Advances in Biology & BioMedicine

www.advancejournals.org
Open Access Scientific Publisher

Research Article

HAEMATOLOGICAL AND BIOCHEMICAL PERTURBATIONS RELATED TO CARDIOVASCULAR DISEASES SEEN IN THE UNIVERSITY HOSPITAL CENTER OF BEFELATANANA ANTANANARIVO MADAGASCAR

Zafindrasoa Domoina Rakotovao Ravahatra[1], Miora Koloina Ranaivosoa[2], Fidiniaina Mamy Randriatsarafara[3], Andriamiadana Luc Rakotovao[1], Andry Rasamindrakotroka[4]

[1]Laboratory Unit of University Hospital Center Joseph Raseta Befelatanana Antananarivo, Madagascar
[2]Paraclinical Training and Biochemistry Research Unit of The Joseph Ravoahangy Andrianavalona, University of Antananarivo, Madagascar
[3]National Institute of Community and Public Health, Mahamasina Antananarivo, Madagascar
[4]Laboratory of Training and Research in Medical Biology, University of Antananarivo, Madagascar

Correspondence should be addressed to **Zafindrasoa Domoina Rakotovao Ravahatra**

Received January 12, 2018; Accepted March 08, 2018; Published March 29, 2018;

Cite This Article: Rakotovao Ravahatra, Z., Ranaivosoa, M., Randriatsarafara, F., Rakotovao, A., Rasamindrakotroka, A.(2018). Haematological and Biochemical perturbations related to cardiovascular diseases seen in the University Hospital Center of Befelatanana Antananarivo Madagascar. Advances in Biology & BioMedicine, 5(1). 1-6

ABSTRACT

Cardiovascular disease is a real public health problem. This study aims to describe the haematological and biochemical perturbations related to this disease in order to ensure a better management of the patients.Thisretrospective and descriptive study covers a period of 20 months at the Laboratory Unit of University Hospital Center Joseph RasetaBefelatanana Antananarivo. All results of haematological and biochemical tests of patients with cardiovascular disease were exploited.Among the 547 patients with cardiovascular diseases, 416 (76.1%) (IC_{95}: 72.2-79.5) had one or more perturbations of the biological tests. As for the biochemical perturbations, 155 patients (28.3%) had high plasma creatinine, 230 patients (42%) had high plasma urea and 84 patients (15.4%) hyperglycemia. The neutrophilic leukocytosis (20.3%), leukopenia (15.7%), normocytic anemia (14.4%), polycythemia (7.5%), thrombocytosis (6.8%) and thrombocytopenia (6.6%) were the most observed haematological perturbations. The elevation of plasma creatinine was significantly associated with normocytic anemia (85.1%) ($p = 0.002$). Patients with cerebral vascular accidents had neutrophilic leukocytosis in the majority of cases (79.4%) ($p = 0.03$).A blood count and a complete biochemical test should be prescribed in any patient with cardiovascular disease to better follow the evolution and the prognosis of the disease in order to improve the management of the patient.

KEY-WORDS: Cardiovascular diseases; leukocytosis; anemia; plasma creatinine

INTRODUCTION

Cardiovascular diseases represent a large public health problem in the world. According to World Health Organization (WHO), 17.5 millions of death have been caused by cardiovascular diseases, that is to say 46% of death by non- transferable diseases(NTD), and therefore it was the first cause of death by NTD in 2012 [1]. Among these deaths 7.4 millions were caused by myocardial infarction (ischemic heart diseases) and 6.7 millions by cerebral vascular accidents. At the world level the prevalence of high blood pressurefor adults ≥ 18 (systolic and/or diastolic blood pressure ≥ 140/90mmHg) was about 22% in 2014 [1]. Cardiovascular diseases such as vascular accidents, myocardial infarction, heart failure, dementia,

kidney failure or blindness are often secondary to high blood pressure. In Madagascar cardiovascular diseases remain the leading cause for 18% of total deaths in all age groups [2]. For this reason, deeper studies on clinical, biological and etiological diagnosis of these cardiovascular diseases should be developed in order to reduce their onset and to improve the patients care. So, the purpose of this study is to describe the haematological and biochemical disorders related to cardiovascular diseases in order to know the progressive stage of the illness and to put forward suggestions related to the patient care.

PATIENTS AND METHODS

This is a retrospective study of descriptive method from May 1st 2015 to December 31st 2016, over a period of 20 months, in the University Hospital Center of Befelatanana Antananarivo Madagascar. All the results of haematological and biochemical profiles of the patients having cardiovascular diseases were operated. The haematological balance was represented by the blood picture which was done on the haematology automaton ABX Pentra 60. The biochemical balances were represented by the plasma creatinine, the plasma urea and the fasting plasma glucose. They were dosed on the Kenza Max Biochemis Try spectrometer according to the Jaffé method for the plasma creatinine and the enzymatic method for the plasma urea and the fasting plasma glucose. As none study was done to determine the normal blood counts of Malagasy people we should use the values of references proposed by the team of experts from the French-speaking group of cellular haematology[3]. Concerning the normal values of biochemical balances, a normal plasma creatinine is less than 137µmol/l for men and less than 104µmol/l for women [4]. The normal plasma urea is between 2.5 to 7mmol/l [5, 6]. Normal fasting plasma glucose is between 3.9 to 5.8mmol/l [6]. Blood glucose between 5.8mmol/l and 7mmol/l corresponds to glucose intolerance or to a fasting moderate hyperglycemia. The diagnosis of diabetes can be established by a fasting plasma glucose ≥1.26g/l (7.00mmol/l) [7]. The parameters of study were the gender, the clinical inquiries, the results of blood counts and the 3 biochemical parameters. The data entry and processing were carried out on the computer software Epi-info 3.5.2. Chi-square tests were used to compare the percentages. The Kappa coefficient was calculated to assess the concordance between plasma glucose and plasma urea. For ethical imperatives the approval of the staff member's supervisor has been achieved before the data collection in the registers. The data entry was realized in anonymous way in order to keep confidentiality. p= 0.05 is the indicative borderline significant.

RESULTS

Among the 547 patients affected with cardiovascular diseases, 270 (49.4%) presented a high blood pressure, 106(19.4%) of decompensated heart failure, 103(18.8%) of cerebral vascular accidents, 61(11.2%) of heart diseases and 7(1.3%) of deep vein thrombosis (Figure 1).One or many biological perturbations were noticed on 416 patients (76.1%) (IC_{95}: 72.2-79.5)About biochemical perturbations: 155 (28.3%) patients presented a raise of plasma creatinine, 230 patients (42,0%) a raise of plasma urea and 84 patients (15,4%) a hyperglycemia (Figure 2).The elevation of the plasma creatinine affected 24.6% of men and 31.1% of women (p=0.09; Non Significant).Among these patients, 3.5 % presented a very high plasma creatinine> 500 µmol/l. Concerning the relation between plasma urea and plasma creatinine, 139 (25.4%) patients presented a simultaneous raise of the 2 parameters and 301 (55%) patients had normal values for the 2 parameters (Table 1).

Therefore, the concordance of results observed between plasma urea and plasma creatinine is 80.4%.Kappa number is (0.804-0.50) / (1-0.50) = 0.608. A good agreement is observed between the results.About haematological perturbations, neutrophilic leukocytosis (20.3%), leukopenia (15.7%), normocytic anemia (14.4%), polycythemia (7.5%), thrombocytosis (6.8%), thrombocytopenia(6.6%) were the most observed (Figure 3).The elevation of plasma creatinine was significantly associated with anemia (40%) ($p<10^{-6}$) (Table 2).In most cases, patients suffering from deep vein thrombosis presented neutrophilic leukocytosis (57,1%) (p=0.10; Non Significant) (Table 3).

Table 1: Relationship between plasma creatinine and plasma urea (n=574).

Plasma urea				
Plasma creatinine	**Normal (n=317)**		**High (n=230)**	
	Effective	%	Effective	%
Normal	301	55,0	91	16,6
High	16	2,9	139	25,4

Table 2: Relationship between plasma creatinine and anemia

	Anemia (n = 123)		**Others (n = 424)**		**p**
	Effective	**%**	**Effective**	**%**	
Normal plasma creatinine	61	15,6	331	84,4	$<10^{-6}$
Highplasma creatinine	62	40	93	60	

Table 3: Relationship betweenneutrophilic leukocytosis and clinical informations.

	Neutrophilic **leukocytosis (n = 199)**		**Others(n = 348)**		**p**
	Effective	**%**	**Effective**	**%**	
Cerebral vascular accident	34	33,0	69	67.0	0,10
Heart disease	17	27,9	44	72,1	
High blood pressure	91	33,7	179	66,3	
Decompensated heart failure	53	50,0	53	50,0	
Deep vein thrombosis	4	57,1	3	42,9	

Figure 1: Distribution of cardiovascular diseases.

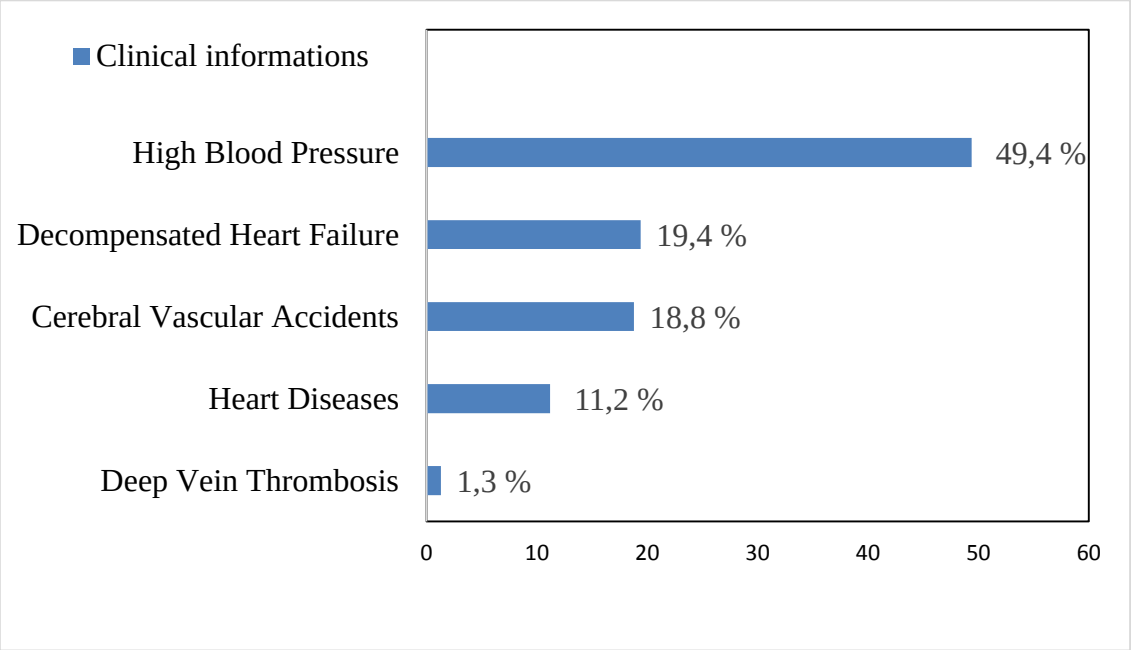


Figure 2: Distribution of Biochemical disturbances.

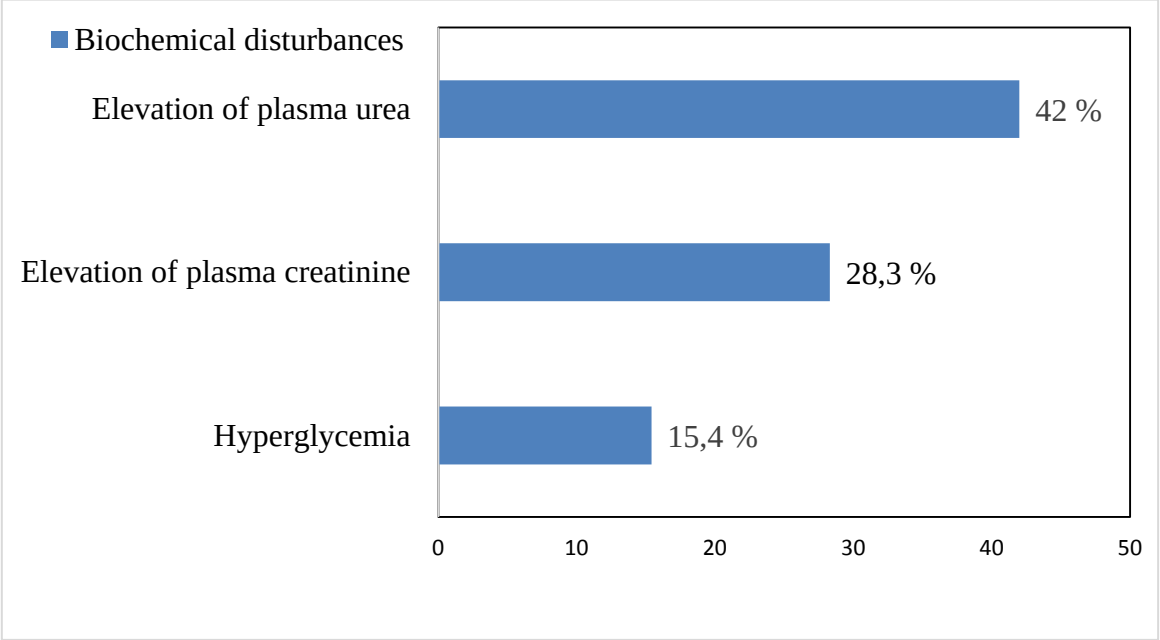
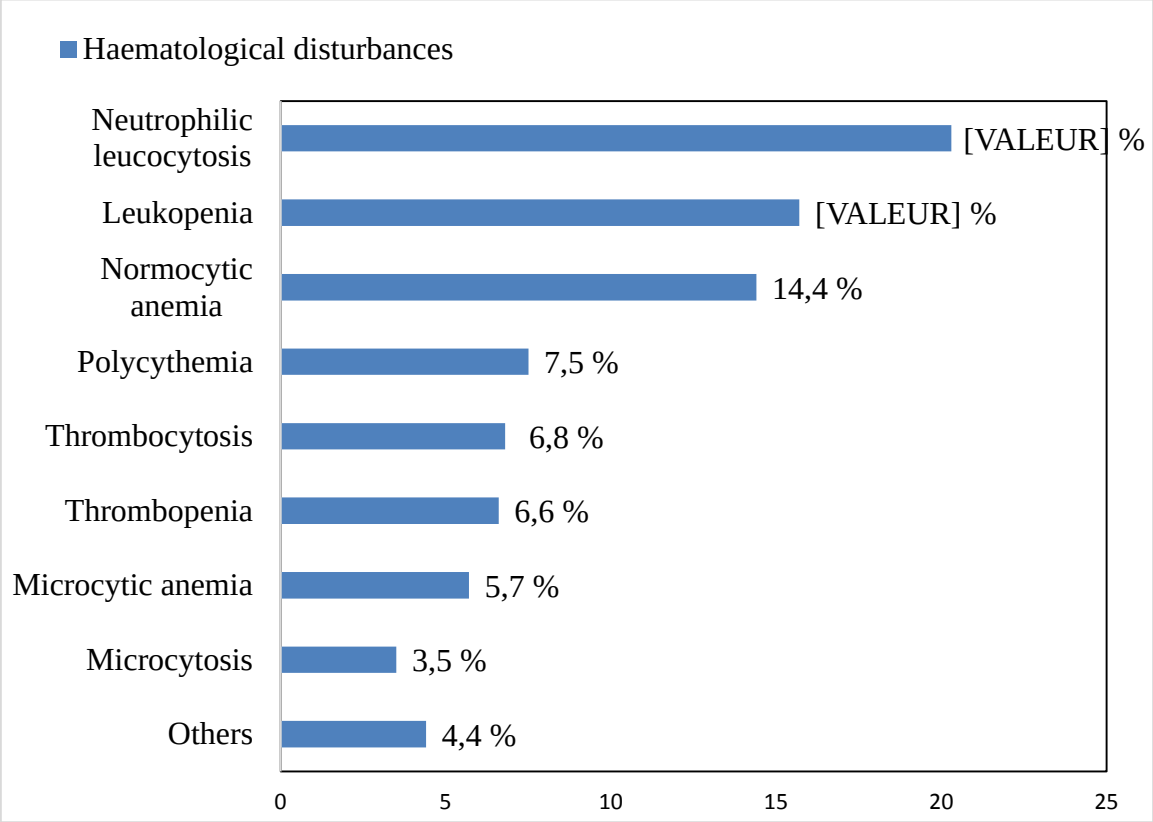


Figure 3: Distribution of haematological disturbances.



DISCUSSION

According to the collected data from the statistics service of the Malagasy Ministry of Public Health in 2013, at the Hospital Reference Centers, the essential high blood pressure represented the second cause of the most frequently reported medical pathologies: 6.4% of outpatient management. Lethality bound to high blood pressure rose to 5.5%[8] as it was reported at the Hospital Reference Centers. It would justify the predominance of high blood pressure in our present study. Similarly, most of the examined cardiovascular diseases represented long-term complications of high blood pressure if the latter was not properly managed [1]. About the results of biological analysis, the high prevalence of haematological and biochemical perturbations in patients with cardiovascular diseases has already testified their adverse effects on human organism. Therefore, they should be taken into account in order to improve monitoring and care for the patients. Likewise, these perturbations may be indicative of other underlying diseases that could be identified by other additional investigations. About plasma creatinine, this parameter was useful for monitoring kidney function of patients with cardiovascular diseases. However, it should be noticed that this parameter presented a lack of sensitivity to assess kidney function. In fact, during the acute renal failure or chronic renal failure, plasma creatinine could stay for a long time within the ranges of usual values whereas glomerular filtration rate was very reduced. And as creatinine production depended on muscle mass, a value in the standards may reflect a moderate kidney failure, while a value above standards does not necessarily testify to a kidney failure [9]. In this way, the assessment of renal function should take in account the glomerular filtration rateand plasma creatinine at the same time. Nevertheless, the literature also points out that the epidemiological specificity remained satisfactory for plasma creatinine. There was small change of plasma creatinine outside the renal impairment [5]. But I could also mention a decrease of plasma creatinine during a post-operative extended period of fasting and slimming, and a rise during nutrition rehabilitation but these changes remained low and generally should not bring a wrong diagnosis. In that respect, an adequate epidemiological specificity of plasma creatinine was used in this study to assess renal function of the patients. Furthermore, although plasma creatinine was an imperfect marker of glomerular filtration rate, nevertheless it kept alert value. In fact, the literature reported that 85% of adults having aglomerular filtration rate< 60 ml/mn/1.73m^3 had a plasma creatinine >137µmol/l for men and > 104µmol/l for women [4]. However, a glomerular filtration rate<60 ml/mn/1.73m^3 characterized undoubtedly a renal failure [10]. So, in this study the rise of plasma creatinine among the two genders already meant a beginning of the renal failure. The very important rise of plasma creatinine (> 500µmol/l) for some patients proved that they were at an advanced chronic renal failure. In fact, chronic renal failure represented the most terrible complication among cardiovascular diseases. However,chronic renal failure stood for an unknown disease, insidious, with a few specific symptoms. Very often it is still diagnosed in a late stage [11]. This fact explained why it was necessary to check patients biochemical balance sheet regularly in order to monitor renal function. Therefore, the complications will be detected early in order to adjust, modify and improve therapeutic care. These measures would allow the control of the complications and the improvement of the patient's life expectancy. Similarly, the earlier the diagnosis and the care were, the more the disease was controlled and the more the complications were limited. Concerning plasma urea, the

simultaneous rise of this parameter with plasma creatinine expressed renal damage. In fact,plasma urea had been used as a marker of renal function. However nowadays, it is no more used because its plasma concentration depends on many factors [12]. Nevertheless, a strong interest is retained within the functional acute renal failure (diagnosis and follow-up), hydro-electrolytic disorders, monitoring in intensive catabolism and the follow-up of dialysed patients [5]. In this study, hyperglycemia among some patients indicates the presence of diabetes associated to cardiovascular disease. The literature also reports that diabetes is one of cardiovascular disease risk factor [13]. The presence of other risk factors may worsen the disease leading to a lot of complications. The presence of other risk factors such as inactivity, obesity, tobacco addiction, metabolic syndrome, dyslipidemia including hypercholesterolemia and hypertriglyceridemia should also be determined in order to control the disease [13]. Concerning haematological perturbations, neutrophilic leukocytosis was the most frequent particularly in the case of deep vein thrombosis. It was probably due to the presence of inflammatory reaction at thrombosis level. Anyway, all vascular accidents such as deep vein thrombosis, acute coronary syndrome and cerebral vascular accidents were all concerned by these inflammatory reactions. For example, cerebral ischemia during cerebral vascular accidents will induce an inflammatory response which is prolonged by a rapid activation of main microglial cells, a production of pro-inflammatory mediator and an infiltration of different types of inflammatory cells (including neutrophils, different sub-types of T lymphocytes, monocytes/macrophages and other cells) in the ischemic cerebral tissue. The collaboration of all the cells contribute to the post-ischemic injuries. Neutrophils are among the first cells to infiltrate at the level of ischemic attack (thirty minutes to a few hours after the beginning of theischemia) with a peak from the first to the third post- ischemic day then the cells rapidly decrease over time [14]. If a rapid care was not put in place, neutrophils would participate to post-ischemic and vascular alterations. This pathophysiology mechanism is also valid for other causes of tissue ischemia such as deep vein thrombosis or acute coronary syndrome. On the other hand, leukopenia is probably due to side effects of medicated therapy which have rapidly been first initiated from the diagnosis of some cardiovascular diseases. Anti-inflammatory and thrombolytic drugs are mainly concerned [15]. About anemia, this anomaly is a frequent disease in hospitals. It is bound to diet, to the way of life, to the physiological state of the individual. Anemia could indicate renal failure which was a serious complication of cardiovascular diseases. In this case, it was a normocytic anemia and it was due to deficit production of erythropoietin by the kidneys [11]. It would justify the association of the anemia with the rise of the creatinine plasma within this study. In fact, erythropoietin is a hormone which boosted the production of red blood cells within the bone marrow[16]. Therefore, the deficit or the lack of erythropoietin will lead to anemia in the long term and justify a regular follow up of the patients blood count affected with cardiovascular diseases. In the case of chronic renal failure, the arrival at a terminal stage is unavoidable for the patients, and the cost of its treatment was a heavy burden at either individual or state level. Furthermore, the presence of anemia could lead to thrombotic events all along cardiovascular diseases. In fact, iron deficiency anemia, secondary to a chronic bleeding would be associated with secondary thrombocytosis and with a hypercoagulable state [17]. At their turn, these thrombocytosis were responsible of deep-vein thrombosis, the source of ischemic accidents such as cerebral vascular accidents or acute coronary syndrome. About polycythemia, another study has also shown the frequency of this anomaly in the case of high blood pressure [18]. On one hand, this polycythemia led to high blood pressure while increasing blood viscosity and slowing the normal flow of blood. On the other hand, this slowdown would promote the formation of blood clots leading to arteriovenous thrombosis [19]. At their turn,these thrombocytosis could lead to ischemic attacks in the absence of a fast care. That was why it was necessary to do other complementary investigations to look for the cause of this thrombocytosis. In fact, the treatment of thrombocytosis and similarly that of thrombosis would prevent thrombotic recurrences. The research of thrombocytosis etiology about patients suffering from cardiovascular disease should have been done mainly in a young patient suffering from unspecified etiology and in the presence of family or personal background of arterial or venous thrombosis. Finally, the encountered thrombocytopenia was always associated with significant risk of intracranial bleeding and cerebral vascular accident, it was willingly serious, particularly when platelets number was under 20,000/mm^3 [18]. Likewise, many affections and some medicated therapy could come with platelet hypoactivity (decrease of adherence and of platelet aggregability) and could be responsible of bleeding complication. Therefore, clinician ought to treat rapidly the thrombocytopenia in order to avoid these complications.

CONCLUSION

Several haematological and biochemical disturbances had been noticed in most of biological tests for patients affected with cardiovascular diseases. These disturbances showed the disease stage of evolution and the presence of risk factor or other underlying associated diseases. Thanks to these tests, the clinician could direct the diagnosis, the therapy and the follow-up of patients having cardiovascular diseases. In practice the clinician should ask for a complete biological test including at least a complete blood count and a renal check-up. So, the patient would be properly looked after and his life expectancy would be improved.

REFERENCES

[1]. WHO. Global Status Report on noncommunicable diseases 2014. WHO/NMH/NVI/15.1.

[2]. WHO. Country profile for noncommunicablediseases. World HealthOrganization, Geneva.2014. AccessedJanuary 12, 2017 on apps.who.int/nmh/countries/mdg_fr.

[3]. Troussard X, Vol S, Cornet E, Bardet V, Couaillac JP, Fossat C, Luce JC, Maldonado E, Siguret V, Tichet J, Lantieri O, CorberandJ; French-Speaking Cellular Hematology Group. Determination of full blood count normal reference values for adults in France.Ann Biol Clin 2014, 72:561-581.

[4]. The National Agency for Accreditation and Health Care Evaluation. Diagnosis of adultchronickidneyfailure. Septembre 2002 :25. AccessedJanuary 15, 2017 www.has-sante.fr.

[5]. Beaudeux JL, Durand G. Biochimie médicale : marqueurs actuels et perspectives. 2ème Edition revue et augmentée. Médecine Sciences Publications. Lavoisier. Paris Septembre 2011 : 607. ISBN : 978-2-257-20472-1.

[6]. Dieusaert P. Guide pratique analyses médicales. 5ème Edition. Maloine. 2009 : 1327.
[7]. Drouin P, Blickle JF, Charbonnel B, Eschwege E, Guillausseau PJ, Plouin PF, Daninos JM, Balarac N, Sauvanet JP. Classification and diagnosis of diabetesmellitus new criteria.DiabetesMetab 1999, 25:74.
[8]. Service des statistiques sanitaires. Annuaire des Statistiques du Secteur Santé à Madagascar année 2013. Ministère de la Santé Publique. Madagascar. Edition Décembre 2014;112.
[9]. Tsinalis D, Binet I. Assessment of renalfunction: plasma creatinine, urea and glomerular filtration rate (GFR).Forum Med Suisse2006, 6:414–419.
[10]. Serrano F, Vidal-Petiot E, Flamant M. Assessrenalfunction. La revue du praticien médecine générale. 2015 ; tome 29 l n° 945 l:2-4.
[11]. Sabi KA, Gnionsahe DA, Amedegnato D. Chronickidneyfailure in Togo : clinical, laboratory, and etiological aspects.Med Trop 2011, 71:74-76.
[12]. Dussol B. Methods of exploration of the renalfunction:Interest and limits of the formulaeallowing to estimate the renalfunction.IMMUNO ANAL BIOL SPE 2011, 26 :6-12.
[13]. Yahia-Berrouiguet A, Benyoucef M, Meguenni K, Brouri M. Survey on the prevalence of riskfactors for cardiovasculardisease in Tlemcen (Algeria). Médecine des maladies métaboliques 2011, 5(4):42-48.
[14]. Rosell A, Cuadrado E, Ortega-Aznar A, Hernández-Guillamon M, Lo EH, Montaner J. MMP-9-positive neutrophil infiltration is associated to blood-brain barrier breakdown and basal lamina type iv collagen degradation during hemorrhagic transformation after human ischemic stroke. Stroke 2008, 39:1121-1126.
[15]. Andres E, Weitten T, Federici L et al. Management of neutropenia in youngadults. Médecine thérapeutique 2008, 14(5):314-321.
[16]. Tremblay R. Anémie et insuffisance rénale chronique. Le Médecin du Québec 2002, 37(6):25 -28.
[17]. Crassard I, Woimant F. Haematologicaldisorders and strokes. EMC (Elsevier SAS, Paris), Neurologie, 17-046-b-15, 2005:1-7.
[18]. Karabacak M, Dogan A, Turkdogan AK, Kapci M, Duman A, Akpinar O. Mean platelet volume is increased in patients with hypertensive crises. Platelets2014, 25(6):423-426.
[19]. Khalid S, Mustapha M, Hamida A, Cosmina FG, Emmanuel A. Thrombocytosispathophysiology, diagnosis and treatment. mt2012, 18(1):11-20.