



Research Article

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Chronic Myeloid Leukaemia: Epidemiological, clinical and paraclinical aspects in two hospitals in Cameroon (DGH and YGH) over 8 years

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Abstract

Background: Chronic myeloid Leukaemia (CML) is a myeloproliferative syndrome characterised by a proliferation of the granular cell lineage. It accounts for 7 to 15% of leukaemia in adults; its incidence in the world is estimated at 1 to 2 cases per 100,000 inhabitants per year. **Aim:** It was to look into the epidemiological, clinical and biological characteristics of CML in our setting. **Methods:** We carried out a retrospective, transverse descriptive study at two hospitals in Cameroon (Douala General Hospital and Yaounde General Hospital). We reviewed files of patients with CML from 2007 to 2014 to collect socio-demographic clinical and biological data and analysed them using Microsoft Excel 2007 and Epi info version 7. **Results:** We made a census of 126 cases with a mean age of 40.8 ± 13.9 years. The mode age was 26-35 years at 29.37% of cases. The male to female ratio was 1:4. Concerning occupation we found out that most (26.2%) had informal jobs, followed by 24.6% were housewives. The majority of patients lived in urban areas (73.8%). The patients were mostly diagnosed during routine examinations (63.5%). Splenomegaly, hepatomegaly and lymphadenopathy represented respectively; 97.6%, 64.3% and 7.1% of cases. We also found bone pain (7.9%), joint pain (6.4%), fever (6.4%). Leucocytosis was found in all patients with a mean of 167238.3 ± 124282.6 cells/mm³. Anaemia was found in 81.7% of cases. It was mild, moderate or severe at 14.3%, 50.8%, 16.6% of cases respectively and haemoglobin concentration varied between 1.2 to 15.3 g/dl with a mean of 9.8 ± 2.2 g/dl. Platelet count varied between 1000 to 2179000 with a mean of 352632.5 ± 268711.7 platelets. We found thrombocytosis in 24.6% of cases and thrombocytopenia in 15.9%. For diagnostic confirmation, 83.3% of patients went through a conventional karyotype, 12.7% an FISH, and 3.2% of cases Convention karyotyping alongside an FISH. One patient had done an RT-PCR. We counted 23 patients who presented with additional anomalies in their conventional karyotyping at 18.3%. **Conclusions:** Chronic Myeloid Leukaemia affects the young adult in our setting and is mostly fortuitously discovered. The tumoral syndrome was mostly already present at diagnosis so as anaemia. Additional genetic anomalies were found. A better understanding of this pathology in our setting could help elaborate state guess for sensitisation of the public and health practitioners.

Keywords: Chronic Myeloid Leukemia, Epidemiological, Clinical and biological.

INTRODUCTION

Chronic myeloid leukaemia is a myeloproliferative syndrome characterised by proliferation of the granular cell lineage [1].

This proliferation is mononuclear and originates from cytogenetic anomalies; the Philadelphia chromosome (ph1), results from a reciprocal translocation t(9,22) which brings into contact an oncological site (ABL), found on chromosome 9 and a particular region of chromosome 22 (bcr) [1]. This translocation leads to the formation of a fusion gene BCR-ABL, brought into evidence in molecular biology by RT-PCR and responsible of the production of excessive and persistent white blood cells at the bone marrow [2,3]. CML progresses in 3 phases, a chronic phase which can last more than 10 years, followed by an acceleration phase of few months and a transformation phase or accusation almost ineluctable and mortal in 3 to 6 [1,4].

CMLMC represents 7 to 15% of leukaemia in adults; its world incidence is 1 to 2 patients /100,000 inhabitants per year. 807 new cases per year are counted in France giving an incidence of 1-2 new cases/100,000 H/an. In Africa, precisely in Algeria the incidence is 0.4/100,000 H/an according to a

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study carried out in 2004 by the Algerian society of Haematology and of blood transfusion (SAHTS) [3,6].

Few studies have been done in Cameroon on CML thus motivating this study which will help us know thus pathology better in our setting and help us elaborate strategies for sensitisation in the future.

MATERIALS AND METHODS

This was a retrospective and descriptive study done on patient files followed up at the onco-haematological units in two hospitals in Cameroon.

This study was done in Cameroon, a country found in central Africa. We recruited our cases in the onco-haematological units of the internal medicine services of Douala General Hospital (DGH) and the oncology unit of Yaoundé General Hospital (YGH). Actually, each time the diagnosis of CML is confirmed the patients are seen to YGH to benefit from free management with respect to the GIPAP (Glivec International Patient Assistance Program). YGH is found at about 239.48 Km from Douala. It's a referral Hospital in the sub region and for the meantime the only centre of management of haematological malignancies.

This study was carried out for a period of 6 months, from January to June 2015. Stored files of patients received from the year 2007 to 2014 were selected that is over an 8 years period.

Included in the study were files of patients diagnosed and documented with CML by cytogenetic studies. We excluded patients with incomplete files.

The sampling was consecutive and exhaustive.

All administrative authorisations of concerned hospitals were obtained as well as ethical approval.

The research variables were;

Sociodemographical: sex, age, residence, place of occupation and educational level.

Clinical:

- Presenting complaint
- General state at presentation
- Tumoral syndrome
- Infections; fever
- Bone and joint pain

Paraclinical:

- Blood count: We looked for anaemia based on WHO classification of 2011. Was considered as anaemia patients having a haemoglobin < 12 g/dl. We equally looked into the white cell count, platelet count and blast count.
- Bone marrow smear: we looked at the content of the slides and hyperplasia of the granular cell lineage.

Cytogenetic: We looked for the Philadelphia chromosome for all patients and for those who didn't have it in their files, a request was done to the CERBA laboratory of France. We equally looked at the additional abnormalities.

-Sokal prognostic index of every patient was found based on this formula: $Index = [\lambda_i(t)\lambda_0(t)] = \exp 0.0116 (age-43.4) + 0.0345 (rate-7.51) + 0.188 [(platelets/700)^2 - 0.563] + 0.0887 (blasts-2.10)$. An online calculator was found on the following link: www.digipills.com/sokal/index.php

Statistical Analysis

The data was entered into a soft and analysed using Microsoft Excel 2007 and Epi info version 7.

RESULTS

Our inclusion criteria helped us select 126 files for our study of which 46 at DGH and 80 at YGH. The mean number of cases per year was 16.

Sociodemographical characteristics

The mean age was 40.8 ± 13.9 years with the age range of 15 to 83 years. The mode age was 26-35 years at 29.37%. The male: female ratio was 1.4.

Those working informal jobs represent 26.2%, followed by housewives at 24.6%. The majority of patients (73.8%): with CML lived in an urban area. In this study 49.2% of patients with CML had a secondary educational level and 26.2% had a tertiary educational. (Table 1).

Table 1: Sociodemographical Classification of patients

Variables	Categories	Proportions (%)
Age	Mean age 40.8 years (15-83)	Age range (years)
	15-25	14(11.1)
	26-35	37(29.37)
	36-45	30(23.81)
	46-55	23(18.25)
	56-65	15(11.90)
Sex	>65	7(5.56)
	Male	74(58.7%)
	Female	52(41.3%)
Residence	Urban	93(73.8%)
	Rural	33(26.2%)

Clinical parameters

The majority of patients (87.2%) had a performance status (PS) in between 0 to 1. In this group, 97.6% of patients presented with splenomegaly at diagnosis. We found out that 64.3% of patients had hepatomegaly; 9 patients (7.1%) presented with lymphadenopathies. We obtained respectively 8% and 6.4% of bone and articular pain presentation. Fever was found in 6.4% of cases (Table 2).

Table 2: Clinical classification of patients

Variables	Categories	Proportions (%)
Presenting complaint	Routine Examination	80(63.5)
	Asthenia	14(11.1)
	Abdominal heaviness	19(15.1)
	AGD	9(7.1)
Performance status	Abdominal pain	4(3.2)
	0-1	110(87.2)
	2-3	16(12.8)
Splenomegaly	4	0(0)
	0cm	3(2.4)
	1-9cm	23(17.6)
	≥ 10 cm	100(80)
Hepatomegaly	Present	81(64.3)
Adenopathy	Present	9(7.1)
Bone pain	Present	10(8)

Joint pain	Present	8(6.4)
Fever	Present	8(6.4)

Biological classification of the patients

All the patients had leucocytosis. In 62.7% of cases the white cell count was greater than 100000 cells/mm³. The mean was at 167238.3 ± 124282.6 cells/mm³ with a range of 13400 et 570000 cells/mm³. The mean neutrophil, basophil and eosinophil counts were respectively; 50.8% for PNN, de 1.7% for PNB and 2.3% for PNE. In this category 103 patients (81.7%) were anaemic at diagnosis. This anaemia was mild, moderate or severe respectively at 14.3%, 50.8%, 16.6 %. the mean haemoglobin concentration was 9.8 ± 2.3 with a range of 1.2 to 15.3 g/dl.

The platelet count varied between 1000 and 2179000 with a mean of 352632.50 ± 268711.7 platelets. The blast ranged between 0 to 66% and the promyelocytes 0 to 55%. The respective means were 7.60% and 3.03%. Of the 126 cases, 119 had a bone marrow biopsy and smear done.

Cytogenetic Classification

In this study group 83.3% of the patients had a conventional karyotype, 13.5% had done a FISH and 4% had both à conventional Karyotype and a FISH. One patient had done a RT-PCR (Table 3).

Table 3: Classification of patients according to the type of laboratory examination

Laboratory exams	Number (n=126)	Proportions (%)
Conventional karyotype	105	83.3
FISH	16	12.7
RT-PCR	1	0.8
Conventional karyotype and FISH	4	3.2

We counted 23 patients with at least one additional karyotype anomalies at 18.25% (Table 4).

Table 4: List of additional anomalies

Cytogenetic anomalies
46, xx, t (9;16;22) (q34; q21;q11)[20]
46, xx, t (9;21;22) (q34; q22; q11) [20]
46, xy, t (2; 9; 22) (12; q34; q11) [20]
46, xx, t (4; 9; 22) (p15; q34; q11) [20]
46, xy, t (7; 9; 22) (q15; q34; q11) [15]
46, xx, t (9; 22; 22) (q34; q11; q12)[20]
46, xy, t (9; 17; 22) (q34; q23; q11) [19] 46, xy [1]
46, xx, inv(9)(p12; q12)+(9; 12)(q34; q11) [19] [30]
46, xx, t (9; 22) (q34; q11)[13] 47; idem, +8 [7]
46, xy, t (9; 22) (q34; q11) [19] 47; idem,+ der(22)+(9;22)(q34;q11) [1]
46,xy,t(9;22)(q34;q11)[9]46,xy,der(9)del(9)(q34)t(9;22)(q34;q11)der(22)t(9;22)(q34;q11)[6]
46,xy,der(9)inv(9)(p12;q13)+(2;9;22)(p13=21,q34;q11,2),der(22)+(2;9;22)(p13~21;q34;q11,2)
46, xy, t (9; 22) (q34; q11) [5] 50,xy,+8;t(9;22)(q34;q11),+14+19,+21[CP15]
46, xy, t (9; 22) (q34; q11) [19]/ 46; idem,+ (12;16)(q13;q13) [1]
46, xy, t (9; 22) (q34; q11) [31] 46; idem,+19;+mar1 [1]
46,xy,t(9;22)(q34;q11)[6]46;idem,del(7)(q21;q31);der(17)+(17;?)(q12;?),der(18)+(18;?)[14]
46,xy,t(9;22)(q34;q11)46,xy,del(6)(q10),t(9;22)(q34;q11)47,xy,+2,+ (9;22)(q34;q11) [20]
46, xy, t (9; 22) (q34; q11) [2]/ 46, idem, t(8;17)(q11;q22)[18]
46,xx,t(9;16;22)(q34;q24;q11)[14]46,xx,idem,del(2)(p16)del(8)(q21),der(17),t(8;17)(q12;p1),+19[6]

The following cytogenetic anomalies 46, xy, t (9; 17; 22) (q34; q23; q11) [19] 46, xy [1] and 46, xy, t (9; 22) (q34; q11) [19]/ 46; idem,+ (12;16)(q13;q13) [1] were the most representatives at the respective frequencies of 3 and 2.

Classification of patients with respect to sokal

The patients having an intermediate risk were many 55.6 % of cases (Figure 1).

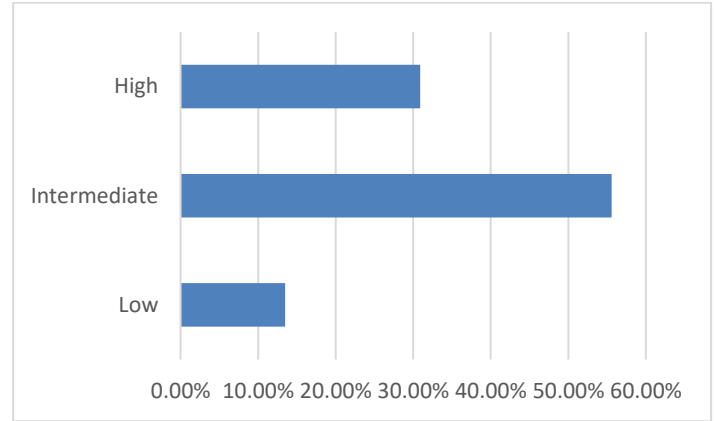


Figure 1: SOKAL Prognostic classification of patients We obtained a predominance of intermediate risk (55.6% of cases).

DISCUSSION

The mean age of our population was 40.8 years with a range of 15 to 83 years. The mode age was that of young adults between 26 to 35ans. This mean age is similar to that of data obtained from most studies done in Europe which was 41 years [8-11]. Djouadi in 2010 in Algeria had a mean age of 43.5 years [3]. Tolo in 2013 in Cote d'Ivoire reported in his study a mean age of 38 years [12]. We can conclude that, just as these other authors, CML is a pathology of young adults. In 58.7% of cases, we noticed a predominance of males with an sex-ratio of 1:4. Our results are similar to those of some African authors confirming the predominance of male with CML. In fact Djouadi and Tolo found respectively a sex-ratio of 1,01 and 2 in favour of men [3,12]. Maynadié *et al* in France in 2012 showed equally a male predominance in their study [4].

In this study, 26,2% of the patients worked in the informal sector, followed by housewives at 24,6%. This predominance of the informal sector can be explained by the number of patients with a particular profession put in this category and also adds to this category those doing jobs such as taxi drivers, caper terse and brick layers. The non-eligible percentage of house wives can be explained by the fact that housewives are in constant contact with toxic products to carry out their household chores especially detergents. They are equally exposed to daily inhalation of domestic gas which contain hydrocarbons.

Of the 126 patients, 73,8% lived in an urban area. This result could be probably due to the high industrialisation of urban areas, it could equally be due to an unequal distribution often population between urban and rural areas. This could equally be explained by the difficulties in carrying out these diagnosis at rural areas due to lack of infrastructures

We obtained 49.2% of cases who has a secondary level of education, followed by tertiary educational level at 26.2%. This predominance of secondary educational level confirms the fact that CML affects the young adults.

CLINICAL DATA

In this study 63.5% of patients were diagnosed during routine laboratory examinations. This result corresponds to data from literature review. It is similar to the number obtained in 2013 by Tolo *et al* [12] notably 63% of patients diagnosed during a routine laboratory examination. Also in Algeria in 2010, Djouadi found out that 90% of the cases were diagnosed during routine laboratory examinations.

The activity index with respect to WHO less than or equal to 2 was found in 87.2% of patients. Our results are different from those of Tolo [12] who had found out that 100% of patients had the WHO active index greater than 2 at the moment of first consultation. This difference could be explained in that our study was carried out in two big towns of Cameroon where workers can benefit from routine laboratory examinations.

Splenomegaly was present at diagnosis in 97.6% of cases. This result is similar to that of Tolo *et al* [12], who had found 100% of splenomegaly in their study group. Some European authors such as auteurs Brière [14], noticed in 90 % of cases, an easily palpable splenomegaly. Our result analysis help us note that 80% of patients had a spleen Greater or equal to 10cm below the left costal margin. This matches with the values noted by Tolo *et al* [12] who found that 74% of patients presented with a splenomegaly greater than 10cm. A predominance of these voluminous splenomegaly is probably due to delay in consultations in modern hospitals.

In our study, 9 patients out of 126 presented with lymphadenopathies giving a promotion of 7.1%. Tolo *et al* found that 6 patients out of 27% with lymphadenopathies giving a percentage of 22%. We convey with Dreyfus that the development of lymphadenopathies is rare and generally considered severe in CMLs [13]. We obtained that 8% of patients presented with bony pain. Our results are different from those found by Tolo *et al* [12], who found out that 48% of patients presented with bony pain. This difference could be explained in that the study of Tolo *et al* was geared towards cases presenting additional anomalies that occur in patients at acceleration phase or accusations. At these disease stages the occurrence of bony pain is more frequent.

BIOLOGICAL DATA

Leucocytosis was a constantly observed anomaly in all our patients. The leucocyte count varied between 13400 cells/mm³ to 570000 cells/mm³ with a mean of a 167238.3 cells/mm³. This mean is similar to that found by Djouadi in Algeria which was 182737.3 cells/mm³ [3]. On the contrary, Guilhot 1993 at Hospital Saint Louis of Paris reported a mean leucocyte count of 100000 cells/mm³ [9]. Comparing our results to that of European literature helped us notice that the mean leucocyte count was higher than what was observed in Europe. This could be explained by the delay in initial consultation.

In our result series the haemoglobin concentration varied between 1.2 to 15.3 g/dl, with a mean of 9.8g/dl. Our results are comparable to those of Djouadi, who found in Algeria a mean haemoglobin concentration of 9 g/dl. Just like this author we can say that the haemoglobin concentration in CML is reduced [3]. Amongst our patients, 103 had anaemia giving a promotion of 81.7 of cases. This can be explained by the delay in consultations.

The platelet count of our study varied in between 1000 to 2179000 cells/mm³ with a mean of 352632.50 cells/mm³. In our study group, 75 patients, that is 59.5% had a normal platelet count, 31 patients that is 24.6% of cases had a platelet count greater than 450000 and only 19 patients that is 15.9% of cases had a platelet count less than 150000. Taking into consideration this result we agree with Broustet *et al* on the idea that the platelet count is most often elevated or normal and exemption ally reduced [11]. The mean blast count and promyelocytes

were respectively 7.6% and 3.03%. Our results are similar to those proposed by Tolo *et al* [12] Considering the mean blast count which was 7% in this study. This could get us to thinking that the majority of our patients were diagnosed at the active phase of the disease. A bone marrow biopsy and film were done for 119 patients, and the totality that is 100% presented a rich smear and hyperplasia of the granular cell lineage. These results are similar to those of Koumeabalo *et al* in 2009 in Mali.

CYTOGENETIC DATA

All our patients had had cytogenetic examinations; they are classified as follows: 105 patients had done a conventional Karyotype that is 83.3%, 16 had had a FISH that is 12.7%, 4 had had both a conventional karyotype and FISH that is 3.2% and 1 patient had done an RT-PCR that is 0.8%. These different results could be explained in that conventional karyotype is the cheapest amongst these examinations. In our study, 23 patients presented with at least one additional anomaly in their karyotype that is 18.25% of cases. Tolo *et al* [12] in 2013, realised a study on additional anomaly concerning 27 cases in Côte d'Ivoire, demonstrating a negative impact of these anomalies in the survival of these patients. In the literature of Bernard Dreyfus, the additional anomalies occur more often at the acute transformation phase but also at the acceleration phase anomalies [13]. This helps us conclude that in our study group at least 23 patients were either in the acute transformation phase or in the acceleration phase at the moment of diagnosis.

SOKAL PROGNOSTIC CLASSIFICATION

We calculated the sokal prognostic index to evaluate their vital prognosis. We obtained a predominance of the intermediate risk at 55.6% that is 70 patients, followed by high risk at 30.9%. Our results are compatible to those of Djouadi in Algérie who showed equally a predominance of the intermediate risk at 47%, followed by high risk at 35% and low risk at 18%. This predominance of intermediate risk could be explained by delay in treatment of these patients initiated by late delay in consultations [3].

CONCLUSION

At the end of this study we conclude that CML is a pathology of the young adult with male predominance in majority those living in urban areas. It's mostly discovered fortuitously and presents clinically with a splenomegaly in the majority of cases, sometimes associated with a hepatomegaly but very rarely associated lymphadenopathies, bone and articular pain which are signs which testify of the gravity of the disease. We equally find a moderate anaemia but this can also be accompanied by severe anaemia in our context. Approximately one in six patients presents with at least one additional anomaly.

Limitations

The number of cases presented in this article is under estimated as only few patients can pay for the cytogenetic examinations in our context. Just as in all retrospective studies some data was not available. Nevertheless, we think that the results obtained permit us appreciate the presentations of this pathology in our context.

Conflicts of interests

The authors declare no conflict of interest.

Authors' contributions

Ngouadjeu Dongho T.E initiated and wrote the article. Ngosso Cedric a selected the cases and participated in editing. Ngo sack Françoise and Chetcha Bernard participated in editing the article. Anne Andong

Mbong contributed in editing this article and translating it in English from French. Mbanya Dora and Ndom Paul supervised the article.

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