

- Intramuscular injection of halothane 6 vol% has been shown to result in higher than normal increases in local pCO2, among patients with known malignant hyperthermia susceptibility.
- Intramuscular injection of caffeine was followed by local measurement of the pCO2; those with known MH susceptibility had a significantly higher pCO2 (63 versus 44 mmHg).

Genetic testing:

- is being performed in a limited fashion to determine susceptibility to MH. In people with a family history of MH, analysis for RYR1 mutations may be useful.

Indications for Muscle Biopsy Testing for MH

- Suspicious clinical history for MH,
- First degree relative of a proband (index case) with a clinical history of MH if the proband cannot be tested (e.g, too young, too old, MH death, not willing to undergo the muscle biopsy, no test centre available),
- Family history of MH where genetic testing is negative for mutation,
- Severe masseter muscle rigidity after succinylcholine administration that is associated with myoglobinuria and/or marked CK elevation ,

Possible Indications:

- Unexplained rhabdomyolysis during or after surgery (may present as sudden cardiac arrest due to hyperkalemia),
- Moderate to mild masseter muscle rigidity with evidence of rhabdomyolysis,
- Exercise-induced rhabdomyolysis Probably Not Indicated Sudden unexpected cardiac arrest during anesthesia ,or early postoperative period not associated with rhabdomyolysis.
- Age less than 5 years or weight less than 40 pounds (insufficient muscle mass)
- Neuroleptic malignant syndrome

North-American Protocol

- Sensitivity of 97% specificity of 85 %• a contracture of ≥ 0.5 g (force) in response to exposure to halothane is considered positive, and a contracture of ≥ 0.3 g in response to 2 mm caffeine is considered positive
- Based on this test, a patient can be categorized as one of the following:MHS -- muscle contracture occurs with both halothane and caffeine; MH-equivocal -- muscle contracture occurs with caffeine or halothane, but not both; or M H-negative -- muscle contracture does not occur with either agent.
- Attempts to enhance the sensitivity, such as measuring the muscle contracture response to ryanodine and to chloro- cresol, have been introduced, and these agents have been somewhat successful in clarifying equivocal cases.
- CHCT (Caffeine Halothane Contracture test)…This is a compilation of a response to 3% halothane taken from an MH patient.
- Three pieces of muscle are shown.
- The muscle is stimulated every 10 seconds and the contraction force is measured and displayed as a quick upstroke.
- When halothane is introduced, a sustained increase in muscle tension is noted, termed a contracture.
- In the top bundle, a 1.2-g contracture is noted.
- A normal response is a contracture of less than 0.5 g
- CHCT• Also positive in central core disease and hypokalemic periodic paralysis.

Clinical Picture of Malignant Hyperthermia

- First clinical case published in 1960 in LANCET, by Denborough and Lovell.
- Association with porcine stress syndrome and malignant hyperthermia

described in early 1970 – the clinical picture of which resembles with malignant hyperthermia in animal model when potent triggering agent is administered.

Clinical picture:

- A hyper metabolic disorder of skeletal muscle.
- Clinical presentation is highly variable and it depends on species, breed, genetic make up, and triggering agents.
- Time of onset : unpredictable, varying from within minutes to several hours of induction; it may even occur in post operative period in the recovery room.
- The most potent triggering agent appear to be induction of anaesthesia with halothane followed by administration of succnylcholine.
- The symptoms appear almost immediately.Presentation is gradual and delayed in onset after the induction with new halogenated anaesthetic agents.

Signs and symptoms

- Tachycardia : one of the earliest but a non specific sign.
- Tachypnea : in spontaneously ventilating patients.• Increased sweating.
- Increased body temperature : late and serious sign of MH and may not be present at the time of the diagnosis.
- During fulminant acute MH, body temperature may increase at a rate of 1.8–3.6°F (1–2°C) every 5 minutes.
- Cyanosis, flushing or blanching of skin.
- Cola coloured urine• masseter spasm or generalised muscle rigidity or both.
- Capnogram – Gradually increasing EtCO2 not related to other possible causes.
- The earliest , the most sensitive and specific sign of M.H Excessive heating and rapid exhaustion of CO2 absorber.
- Other possible causes: Hypoventilation Other causes of Hyper metabolism,
- Partial airway obstruction Absorption of CO2 from exogenous source equipment malfunction.
- Biochemical parameters..
- Respiratory with or without metabolic acidosis.– Hypercarbia– Hyperkalemia– Hyper calcemia– Hyper phosphatemia.– Lacticacidemia.– Myoglobinuria.
- Increase in creatinine kinase: neither a constant feature nor signifies increase muscle metabolism in intra operative period– Abnormal coagulation tests ,

Outcome

- Mortality un acceptably high.
- Mostly due to failure to recognize the syndrome in the early phase.Earlier death rates were 80%
- Now come down to < 5% after introduction of dandrolene sodium.
- There is 25% recrudescence rate in 1st 24- 36 hrs.
- Even after successful treatment there may be prolonged muscle pain and weakness (chronic slowly progressive myopathy) for which physical rehabilitation may be necessary.
- Dysarrythmia from markedØDeath results from…. sympathetic stimulation and Severe spasm makingØHyperkalemia intubation and ventilation Myoglobinuric renal failure¬impossible Ø Disseminated intravascular coagulation.Ø(acute tubular necrosis).
- Multi organ failure when core temperature is¬Neurological damage. elevated beyond critical temperature (>43 deg c).

Diagnosis

Tests that may be done include:

Blood clotting studies (PT, or prothombin time; PTT, or partial thrombloplastin time)

Chem-20, including CPK (creatinine phosphokinase, a muscle protein destroyed during the acute illness)

Genetic testing to look for defects in the RYR1 gene

Muscle biopsy

Urine myoglobin (muscle protein) determination

- Muscle rigidity (generalized rigidity including severe masseter muscle rigidity),
- Muscle breakdown (CK >20,000/L units, cola colored urine or excess myoglobin in urine or serum, potassium above 6 mmol/l),
- Temperature increase (rapidly increasing temperature, T >38.8°C),
- Other (rapid reversal of MH signs with dantrolene, elevated resting serum CK levels),
- Family history (autosomal dominant pattern).

Diagnosis of an Attac During Anesthesia

The earliest signs are:

- early Masseter Muscle Contracture following administration of Succinylcholine,
- a rise in End-Tidal Carbon Dioxide Concentration (despite increased minute ventilation),
- unexplained Tachycardia,
- muscle Rigidity,
- tachypnea (in a spontaneously breathing patient),
- cyanosis,
- hypertension,
- cardiac dysrhythmias ,
- Hyperthermia -Temperature increase (rapidly increasing temperature, T >38.8°C)

So, Core body temperatures should be measured in any patient undergoing general anesthesia longer than 20 minutes. Blood Tests shows:

- Hyperkalemia- above 6 mmol/l
- increased Phosphate (leading to decreased Calcium) and—if determined—raised Myoglobin;
- Metabolic acidosis and Respiratory Acidosis
- a raised Creatine Kinase level (CK >20,000/L units)
- Muscle breakdown (CK >20,000/L units),
- cola colored Urine or excess myoglobin in urine or serum,
- Severe Rhabdomyolysis may lead to acute renal failure, so kidney function is generally measured on a frequent basis.

Differential Diagnosos

- Pheochromocytoma,
- Thyrotoxicosis (thyroid storm)
- Sepsis
- Transfusion reactions (acute haemolytic and non haemolytic)
- Allergic reactions
- Central nervous system dysfunction (pontine hge, hypoxic ischemic

encephalopathy etc.)
- Neuroleptic malignant syndrome,
- Alcohol withdrawal,
- Drug interactions (MAOI and meperidine)
- Differential Diagnosis- Thyrotoxicosis Pheochromocytoma :MH -MH Thyrotoxicosis -Pheochromocytoma↑ ETCO2 (End Tidal CO2)↑ ETCO2 +++ +++ ++ ++ ++ ++↑ HR↑ HR +++ +++ +++ +++ +++ +++↑ BP↑ BP + + ++ ++ +++ +++RigidityRigidity ++ ++ +/- +/- --AcidosisAcidosis +++ +++ -- + +

Diseases associated with MHS

- Central core disease.
- Multicore myopathy or Evan's myopathy or MH myopathy.
- King Denborough syndrome.
- Rhabdomyolysis, but not- MH,
- Brody's disease
- Deficient calcium adenosine triphosphatase
- McArdle's disease
- Myophosphorylase B deficiency
- Dystrophinopathies and other abnormalities of the structural proteins in the muscle membrane there is chronic elevation of CK indicating chronic rhabdomyolysis,
- Post operative myoglobinurea may be the only sign of M.H without any other sign of increased muscle metabolism,- But d/d (day doses) of post operative myoglobinurea is large.

Anesthesia for the Patints Susceptible to MH

- Patients susceptible to MH can be safely anesthetized using non triggering agents• primary regional anaesthetic technique is also appropriate when feasible, all local anaesthetic are considered safe.
- Core temperature and minute ventilation should be monitored closely in all patients.
- To "clean" the anaesthesia machine and ensure that the patient will not be exposed to trace anaesthetic gases.
- To use fresh anaesthetic circuit..and use of vaporizer free machine if possible.
- Flushing the anaesthesia machine with high-flow oxygen (at least 10 L/

minute) for 20 minutes,
- Placing tape over the vaporizer canisters to avoid accidental administration
- The re breathing bag should be attached to the distal end of the ventilator circuit with at least 5 ventilator cycles per minute during the 20- minute flushing.
- The CO2 absorber should be replaced with a fresh absorber
- Dantrolene is not required prophylactically but should be readily available.
- Postoperative observation for 4 hours is recommended for patients

Anesthetic Protocol of different Myopathy or Myotonic Disorders

- The anaesthetic protocol of different myopathy or myotonic disorders and M.H are more or less same.
- But what differs….is that..:
- The implications of a diagnosis of X-linked myopathy, myotonia, or autosomal-dominant ryanodine receptor mutation that are quite different for the rest of their family.

A very much related condition

- Masseter muscle rigidity (MMR).• Defined as jaw ms rigidity along with limb ms flaccidity after administration of succinylcholine (scch) impeding intubation and persisting for > 2 mins.
- MMR may be the first sign of MH, or it can develop during an MH episode. However, it may also occur as an exaggerated response to succinylcholine (scch) in normal individuals.
- Slow tonic fiber of masseter and lateral pterygoid ms responds to depolarising ms relaxant with contracture, the reason of development of MMS (masseter muscles spasm).
- May occur even after pretreatment of defasciculating dose of NDMR (non depolarising muscle relaxant).
- The most common response to succinylcholine is "jaw stiffness" that is subclinical and can only be detected using special measuring devices. This is a normal response to succinylcholine and is considered to be of no prognostic significance with respect to MH.
- A greater increase in masseter spasm (MMS) is called "jaw tightness that interferes with intubation." This group may be quite large (1–2%) in children who are administered halothane and succinylcholine.

- A small but unknown number of these patients are at risk for MH.
- The most severe form of masseter muscle spasm has been characterized as "the mouth could not be opened" or "jaws of steel." This group is documented to have an increased incidence of fulminant MH and increased mortality if the triggering agents are continued.
- MMS may occur in normal persons. 30% of patients with MMS prove to be MH susceptible. Additional signs increase likelihood of MH 50 – 60% if metabolic signs present, 70 – 80% if muscle signs present,
- May be the first indication of previously unsuspected muscle disease particularly myotonic conditions..
- If possible abandon surgery
- Otherwise choose to MH safe technique,
- Allow 15 min to get the patient stabilised..monitor ETCO2, temperature, and consider arterial line,
- Investigate: blood for CK within 24 hr period, and first voided urine for myoglobin
- But the scale lacks sensitivity and early termination of crisis would not yield sufficient score indicative of malignant hyperthermia.
- Patients rated D6 are encouraged to go for ms biopsy test.

Who ansthetic drugs are safe?

Other anesthetic drugs are considered safe. These include local anesthetics (lidocaine, bupivacaine, mepivacaine), opiates (morphine, fentanyl), ketamine, barbiturates, propofol , etomidate, benzodiazepines. The nondepolarizing muscle relaxants pancuronium, cisatracurium, atracurium, mivacurium, vecuronium and rocuronium also do not cause MH. There is mounting evidence that some individuals with malignant hyperthermia susceptibility may develop MH with exercise and/or on exposure to hot environments.

- Local anaesthetics
- Droperidol

Acute management of an MH crisis

1. Declare crisis: Call for help, MH cart
2. Notify surgical team: Determine best time to abort procedure, assist with active cooling of patient,
3. Stop exposure to triggering agents: Discontinue volatile agents, hyperventilate

with high fresh gas flows using 100% oxygen. termination of use of volatile anaesthetics and succinylcholine. removal the **vaporizer** and use of new circuit.• flushing the anaesthesia machine with high-flow oxygen (at least 10 L/minute) for 20 minutes,

4. Do not change anesthesia machine.
5. Switch to nontriggering anesthetic technique: total IV anesthesia.
6. Administer 2.5 mg/kg of dantrolene in repeated doses based on clinical and laboratory response.
7. Each vial contains 20 mg of Dantrolene and 3 g of Mannitol.
8. Mix with only preservative-free sterile water.
9. Obtain additional peripheral or central venous access, as indicated.
10. Place arterial catheter for continuous monitoring of hemodynamics and vascular access for frequent blood sampling.
11. Place Foley catheter to monitor urine output.
12. Initiate and continue active cooling of patient as indicated.
13. Address metabolic and electrolyte derangements.
14. Transfer to intensive care unit for further treatment and continuation of dantrolene.

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Treatment with Dandrolene

1. Dantrolene sodium was first introduced in 1979 as an injectable antidote for acute MH. Prior to that time, the drug was available in an oral formulation for use as an adjunct in the treatment of muscle spasticity associated with spinal cord injury or cerebral palsy,
2. Dantrolene sodium inhibits the release of calcium from the SR (sarcoplasmatic reticulum) by binding to RYR1 and reverses the effects of MH i.e uncouples depolarisation with contraction. Fast contracting twitch ms are affected more than slow contracting antigravity ms (musculo-sceletical).
3. Administration of 2-3 mg/kg dantrolene intravenously. Repeat every 5 –10 min up to 10 mg/ kg , till metabolic symptoms are controlled,
4. After initial stabilization, Continue intravenous dantrolene for at least 24

h after control of initial episode (approximately 1 mg/kg q 6 h). Watch for recrudescence by monitoring in an intensive care unit (ICU) for 36 h. Recrudescence occurs in about 25% of MH cases,

5. Dose : 2- 3 mg /kg initially.. To be repeated every 5 – 10 min upto 10 mg/kg to control clinical signs of hypermetabolism,
6. To continue upto 24- 48 hrs to prevent recrudescence and worsening of rhabdomyolysis.,
7. Generally safe in clinically recommended dose,
8. Has no effect on cardiac or smooth muscle,
9. Side effects include:
   - nausea, malaise, light headedness,
   - muscle weakness,
   - irritation and phlebitis at the intravenous site due to the high pH of the drug,
   - Hepatotoxicity after long term oral use of the drug,
   - Respiratory muscle weakness may occur when large doses are used or whenadministered to patients with an neuromuscular disorder.

Azumolene

- Is a 30-fold more water-soluble analogue of dantrolene that also works to decrease the release of intracellular calcium by its action on the ryanodine receptor.
- In MH susceptible swine, Azumolene was as potent as Dantrolene.
- It has yet to be studied in vivo in humans, but may present a suitable alternative to dantrolene in the treatment of MH.
- Azumolene has also been shown to be as effective as dantrolene at preventing and reversing contracture in in vitro experiments with human skeletal muscle.
- Furthermore, elucidating earlier ideas on the pathogenesis of malignant hyperthermia, researchers point out that it may be “as much a syndrome of exaggerated Ca2+ entry as it is of exaggerated Ca2+ release.

ICU Treatment (Reanimation Room Treatment)

1. Monitor core temperature, electrocardiogram, arterial blood pressure, and urine output.

2. Active surface cooling , naso gastric and rectal lavage with cold saline but avoid overcooling to body temp < 38 deg. c
3. Adequate Hydration with saline preferably cold.•
4. Management of acidosis with i.v bicarbonate 1-2 meq/kg iv if not rapidly improved with dantrolene.•
5. Maintenance of urine output with mannitol (0.25 gm/kg iv) and loop diuretics (frusemide 1 mg/kg iv). Forced alkaline diuresis.
6. Correction of Hyperkalemia with glucose-insulin, and calcium.
7. Cardiac dysarrhythmia usually responds to correction of Hyperkalemia acidosis. Persistent **arrhythmias** may be treated with standard anti arrhythmic like procainamide or lidocaine,
8. CCB s (Calcium Channel Blocker) should not be preferably used,
9. Continue intravenous dantrolene for at least 24 h after control of initial episode (approximately 1 mg/kg q 6 h),
10. Watch for recrudescence by monitoring in an intensive care unit (ICU) for 36 h. Recrudescence occurs in about 25% of MH cases,
11. Ensure adequate urine output by alkaline diuresis because myoglobinuria is common,
12. Follow coagulation profile watching for the occurrence of disseminated intravascular coagulation (DIC),
13. Measure creatine kinase (CK) every 6 h until falling then at least daily until normal. CK may remain elevated for 2weeks. To be kept in mind that baseline CK may be elevated in some patients post operatively,
14. Counsel patients and families regarding testing and future anaesthetics.

Possible Complications

- Amputation
- Breakdown of muscle tissue (rhabdomyolysis)
- Compartment syndrome (swelling of the hands and feet and problems with blood flow and nerve function)
- Death
- Disseminating intravascular coagulation (abnormal blood clotting and bleeding)
- Heart rhythm problems
- Kidney failure
- Metabolic acidosis
- Respiratory dysfunction (fluid buildup in the lungs)
- Weak muscles (myopathy) or muscular dystrophy (deformity)

Prognosis

Prognosis is poor if this condition is not aggressively treated. In the 1970s, mortality was greater than 80%; with the current management, however, mortality is now less than 5%. Repeated episodes or untreated episodes can cause kidney failure. Untreated episodes can be fatal.

Prevention

- If you or anyone in your family has malignant hyperthermia it is very important to tell your doctor, especially before having surgery with general anesthesia.
- Using certain medications can prevent the complications of malignant hyperthermia during surgery.
- Avoid stimulant drugs such as cocaine, amphetamine (speed), and ecstasy. These drugs may cause problems similar to malignant hyperthermia in people who are prone to this condition.
- Genetic counseling is recommended for anyone with a family history of myopathy, muscular dystrophy, or malignant hyperthermia.

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Her2 In Gastric Cancer In Albania

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General background

Gastric cancer (GC) is the fourth most common cancer in Albania. HER2-positivity rates in GC are reported with a wide range. There is no data for it in Albania.

Materials and method

A total of 192 patients, with primary GCs was retrospectively analyzed for HER2 overexpression by IHC. Dual SISH, was used in only 20 GCs with equivocal results. We dispersed HER2 results by: gender and age, histopathological diagnosis and stage, type of the specimen. The results were compared.

Results

We examined by IHC 73.4% (141 cases) surgical and 26.5% endoscopic biopsies: 18.4% (26 cases) and 15.7% (8 cases) HER2 3+, respectively. HER2 overexpression (3+) was detected in 17.7% (34 cases). HER2 equivocal (2+) was detected in 24.5% (47 cases). 17.8% , 14%, 4.7% were respectively intestinal type, diffuse, signet ring and the rest adenocarcinoma NOS. GC prevailed in the group age of 61-70 yrs

(31.70%;), followed by 51-60 yrs (25%), 22.9% in 71-80-yrs. 20 cases analyzed by SISH, showed Her2 amplification in 40% (8cases). Economical restrictions and problems with preanalytical phase made it impossible to evaluate by SISH all 20 cases.

Conclusion

17.7%of Albanian patients with primary GC were HER2-positive on IHC. There is no difference in biopsy and surgical specimen results. Economical restrictions can influence the results.

General background

Gastric adenocarcinoma is one of the most frequent neoplasms in the world. Its incidence varies from country to country, having higher incidences in Japan, Chiles, Finland, and a low incidence in Thailand and in most parts of Africa. In United States, the incidence of gastric cancer has decreased during the last 50 years and actually it has an incidence of 10 cases per 100 000 inhabitants.[1]

In Albania, in 2008, the population was 3,170,048. According to INSTAT 45% of the population lives in the urban areas, 55% lives in the rural areas. The median survival age is 72.1 years for males and 78.6 years for females (2005-2008). Gastric cancer has a survival rate of 5 years of approximately 5-20%. Yet, there is no standard chemotherapy for patients with gastric cancer in the world.

In patients without metastasis and with tumors resectable by surgery, the main therapy (with curative purpose) is surgical excision, followed by chemotherapy or radiotherapy, according to the stage and type of tumor. The carcinomas of the antrum, body and fundus can be divided in two main histologic types: intestinal and diffuse (Lauren classification) which have different causes, different precursor lesions and different growth rates. [4]

The terminology used and the histopathologic evaluation have interobserver subjectivity mostly for two important elements of carcinogenesis, that are, atrophy and dysplasia. Microscopically, even in the early gastric cancer, also in the advanced forms, the histologic aspect is similar, with glands being from well differentiated, to moderately and poorly differentiated. There is also a subtype with cells with the aspect of "signet ring".[3] There aren't yet specific molecular markers for the diagnosis of gastric cancer, even though the later is rarely a challenge for the pathologist. The amplification of HER2/Neu seems to be a marker of the ability to metastasize and a marker of poor prognosis. This can result in an effective target for the therapies with molecular base. [2]

Materials and method: We have conducted an epidemiologic study on the status of HER2 in gastric cancer in our country. This is a retrospective and prospective study, that consists in the collection of 192 cases (paraffin blocks) of endoscopic biopsy specimens, but also in surgical specimens of two central laboratories of Pathologic Anatomy (Laboratory of Morphologic Diagnosis and the Central Laboratory of Pathologic Anatomy, NUHC "Mother Theresa"). All the samples were examined for the expression of HER2 with immunohistochemical method and some with HER2/SICH. We have analized the data of the pathologic reports to check the correlation between the presence of HER2 expression and clinical-pathologic features. The immunohistochemical exam is performed with the manual method with the antibodies HercepTest™ (Dako), but also with the automatized method with BenchMark XT with the antibody anti-HER-2/neu (4B5) Rabbit Monoclonal, also SISH utilizing INFORM HER2 DNA Probe. All the data were analized utilizing Microsof Excel.

Results: From 192 cases examined, the demographic data show a median age of approximately 58.4 years, predominantly of the group age 6-71 yo (Table 1). In all the cases examined, 69 cases (35%) were endoscopic samples and 123 cases (65%) were surgical specimens. 9 cases (4.7%) were T4, 91 cases (47.4%) were T3, 23 cases (11.98%) were T2 and 69 cases (35%) had no tumor stage (corresponding to endoscopic biopsies). From all the cases examined with immunohistochemistry for HER2, HER2 0 was found in 53 cases, HER2 1+ in 57 cases, HER2 2+ in 47 cases and HER2 3+ in 34 cases. In 47 cases that resulted HER2 2+ (equivocal), which were impossible to be defined with immunohistochemistry for the status of amplification of HER2 gene, we have performed SISH for 20 cases, with the following results: SISH positive in 8 cases (17%) and SISH negative in 12 cases (15.5%) (table 2).

After correlating the histologic subtype with HER2 expression, it resulted that poorly differentiated adenocarcinomas (G3) had overexpression of HER2 (Her2 3+) more than well differentiated ones (G1) (respectively 23.5% vs.11.7%). Mucinous adenocarcinomas mostly have no amplification of HER2 gene, respectively 15.2% Her2 0 and 3.5% Her2 1+, and zero cases with Her2 3+. Similar data are also for the carcinoma with signet ring cells, 2.9% of which being Her2 3+ and 8.4% Her2 0.

Also, even though intestinal type adenocarcinomas have a favorable prognosis in comparison to diffuse subtype, in our study, 8.8% of the cases with intestinal type cancer had amplification of HER2 gene and 20.4% of diffuse infiltrative carcinomas don't have amplification of HER2 gene (table 3).

After correlating the expression of HER2 with pathologic stage, we found no significant difference between the stage and expression of HER2 (HER2 3+) in our study ((T4 2.9%, T3 35.3%, T2 8.8% and 52.5% not specified).

TABLE 1,2,3 of median age, dispersion of Her2 and correlations with the histologic type and stage.

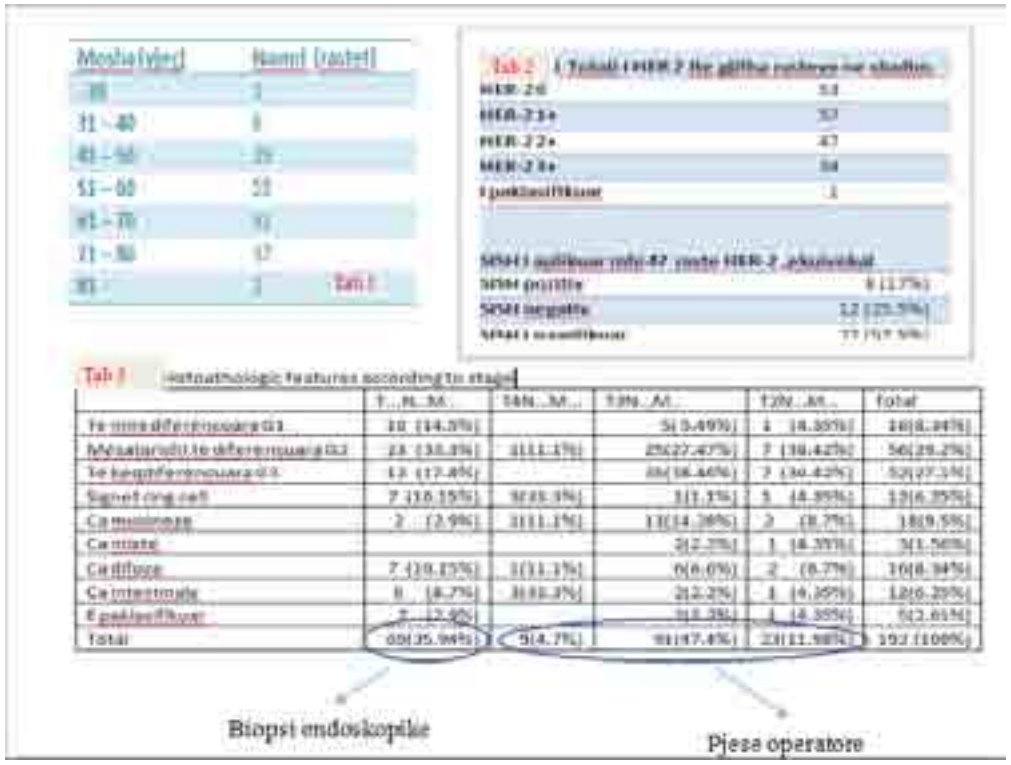
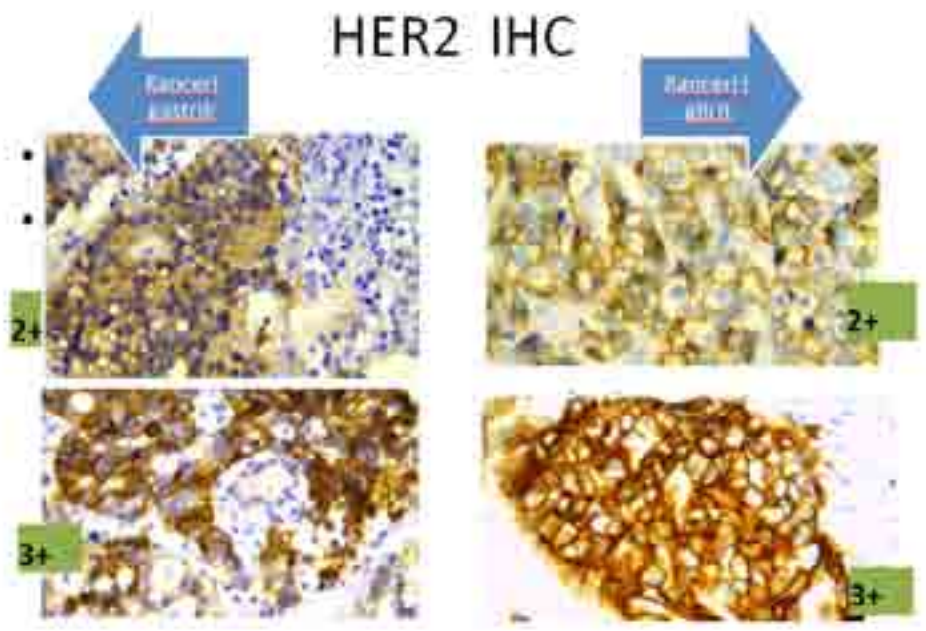


FIGURE 1 Correlation of HER2 expression in endoscopic samples and surgical specimens.

Discussion: In patients with gastric cancer and gastroesophageal cancer, the amplification of HER2 identifies the patient that will benefit from therapy with Trastuzumab. The evaluation of HER2 status is, however, influenced by the preanalytic and postanalytic parameters, as reported also for breast cancer. [2]

In a study of Kapelessor et.al, from 5426 tissue fragments examined with microprobes, HER2 was found mostly expressed in intestinal type and in the cancers of low grade and had no correlation with the age, gender, stage, and tumor location. Even in a study of Moelans CB and co., it was seen a low expression of HER2 in early gastric cancer. In our study the data are different, with amplification found in poorly differentiated subtypes and intestinal subtype. The abovementioned data can be explained with the biologic characteristics of gastric cancer in our country, or, another hypothesis, can be also not standardized protocol of TNM reporting system that produces variables that can influence the result. However, 17,7% of our cases express HER2 and can be a group that can benefit from targeted therapy. [5]

FIGURE 2 The difference of expression of HER2 in gastric cancer and breast cancer.



The evaluation of HER2 is done utilizing microscopic examination through a semiquantitative method, based in the intensity of staining of the nuclear membrane, also the stain of the entire perimeter of this membrane. There is a difference of evaluating HER2 in the materials from breast cancer and gastric cancer. This difference is reflected also in the guidelines published for this exam. [6]

In endoscopic biopsies, which are small biopsies with crush artifacts, especially in the periphery of the tissue, with inflammatory infiltrates, HER2 score can be influenced by artifactual changes. Even in the guidelines, there is a difference of interpretation of small endoscopic biopsies and surgical specimens. In our study there is no significant difference of expression of HER2 (HER2 3+) among endoscopic biopsies and surgical specimens (respectively 15 and 19 cases, figure 2). In gastric cancer, the status of HER2, at least partially, is influenced by the variation in the methodology used, in the instruments and the experience of the technician that perform the test. [7]

One of the main reasons of our study in both labs was exactly the quality control done utilizing the comparison of the results among the laboratories and the methods used by each. In one study of Rüschoff J et al., there is a variability between immunohistochemistry and SISH. [8]

In one study of Mrklic et al., to evaluate HER2 in gastric cancer and its scoring system and to standardize the method, the results of IHC method were compared to SISH, not only inside the laboratory, but also among different centers that have participated in this study. [9]

Conclusion: The examination of HER2 is performed from nearly a decade in Albania, mostly for gastric cancer. It has changed from manual to automatized method. Mostly, this exam was performed only in one laboratory that was the central laboratory of immunohistochemistry. actually, new centers are being developed. HER2 is expressed approximately in 30% of the patients with breast cancer and in 17.7% of the patients with gastric cancer. Sharing the methodology among the laboratories will improve quality assurance for HER2 testing.

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HER2 testing in gastric cancer: a practical approach Josef Rüschoff[1,2], Wedad Hanna[3], Michael Bilous[4], Manfred Hofmann[2], Robert Y Osamura[5], Frédérique Penault-Llorca[6], Marc van de Vijver[7] and Giuseppe Viale[8]

Esbl (Extended Spectrum Beta Lactamase) Infections - An Emerging Problem in Children

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Background and aims

There is an emergence of infections with ESBL-producing micro-organisms recently. They remain poorly characterised in children. We sought to characterise children in a teaching hospital from whom an ESBL-producing organism had been isolated.

Methods

We identified all children under sixteen years of age who had ESBL-producing organism isolated in the year 2016 in children admitted to pediatric hospital at University Hospital centre "Mother Theresa", Tirana. The referral source was contacted for further information where possible. Clinical details and treatment were analysed to determine likelihood of infection or colonisation.

Results

Fifteen children were identified, aged three months to nine years. Thirteen isolates were obtained from urine, one each from a wound swab and a cough swab. Three isolates were obtained from hospitalised children, but only one of these needed treatment. This child presented with lymphadenitis and continued to be pyrexial and irritable despite treatment with cephalosporin. Subsequently ESBL producing organism was isolated from the urine and she responded to appropriate antibiotic. Data was available for nine out of twelve patients originating from the community. Of these, four had repeat specimens which didn't grow ESBL-producer again. Three were treated and two remained asymptomatic and well.

Conclusions: ESBL-producing organisms are increasingly isolated in children, but from our review appear frequently to be colonisers rather than pathogens. However, it is very important to be vigilant about the possibility of ESBL infection in children especially if they fail standard antibiotic therapy.

Introduction

Resistance of Gram-negative bacteria to antibiotics has increased at an alarming pace over the last two decades, particularly the emergence of Enterobacteriaceae resistant to third-generation cephalosporins and aztreonam1 which is commonly associated with the expression of extended-spectrum beta-lactamases (ESBLs) (1). These enzymes confer resis ance to nearly all beta-lactam antibiotics such as ceftazidime, cefotaxime, ceftriaxone, monobactam – aztreonam, and related oxyimino beta-lactams (2). If Enterobacteriaceae are resistant to one of the extended-spectrum cephalosporins, it means they are therapeutically resistant to all the cephalosporins even though antimicrobial sensitivity is indicated in the laboratory test results (3). Moreover, many ESBL-producing Enterobacteriaceae are also resistant to other antimicrobial agents such as aminoglycosides, trimethoprim, and the quinolones which poses a serious antibiotic management problem as the genes for ESBL production are easily transferred through plasmids (4). ESBL-producing Enterobacteriaceae have worldwide distributions with varying degree of prevalence in community as well as hospitals (5). Nowadays, infections due to ESBL-producing Enterobacteriaceae are concerning for many reasons including increased hospital costs, length of stay, and mortality rates (6). For the pediatric population, blood stream infections and urinary tract infections (UTIs) due to Enterobacteriaceae resistant to ESBL are an emerging problem.1 This alerts clinical microbiologists to identify these ESBL-producing organisms parallel to

antimicrobial susceptibility testing even in resource-limited settings by applying simple screening and confirmatory methods. Data obtained from such methods are so valuable to develop appropriate institutional-based drug therapy guieline (7). Though various phenotypic ESBL detection methods have been described, implementation of highly sensitive and specific methods in resource-limited areas is challenging yet. Infections caused by ESBL- or plasmid-mediated AmpC-producing Enterobacteriaceae are often treated by carbapenems (e.g., ertapenem, imipenem, meropenem, and doripenem) which are antimicrobials of last resort and crucial for the management of life-threatening health care-associated infections. However, due to recent emergence and spread of imipenem/meropenem-resistant Enterobacteriaceae throughout the world, clinical utility of this group of antibiotics is under threat. Production of carbapenemases that are capable of hydrolyzing the carbapenems and loss of outer membrane proteins are major mechanisms through which Enterobacteriaceae develop resistance against this group of drugs (8). The aim of the study was to estimate the frequency of ESBL-producing organism.

Materials and methods

We identified all children under sixteen years of age who had ESBL-producing organism isolated in the year 2016 in children admitted to pediatric hospital at University Hospital centre "Mother Theresa", Tirana. The referral source was contacted for further information where possible. Clinical details and treatment were analysed to determine likelihood of infection or colonisation. Demographic characteristics of the patients were recorded using predesigned sheets after obtaining informed consent. From the UTIs-suspected children, first morning mid-stream urine samples were collected using sterile wide-mouth container. The study participants' parents/guardians were given appropriate instructions before providing urine samples. Urine specimens immediately after collection were brought to microbiology laboratory for bacterial analysis.

Culture and identification

Enterobacteriaceae were classified to species levels using triple sugar iron, indole, citrate, urea, lysine decarboxylase, and motility. After identification, each Enterobacteriaceae was subjected to ESBL and carbapenemase detections as per Clinical and Laboratory Standards Institute (CLSI) and European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines.11,12

Drug susceptibility patterns

The disk diffusion was performed, and after 16–18 hours of incubation at 37°C, zone of inhibition was measured and interpreted as recommended by the CLSI.11 Using a sterile wire loop, three to five pure colonies were picked from MacConkey agar and emulsified in nutrient broth. Standard inoculums adjusted to 0.5 McFarland using McFarland Densitometer were swabbed onto Muller-Hinton agar (dispensed on 100 mm plate). Drug susceptibility testing of all Enterobacteriaceae was performed using disk diffusion method against amoxicillin (30 µg, BD), amoxicillin-clavulanic acid (30 µg, BD), chloramphenicol (30 µg, BD), gentamicin (10 µg, BD), sulfamethoxazole-trimethoprim (1.25 µg, BD), cefotaxime (30 µg, BD), cefoxitin (30 µg, Oxoid), tetracycline (30 µg, BD), nitrofurantoin (300 µg, BD), norfloxacin (5 µg, BD), imipenem (10 µg, Oxoid), and meropenem (10 µg, Oxoid). In this study, multidrug resistance was defined as simultaneous resistance to two or more drugs of different classes of antimicrobial agent.

ESBL detection

Initial screening of Enterobacteriaceae for ESBL was done based on diameters of zone of inhibitions produced by ceftazidime (30 µg, BD), ceftriaxone (30 µg, BD), and cefotaxime (30 µg, BD) according to the CLSI screening criteria. The breakpoints indicative of suspicion for ESBL production were ≤22 mm for ceftazidime, ≤25 mm for ceftriaxone, and ≤27 mm for cefotaxime. A combined disk method was used as a confirmatory phenotypic method for ESBLs detection according to CLSI. Ceftazidime (30 µg, BD) and cefotaxime (30 µg, BD) disks alone and their combinations with clavulanic acid (30 µg/10 µg) were used for phenotypic confirmations of ESBLs presence. A ≥5 mm increase in zone diameters for either of the cephalosporin disks or their respective cephalosporin/clavulanate disks was interpreted as ESBL producer. Double-disk synergy method was compared against combination disk method for detection of ESBL to know if it was the best suitable phenotypic method in resource-limited routine bacteriology laboratory. The antibiotic disks used were ceftriaxone (30 µg, BD), cefotaxime (30 µg, BD), ceftazidime (30 µg, BD), aztreonam (30 µg, BD), and amoxicillin/clavulanic acid (20/10 µg, BD) according to EUCAST.12 The four antibiotics were placed at distances of 20 mm edge to edge from the amoxicillin/clavulanic acid disk that was placed in the middle of the plate. After 24 hours of incubation, if an enhanced zone of inhibition between either of the cephalosporin antibiotics and the amoxicillin/clavulanic acid disk occurred, the test was considered as ESBL positive.

Results and Discussion

Fifteen children were identified, aged three months to nine years. Thirteen isolates were obtained from urine, one each from a wound swab and a cough swab. Three isolates were obtained from hospitalised children, but only one of these needed treatment. This child presented with lymphadenitis and continued to be pyrexial and irritable despite treatment with cephalosporin.

Enterobacteriaceae were isolated from urine specimens. Majority of Enterobacteriaceae (69.2%, n=9/13) were isolated from urine cultures. The most frequent isolates were K. pneumoniae (30.8%) and E. coli (23.1%).

Other Enterobacteriaceae isolates were Morganella morganii and Enterobacter aerogenes. All Enterobacteriaceae showed the highest resistance to amoxicillin (89.1%), sulfamethoxazole-trimethoprim (83.6%), and cefotaxime (85.5%), and least resistance to nitrofurantoin (36.9%), imipenem (12.2%), and meropenem (14.6%). The frequent isolates K. pneumoniae (57.57%, n=19/33) showed the highest resistance to cefotaxime(100%), amoxicillin (94.7%), amoxicillin-clavulanic acid (89.5%), sulfamethoxazole-trimethoprim (89.5%), and gentamicin (89.5%). They showed the lowest resistance to imipenem (10.5%), meropenem (15%), and norfloxacin (15.8%) compared to the other tested drugs. In our study, cefotaxime was least effective (100% resistance) against K. pneumoniae (57%,), M. morganii.

Subsequently ESBL producing organism was isolated from the urine and she responded to appropriate antibiotic. Data was available for nine out of twelve patients originating from the community.

Of these, four had repeat specimens which didn't grow ESBL-producer again. Three were treated and two remained asymptomatic and well.

Inappropriate and incorrect administration of antimicrobial agents in empirical therapies, lack of appropriate infection-control strategies which can cause a shift to increase in prevalence of resistant organisms in the community, and the selective pressure created for the use of third-generation cephalosporins have been described as most important factors in the appearance of ESBL-producing strains, though many reasons can be responsible and mentioned (9).

All ESBL-positive *Enterobacteriaceae* showed the highest resistance to amoxicillin (89.1%), sulfamethoxazole-trimethoprim (83.5%), and cefotaxime (85.5%). It means that the use of these antibiotics for the treatment of infection caused by ESBL-producing strains may result in failure in significant proportion of cases. The choice of antibiotic agents effective against ESBLs-producing species is currently limited, which may cause serious therapeutic problems in the future (10). In our study, the organisms were only susceptible to norfloxacin (63.9%) and cefoxitin (50%) compared to other commonly tested drugs.

Conclusion

The increasing frequency of ESBL-producing Enterobacteriaceae among children is an important problem for both microbiologists and clinicians. In resource-limited settings, double-disk synergy method can be implemented for screening and confirming ESBL production that might give valuable information for appropriate antibiotics selection and controlling the spread of ESBL-positive Enterobacteriaceae. However, it is very important to be vigilant about the possibility of ESBL infection in children especially if they fail standard antibiotic therapy.

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