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Meanders of an Atypical Research Work on *Helicobacter pylori* in the Democratic Republic of Congo: Influence of HIV and other Factors and Study of some Interesting Cases

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Abstract

During the 3rd Euro case reports in Valencia, Spain, a strange medical case taking place in the DRC has been presented. Indeed, while the Congolese population is, until now, convinced of the existence of massive criminal poisonings, throughout the national area, originating from the East region of the country, we incredibly observed and demonstrated that actually, the phenomenon is a silent, surprising and unexpected *Helicobacter pylori* epidemic with numerous extra-digestive pathologies. The present subject will deal with picturesque meanders by which our research work passed, lengthening it to more than twenty years before getting appropriate results. The presentation will start by a brief summary of the DRC *Helicobacter pylori* phenomenon described in Valencia and hypothesis raised for better knowledge of *Helicobacter pylori* infection, at the international level. In a second time, it will focus on the influence and consequences of some followed factors in our study: HIV infection, political situation in DRC, lack of equipment and financial means, population ignorance, traditional practitioners' cupidity, deficiency of south-North collaboration, and so on. Afterwards, two interesting incredible extra-digestive DRC *Helicobacter pylori* cases observed in our study will be discussed. Finally a brief conclusion will present some useful propositions drawn from the experience of this DRC *Helicobacter pylori* research work.

Keywords: *Helicobacter pylori*; Extra-gastric pathologies; RD Congo; Euro case reports; Karoo phenomenon; HIV influence

Introduction

In 1990, in the Democratic Republic of the Congo, Mobutu's regime was at its end and political, social, cultural country environment was very bad. The country was under general international embargo for political reasons. All partners of education of Congolese universities left the country and all of our laboratories lacked of equipment. Medical situation was also bad because of the HIV general infection which was at its top in the country.

It's in that period of time that we started at the Laboratory of Toxicology of the University of Kinshasa a cross-sectional study of a strange disease present in DR Congo since a few decades, characterized by huge digestive and extra-digestive pathologies, considered by Congolese population as a result of massive criminal poisonings throughout the country. Internal heat, suffocation, mental confusion, heart pain, intense tiredness and loose of weight were the principal symptoms of that phenomenon.

During the 3rd Euro case reports in Valencia Spain, in 2016, the strange medical case taking place in DR Congo has been presented. Indeed, contrary to the conviction of the Congolese population about the existence of massive criminal poisonings, throughout the country, we incredibly observed and demonstrated, in 2010, a surprising and unexpected *Helicobacter pylori* epidemic with numerous extra-digestive pathologies.

This paper deals with the presentation made during the 5th Clinical and Medical Euro case reports held in Paris, France in 2017 September 07 to 08, explaining picturesque meanders by which our research work passed, before getting appropriate results. According to the presentation, it will focus first on a brief summary of *Helicobacter pylori* phenomenon described in Valencia and hypothesis raised for the better knowledge of *Helicobacter pylori* infection, at the international level. Afterwards the influence and consequences of some delaying factors will be presented. Finally, two extra-digestive *Helicobacter pylori* cases observed in our study will be discussed.

Methods

Study design and sample

This paper is based on a cross-sectional study conducted on Karoo patients received at the Laboratory of Toxicology of the University of Kinshasa from January 2005 to June 2016. The study protocol has been submitted to the Internal Review Board of the Faculty of Pharmaceutical Sciences of the University of Kinshasa and it has been conducted according to the principles of the Helsinki Declaration (Ethical Principles of Medical Research Involving Human Subjects) as amended in 2013.

Variables of study

Questionnaire for data collection included three parts. The first part concerned socio-demographic variables: age, sex, educational level and

marital status. The second part described "Karoo phenomenon": symptoms, origin, circumstances of poisoning, traditional diagnostic and treatment, opinions of Karoo patients on this phenomenon. The third part addressed the relationship between "Karoo phenomenon" and *Helicobacter pylori*. Scientific parameters were: saliva pH, toxicological screening (Thin layer chromatography, and UV spectrophotometer), Blood sedimentation rate, Alanine Aminotransferase test (ALAT), Aspartate Aminotransferase test (ASAT), Urea, Creatinine, *Helicobacter pylori* (Chromatographic serological method), Hemoglobin, and Glucose.

Case reports

Two cases were reported: a patient's case, and a post-mortem case. The two cases have been selected for their especial feature. Patient's case concerned a woman of 36 year's old, single, employed in a private communication enterprise. The post-mortem case concerned a 40 years old man, married, self-employed. They were both positive to *Helicobacter pylori* with extra-digestive evident signs, displayed in photos in attachment.

Results

Population of study

Table 1 shows that the population of study included 402 patients received at the Laboratory of Toxicology of the University of Kinshasa from January 2005 to June 2016, 277 males and 125 females. Patients from 20 to 50 years old were more represented in the population of study but there were also 21 patients beyond 50 years old and 4 children less than 5 years old. Unmarried patients were 181 (45%) while the currently married patients were 193 (48%). The number of patients received was in ascendant progression: 40 (9.9%) from 2005 to 2009, 56 (13.6%) from 2010 to 2013 and 306 (76.1%) from 2013 to 2016.

Variables	Patients	Percentage
Sex		
Male	277	68.9
Female	125	31.1
Total	402	
Age (years)		
0 – 5	4	0.9
6 – 20	21	5.2
21 – 50	349	86.9
<50	28	6.9
	402	
Educational level		
No education	55	13.6
Primary	97	24.1
High	145	36
Higher	105	26.1
Current marital status		
Unmarried	181	45
Married	193	48
Formerly married	28	6.9
Residence		
East of the country	185	46
Kinshasa	143	36
Other provinces of west of the country	74	18
Patients progression from 2005 to 2016		
2005 – 2009	40	9.9
2010 – 2012	56	13.9
2013 – 2016	306	76.1

Table 1: Socio-demographic variables (n=402).

Characteristics of Karoo poisoning

Symptoms: Symptoms were diversified. They were digestive but most extra-digestive as well, divided in general and nervous symptoms (Table 2).

Digestive Symptoms	General Symptoms	Nervous Symptoms
Heat in the stomach and thorax	Weight loss	Vertigo
Intense abdominal pain	High internal heat	Early aging
Throat dryness	High transpiration	Frequent forgetting
Tongue and mouth burn	General and sexual tiredness	Mental confusion
Hyper-salivation	Suffocation	Consciousness loss
Nausea without vomiting	Anemia	Memory disorders
Regurgitation	Skin allergy	Hallucinations
Constipation	Skin blackening	Intermittent hands shaking
Loss of appetite	High blood pressure	Paralysis
Bitter taste of food and beverages	Sensation of something moving under the skin	Electroencephalogramm disturbance
Alkaline Saliva	High blood sugar	Sensation of something moving into the head
Increase of Saliva viscosity	Increase of blood viscosity	Blurred vision
Stomach distending	Pricking sensation	Frequent drowsiness
Sanguinolent spit	Heart palpitations	
Anorexia	Hormonal disorders on women	
Diarrhea	Hard breathing	

Stomach buzz	Breathlessness	
Sensation of stomach fullness	Increase of blood alkalinity	

Table 2: Symptoms collected in DR Congo.

Opinions of patients on Karoo phenomenon

Table 3 presents opinions of patients on Karoo phenomenon. Most patients thought that Karoo symptoms could last months (275, 68.4%) or years (58, 14.4%). The eastern of the country was identified unanimously as the principal site of Karoo poisoning (402, 100%). Four principal symptoms were identified: internal heat (282, 70.1%), bitterness of food and beverages (257, 69.9%), intense tiredness (275, 68.4%) and inexplicable loss of weight (269, 66.9%). In case of Karoo poisoning, preference was to visit traditional practitioners instead of going to the hospital. Three traditional diagnostic tests were pointed out, all conducted on patients' saliva. Traditional treatment was centered on the honey, sometimes mixed to lemon and garlic juice (402, 100%). The recourse to the Laboratory of Toxicology was directed by two main reasons: traditional treatment failure (388, 96.5%) and the need of scientific diagnosis (346, 86%).

Variables	Patients	Percentage
Duration of "Karoo symptoms"		
Days	120	29.8
Weeks	143	35.5
Months	275	68.4
Years	58	14.4
Principal poisoning site		
East of the country	402	100
Kinshasa	46	11.4
Other provinces of west of the country	20	4.9
Principal sign of Karoo poisoning		
Bitterness of food or beverages	257	69.9
Nausea without vomiting	198	49.2
Tiredness	275	68.4
Internal heat	282	70.1
Inexplicable loss of weight	269	66.9
Reasons for going to traditional practitioners instead of to the hospital		
Traditional practitioners are Karoo specialists		
They have a rapid and efficient test	402	100
They have efficient treatments	402	100
At the hospital there is no test for poison	196	48.7
At the hospital Karoo poisoning is denied	368	91.5
There is no modern efficient treatment	402	100
Modern medicines get Karoo poisoning worse	402	100
	402	100
Principal traditional test made on patients' saliva		
Spit in a glass of water	385	95.7
Spit on a tongue of a yellow paper	242	60.1
Spit in a tender leaf of a plant	80	19.9
Traditional treatment		
Strong medicinal laxatives plants extracts	195	48.5
Mixture of lemon, garlic and honey	402	100
Other unknown mixtures	72	17.9
Honey	402	100
Reasons for coming to Laboratory of Toxicology		
Traditional treatment failure	388	96.5
Need of a scientific diagnosis	346	86
Danger of medicinal plants	88	21.8
Need of scientific control	261	64.9

Table 3: Opinions of patients on Karoo phenomenon (n=402).

Biological parameters

Table 4 shows biological parameters checked. Toxicological screening and Saliva alkalinity determination were performed in all the patients from 2005 to 2016. The others biomarkers (*H. pylori*, sedimentation rate, hemoglobin, ASAT, ALAT, creatinine and urea) were recorded only since 2013, in 306 patients. *H. pylori* and saliva alkalinity were positive to all patients examined. Sedimentation rate was high (<10 mm/h) in most patients (270, 88.2%). The toxicological screening was positive in 46 (11.4%) patients; the toxic in cause in every case was paracetamol. ALAT and ASAT were normal for most patients (260, 84.9%). The eradication of *H. pylori* was obtained in 280 patients (91.5%). Symptoms were also cleared in 280 patients (91.5%). Resistance rate to treatment was then 8.5%. Iron deficiency anemia was present in 80 patients (26.1%).

Parameters	Patients	Percentage
Toxicological screening (n=402)		
Positive	46 (paracetamol)	11.4
Negative	356	88.5
Saliva alkalinity (n=402)		
Yes	376	93.5
No	26	6.4
H. pylori (n=362)		
Positive	362	100
Negative	0	

Negative after treatment	280	91.5
Still positive after treatment	26	8.4
Clearance of the symptoms after treatment	280	91.5
Hemoglobin (n=306)		
Normal	226	73.8
Abnormal (under the norm)	80	26.1
Aspartate amino transferase ASAT (n=306)		
Normal	260	84.9
Abnormal (up to the norm)	46	15
Alanine amino transferase ALAT (n=306)		
Normal	260	84.9
Abnormal (up to the norm)	46	15
Creatinin (n=306)		
Normal	302	98.6
Abnormal (up to the norm)	4	1.3
Urea (n=306)		
Normal	302	98.6
Abnormal (up to the norm)	4	1.3
Blood sedimentation rate (n=306)		
Normal	36	8.9
Abnormal (up to the norm)	270	88.2

Table 4: Results of biological parameter.

Case reports parameters

Patient's case parameters

BIOLOGICAL PARAMETERS		SYMPTOMS
Helicobacter pylori	Positive	Feet swelling
Blood sedimentation rate	85 mm/h (<10 mm/h)	Internal heat in stomach and thorax
Alanine aminotransferase	24 U/L (0-41 U/L)	Dizziness
Aspartate aminotransferase	28 U/L (0-31 U/L)	Headache
Urea	30 mg/dl (15-45 mg/dl)	Intense tiredness
Creatinine	1,2 mg/dl (0,5 – 1,5 mg/dl)	Cough

Table 5: Patients' case parameters.

Post-mortem case parameters

BIOLOGICAL PARAMETERS		AUTOPSY FINDINGS
Helicobacter pylori	Positive	Gut distending
Blood sedimentation rate	-	Stomach distending
Alanine aminotransferase	-	Brain congestion
Aspartate aminotransferase	-	Lungs congestion
Urea	-	Cyanosis of lips, fingers and toes
Creatinine	-	Tongue biting
-	-	Pallor of hands palms and of sole of the feet
-	-	Cardiomegaly
-	-	Eyes red coloration
-	-	Nose bleeding
-	-	Gastric bleeding

Table 6: Post-mortem case parameters.

Discussion

Summary of main findings

The strange phenomenon characterized by huge extra-digestive pathologies, current in Democratic Republic of Congo, considered as massive criminal poisoning, appeared actually caused by *Helicobacter pylori*. (ii) Its characteristics and symptoms have been collected (Table 2). (iii) *Helicobacter pylori* outbreak in DRC needed environment activator factors. (v) Patients' saliva was alkalized by gas ammonia flying up from stomach to mouth. (vi) Gas ammonia and carbon dioxide are responsible of huge patients' extra-digestive pathologies. Carbone dioxide combines causticity and redoubtable fatal asphyxia power, as demonstrated in the post-mortem case.

Helicobacter pylori infection

Helicobacter pylori, is well known worldwide. It largely colonizes humans since immemorial time, in both developing and developed countries [1-24]. It's widely involved in gastritis, asymptomatic for most infected individuals. A small proportion of infected individuals develop more dangerous gastritis involving peptic ulceration and gastric malignancy [22,25-33]. *Helicobacter pylori* is responsible for tremendous morbidity and mortality throughout the world [6,7,12,14-16]. Normally originated in Africa, *Helicobacter pylori* has

been carried with human populations around the world after their departure from Africa [26,29]. *Helicobacter pylori* infected persons increase risk of developing gastric cancer. Many factors and cofactors influence gastric cancer development [8,10,32-34]. *Helicobacter pylori* virulence is under the control of *Helicobacter pylori* gene factors [25,27,30,31]. There is actually an important change in the relationships between *helicobacter pylori* and humans, caused by modern life change in gut micro-ecology [19,29]. In Africa, *Helicobacter pylori* infection displays a specificity called "African enigma" related to the fact that, in spite of a high *Helicobacter pylori* contamination in Africa, often from early childhood, gastric cancer prevalence is inexplicably low [6,17,21].

DRC *Helicobacter pylori* phenomenon

Congolese population is, until now, convinced that the phenomenon current in DR Congo is a consequence of massive criminal poisonings. Yet, our study established, in 2010, an unexpected interesting link with *Helicobacter pylori*. According to Table 4, the 362 patients received at the Laboratory of Toxicology of the University of Kinshasa for poisoning suspicion, were all positive to *Helicobacter pylori*. They were all characterized by huge extra-digestive pathologies (Table 2). Main pathologies identified were: internal heat (282, 70.1%), bitterness of food and beverages (257, 69.9%), intense tiredness (275, 68.4%) and inexplicable loss of weight (269, 66.9%). Following other hypothesis was raised in our study: (i) numerous extra-digestive pathologies observed, indicated a free and massive passage of ammonia and carbon dioxide to the blood. (ii) Ammonia and carbon dioxide released in stomach by the reaction urea-urease, in gaseous state, should be eliminated in stools. (iii) In case of constipation however, ammonia and carbon dioxide, still in gaseous state, could go up along the esophagus to the mouth and lungs and from there to the blood stream. (iv) A double intoxication then occurs, justifying numerous extra-digestive pathologies described in Table 2. (v) This statement is in perfect harmony with recent literature which reports more and more extra-digestive pathologies linked to *Helicobacter pylori* [23,28,35-41].

Proposed improvements on *Helicobacter pylori* infection

Under the light of our study, some following improvements would be proposed for best *Helicobacter pylori* infection understanding: (i). *Helicobacter pylori* infection should be named *Helicobacter pylori* toxic-infection to take count of the intoxication component present in many cases of *Helicobacter pylori* infection as frequently stated in recent literature. (ii). *Helicobacter pylori* extra-digestive symptoms should be definitely recognized as part of *Helicobacter pylori* infection. (iii) Passage of *Helicobacter pylori* toxins in blood via lungs way should be acknowledged. (iv). *Helicobacter pylori* treatment should be reevaluated to take in count the intoxication component. Our study suggested that toxicological eliminating treatment should always be combined to *Helicobacter pylori* medical eradication treatment. (v). the development of a rapid *Helicobacter pylori* diagnosis method based on ammonia identification in saliva and in stools could be useful.

An atypical wandering research work

Our research work took a long time before getting suitable results because, mainly, of unfavorable political, social, cultural and scientific environment of the end of Mobutu's regime in DR Congo and the war it generated. The international political embargo imposed to DR Congo since 1990, provoked lack of equipment, lack of financial means for research and lack of useful South-North collaboration. Secondly, Karoo poison was not only unknown but invisible physically as well.

Thirdly, rumors, traditional believe of Congolese population and cupidity of traditional practitioners played an important impairment role. For example, as reported in Table 3, modern medicines were reputed to be inefficient against Karoo poison. The use of modern medicines, especially by perfusion, was even thought to rapidly lead to death. The consequence was that in many villages, most in the eastern region of the country, people avoided going to the hospital, for any disease. As it could be guessed, HIV/AIDS, tuberculosis and malaria took big advantage of this situation.

Some symptoms reported in Table 2, like intense tiredness, anorexia and most significant loss of weight was commune to Karoo phenomenon and to HIV. The confusion with HIV was a major complication factor in our study.

Opinion of some Congolese medical staff, denying findings concerning the role of *Helicobacter pylori* in Congolese Karoo phenomenon was also an important source of wandering.

Case Reports

As displayed in Figures 1-6, patient's case main pathology was feet swelling. *Helicobacter pylori* was positive, blood sedimentation rate high (85 mm/h), alanine aminotransferase, aspartate aminotransferase, urea and creatinine, were in normal range (Table 5). No hypertension and diabetes diseases. Swelling was accompanied by internal heat in stomach and thorax, dizziness, headache, reflex cough, and intense tiredness (Table 5). Feet swelling was attributed to *Helicobacter pylori* CO_2 toxin, after its passage to the blood via the lungs way, as stated in this study. Activated charcoal guaranteed feet deflating within ten days (Table 5).

Figure 1: Gut distending photo forensic medicine institute/ Kinshasa.

Figure 2: Stomach distending photo forensic medicine institute/ Kinshasa.

Figure 3: Brain Congestion photo forensic medicine institute/ Kinshasa.

Figure 4: Right Lung Congestion photo forensic medicine institute/ Kinshasa.

Figure 5: Fingers and toes cyanosis photo forensic medicine institute/Kinshasa.

Figure 6: Feet swelling photo Shafali/Kinshasa.

The post-mortem case was received, from Forensic Medicine Institute of General Hospital of Kinshasa for toxicological analysis, after a suspect death. Death occurred suddenly, at home, during the night, after the return from a friend's party. Immediately after death, stomach inflated extremely at an incredible speed. Autopsy findings were unexpected and amazing. Autopsy statement revealed full of abnormalities, notably: Gut distending, Stomach distending, Brain congestion, Lungs congestion, Cyanosis of lips, fingers and toes, Tongue biting, Pallor of Hands palms and pallor of sole of the feet, Cardiomegaly, Eyes red coloration, Nose bleeding, Gastric bleeding (Table 6). All those abnormalities were identified as sign of double intoxication by gas ammonia and carbon dioxide. Death occurred bluntly after brutal carbon dioxide asphyxia. *Helicobacter pylori* was incriminated, as the deceased was a known *Helicobacter pylori* chronic gastritis patient. Those two cases, selected among many others, were significant testimony of the findings of this study.

Conclusion

Our research work was very time consuming because it did face many obstacles. In spite of all problems faced, we did never give up. Results got after a so long period of time beyond 20 years of wandering, seem impressive. It's necessary not to forget that in spite of all disturbances in Sub-Saharan African countries, many scientific researchers are there, trying painfully to contribute to the improvement of scientific world knowledge.

We think necessary to develop more scientific collaboration and networks between researchers from developing and developed countries, far beyond political considerations.

We encourage young research workers, to never give up. They have to know that in any research work, without a bit wandering mind, phenomenal results could never be achieved.

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