Genetic Diversity of Human Immunodeficiency Virus Type 1 in the Democratic Republic of Congo: a review of available data

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Abstract

Background: HIV has a genetic diversity that is equal to the complexity of the follow up of patients. The classification of the different variants has allowed us to understand the virus, the geographical distribution and evolution of the pandemic and to better guide the follow up and the care of patients infected by HIV.

Aim & Objectives: Review the specifics of the HIV epidemic in the Democratic Republic of Congo (DRC), in terms of different molecular variants of HIV compared to different geographical location published for the country.

Methods/Study Design: The search of the literature and abstracts presented at conferences with the subject of interest to identify different variants of HIV type 1 in the DRC on the websites of research. Online search was based on the following key words: "HIV subtype, DRC", "genotype, HIV, DRC" and "HIV strains in the Democratic Republic of Congo". It was restricted to the published literatures and presented abstracts between 1997 and 2012. Socio-demographic information of the sample, measurement methods and objectives were considered in the evaluation of the search results.

Results/Findings: According to manuscripts published since 1997, we have noticed a dominating prevalence of group M (100%) and of sub-type A at 50.40% [31.2-68.9] for the entire country. In the Eastern part, variants A (44.73%) are dominant on variants C (12.20%), G (11.5%), D (9.12%) and U (7.24%). In the Center, variants A (62.57%) are followed by variants C (10.32%), H (5.02%), U (4.3%) and D (3.9%). In the Western part, variants A (40.91%) are followed by variants G (19.29%), D (10.5%), F (5.65%) and C (4.51%). For the entire country, variants are found in the following order: A (49.40%), G (10.73%), C (9.01%) and D (7.86%). The differences between and within groups are statistically significant for each variants.

Conclusion: Several variants of HIV type 1 circulates throughout the DRC. The most prevalent strains (A, G, C and D) in the DRC are all of Group M (Major). The high number of recombinant forms (CRFs) shows the diversity and dynamics of the virus in this country. This diversity will quickly become a big problem for the fight against HIV in the DRC.

Key words: HIV-1, variants, geography, Democratic Republic of Congo

Introduction

The Human Immunodeficiency Virus (HIV) has genetic diversity which is equal to the complexity of its management. The classification of types, groups, sub-groups, sub-sub-groups and different recombinant forms (CRFs-Circulating Recombinant Forms) or mutant allows for a better understanding of the virus, geographical distribution and evolution of the pandemic.[1-13] It also helped to better guide the management of patients infected with HIV.[2,5,10,11] The Group M (Major) is the dominant group in Central Africa.[1-19] The distribution of this group in Africa and the Democratic Republic of Congo (DRC), in particular, is very heterogeneous, and it follows a specific and complex algorithm.[15-17] This distribution is highly dynamic, scalable and unpredictable and could continue to diversify as long as the virus circulates.[7] There is a very large group M genetic diversity in the sub-Saharan region of Africa.[1-21]

The first case of HIV group M has been documented from a blood sample collected in 1959 in Kinshasa, DR Congo (Leopoldville, Belgian Congo).[22] The DRC, located in the center of Africa, has the largest number of variants of HIV type 1, particularly in terms of group M subtypes, sub-subtypes and CRFs circulating throughout the country.[12,17,23,24-41] With the development of molecular biology techniques in the field of diagnostic virology, classification of HIV strains is updated document and we see new strains circulating in different countries.

To determine the types, subtypes, sub-subtypes and CRFs circulating in DRC research genotyping strains have been made in recent years in some cities. These studies were conducted in Bukavu (South Kivu),[30] Bwamanda (Equateur province),[24] Kimpese (Bas Congo),[25] Kinshasa (Kinshasa province),[24] Kisangani (Orientale Province),[26,30] Likasi[31] and Lubumbashi[26] (Katanga province), and Mbuji Mayi (Kasai Oriental).[24] These give us a geographical representation of partial strains circulating in DRC based on the territorial geography: East (Bukavu, Kisangani, Likasi, and Lubumbashi), West (Kinshasa Kimpese) and Centre (Bwamanda, Mbuji Mayi). In our context, the East includes the provinces of Katanga, Maniema, North Kivu, South Kivu and Orientale Province. The Center includes the provinces of Kasai Occidental, Kasai Oriental and Equateur. The West includes the provinces of Bandundu, Bas-Congo and Kinshasa.

The objective of this analysis is to review the specifics of the HIV epidemic in the Democratic Republic of Congo, in terms of molecular variants of human immunodeficiency virus in relation to geography published in the country.

Methods

We searched the literature and abstracts presented at conferences with the subject of interest to identify different variants of HIV type 1 in Democratic Republic of Congo (DRC). The research literature on these different strains was done on the internet websites following research: (i) MEDLINE / PubMed, (ii) POPLINE electronic database of published documents, (iii) data of access public articles presented at conferences, (iv) scientific report published on the Internet, (v) Google Scholar, and (vi) Cochrane Library. This online research was based on the following key words: "HIV subtype, DRC", "genotype, HIV, DRC" and "strains of HIV in the Democratic Republic of Congo".

The search was limited to published works and abstracts presented over the past 15 years (1997 to 2012). The manuscripts were selected according to the relevance of the results and the representativeness of the sample. The demographic information of the sample, measurement methods and objectives were considered in the evaluation of articles. Reading various articles allowed excluding items that do not relate directly circulating strains in the Democratic Republic of Congo.

Outcome analysis was made with SPSS version 17.0 for Windows. Student's t test and analysis of variance were used to compare and evaluate the different results.
The results are expressed as a percentage and average percentage extremes [minimum-maximum].

Results

A literature search was performed by systematic interrogation of bibliographic databases and medical scientists over a period of 15 years. A step common to all studies is to systematically seek recommendations, systematic reviews, Meta-analyzes and other assessment work already published nationally and internationally. Several useful websites (government agencies, societies, etc.) were consulted.

Documents that were not accessible by conventional circuit dissemination of information (gray literature) were sought by other means available. The review of references cited in the articles analyzed to select items not identified during the interrogation of different sources of information.

Several manuscripts had as objective the identification of strains circulating in Democratic Republic of Congo (DRC).

According to the articles and abstracts of conferences published since 1997, we found a prevalence dominant group M (100%) and subgroup A 50.40% [31.2 to 68.9] in the throughout the DRC. In the East, influenza A (44.73%) are dominant strains C (12.20%), G (11.5%), D (9.12%) and G (7.24%) (Table 1). Centre, influenza A (62.57%) followed by strains C (10.32%),

H (5.02%), U (4.3%) and D (3.9%) (Table 2). In the West, the influenza A (40.91%) are closely followed by strains G (19.29%), D (10.5%), F (5.65%) and C (4.51%) (Table 3).

For the whole country, the strains are found in the following order: A (49.40%), G (10.73%), C (9.01%) and D (7.86%) (Table 4). Differences within and between groups are statistically significant for the different strains (p> 0.001).

Figure 1 gives us a picture of the distribution of different variants of HIV type 1 in the country.

Discussion

This work was to identify the different variants of the Human Immunodeficiency Virus (HIV) circulating in the Democratic Republic of Congo (DRC) in the publications made since 1997.
Several papers have been published as a direct objective the identification of different strains circulating in the DRC. Other work has been done to clarify on what had already been published by the same groups. Some others have addressed the genetic diversity of HIV in the DRC in general terms (continental or global).

To the east of the country to the towns of Bukavu (Bk) in the province of South Kivu, Kisangani (Ks) in the Eastern Province, Lubumbashi (Lu) and Likasi (Lk) in the province of Katanga, the group M is the most common. A variant is the most abundant with an average of 44.73% (53.0% in Bukavu, Kisangani 34.75% to 39.6% in Lubumbashi, Likasi 45.45%). The difference between the different prevalences of A is statistically significant (p> 0.001). Variant B was found in Bukavu and Kisangani respectively 1.2% and 4.8%. All other variants were found in this part of the country at different prevalences: C (Bk-18, 1%, 2-Ks, 78%, Lu-9, 4%, Lk-18, 2%), D (bk-1, 2%, 12-Ks, 3% Mo-13, 9%, Lk-9, 1%), F (bk-4, 8%, 3-Ks, 98% Mo-1, 4 % Lk-0), G (Bk-4, 8%, 21-Ks, 7%, Mo-10, 4%, Lk-9, 1%), H (Bk-1, 2%, 6-Ks , 5%, Mo-6, 25%, Lk-0), J (Bk-0, Ks-1, 2%, Mo-1, 4%, Lk-18, 2%), K (Bk-0, ks-0, Lu-2, 8% Lk-0) and U (Bk-13, 2%, 8-ks, 18% Mo-7, 6%, Lk-0). Intragroup differences in prevalence (p> 0.001) due to the location of cities, the influence of neighboring countries and the movement of populations in the region.

Center of the country, in the cities of Bwamanda (Bw) in the Province of Ecuador and Mbuji-Mayi (Mb) in the province of Kasai Oriental, only group M variants circulating. A variant is dominant at 62.6% [55.8 to 68.9] (68.9% and 56.25% Bwamanda in Mbuji-Mayi). The difference between the different prevalence's of A is statistically significant (p> 0.001). Alternatives B (2.2%) and E (6.7%) were identified Bwamanda and not in Mbuji-Mayi. Variants C (20.65%), D (7.95%), G (2.8%), J (5.15%) and CRF02_AG (2.33%) have been described in Mbuji-Mayi without been found to Bwamanda. Variants F (Bw-2, 2% Mb-0, 85%), H (Bw-8, 9%, Mb-1, 15%), K (Bw-4, 4% Mb-0, 85 %) and U (Bw-6, 6%, Mb-2, 01%) were identified in two cities with statistically significant differences in prevalence (p> 0.001). Although the two cities are included in the central part of the country, is located north Bwamanda with border countries like the Republic of Congo and the Central African Republic while Mbuji-Mayi is situated in the south near the Katanga province and as a country with border of Angola.

To the west of the country to the cities of Kinshasa (Kn) in the province of Kinshasa and Kimpese (Kp) in the province of Bas Congo, group M is dominant. A variant is the dominant 40.91% [23.0 to 47.5] (34.32% and 47.5% in Kinshasa to Kimpese). The difference between the prevalence was statistically significant (p> 0.00). Variants J (1.66%), K (1.12%), U (3.48%), CRF01_AE (4.95%), CRF02_AG (0.5%), CRF05_DF (0.35%) and CRF11_cpx (0.17%) present in Kinshasa are not identified Kimpese. Variants C (Kn-7, 42%, Kp-1, 6%), D (Kn-11, 2%, Kp-9, 8%), E (Kn-0, 14%, Kp-3, 2 %), F (Kn-4, 8%%, Kp-6, 5%), G (Kn-17, 28%, Kp-21, 3%) and H (Kn-3, 89% 4-Kp 9%) were identified in the two cities. The difference in the prevalence of sub-group was significant (p> 0.001). Kinshasa has a greater diversity of strains compared to Kimpese. The latter is a rural town while Kinshasa is a city where there are people who come from the four corners of the country and even neighboring countries.

The subgroup B is more prevalent in Europe and North America.[1-13] Many publications do not mention it in Central Africa was affirmed by Huang et al[35] published in 2009 they did not detect the subgroup B in the Democratic Republic of Congo. While Vidal et al have published 2.4% of the sample Bwamanda infected with subgroup B in 1997 [24] and Eiji et al have published 4.8% for the subgroup B in Kisangani in 2006 and 1.2% in Bukavu in 2007.[30] Peeters et al published in 2003 only 0.4% of samples from the DRC subgroup B.[19] This discrepancy may be due to a factor of time, location and sampling.

The subgroup K is found in the DRC with an average of 2.25% [0.0 to 4.4] (Bwamanda-4, 4%, Kinshasa-1, 12% Lubumbashi-2, 8%, Mbuji Mayi-0.85%). This subgroup is rarely documented even in Central Africa. Kandathil et al in 2005 confirmed that this subgroup is unique to Cameroon and the DRC.[3]

The geographical distribution of HIV-1 variants in the DRC is closely related to the distribution of variants in neighboring countries.[26] Neighbors Northeast (Sudan[42], Uganda[15,43-46], Rwanda[15,47], Burundi[15,48,49]), the predominant strains are D, C, A and B. While in neighboring South East (Tanzania[15,50,51], Zambia[15,52] and even Kenya[15,52-54]), the dominant strains are A, C and D. This would explain the difference in prevalence between the East Kisangani / Bukavu and Lubumbashi north-east / south-east Likasi. The southern neighbor, Angola[15,55-57], a dominance of strains A, C and H, which is reflected in Kinshasa and Kimpese. The western neighbor, the Republic of Congo[15,58-60], a dominance of strains A, D and G, which is also reflected in Kinshasa and Kimpese. Neighbor of North, Central African Republic[15,61,62], a dominance of strains A, B, D and CRF01_AE is reflected on Bwamanda. The rural exodus (to major cities such as Kinshasa, Lubumbashi and Mbuji Mayi), the displacement of victims of war in the East as well as the movement of people across borders of the DRC makes this difficult to control pandemic for the country.

Conclusion

Several variants of HIV type 1 circulating through the Democratic Republic of Congo. Distribution is a mosaic, it is different depending on the province, the distribution in the country and the methods used. In general, the most prevalent strains (A, G, C and D) in the DRC are all

Group M (Major). The high number of recombinant forms (CRFs) shows the diversity and dynamics of virus in this country. This diversity could quickly become a big problem for the fight against HIV in the DRC.

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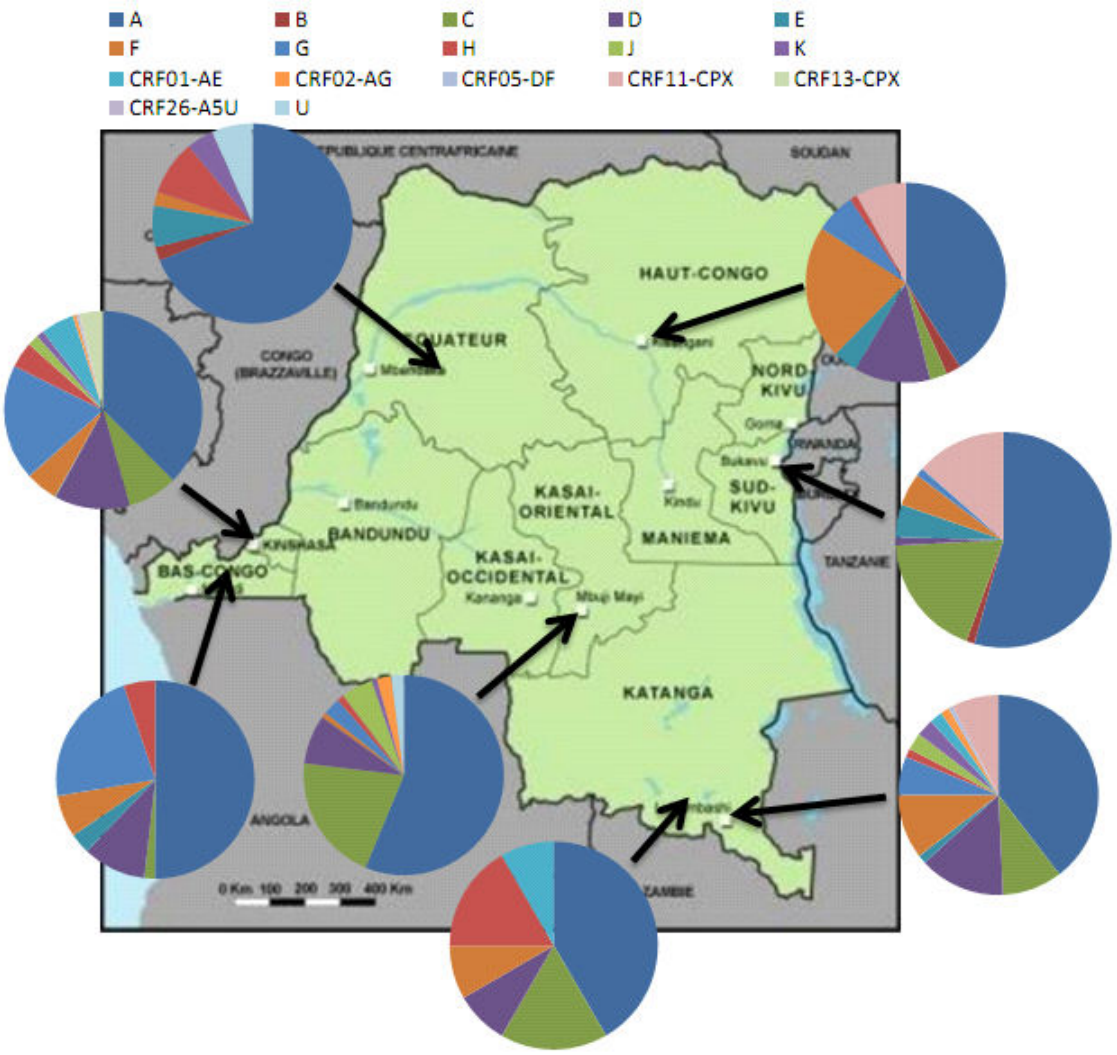

Figure 1: Geographic distribution of HIV variants

Table 1 : Variants circulating in the **Eastern** portion (Bukavu, Kisangani, Lubumbashi, Likasi)

Types/Sous-types/CRFs		Kisangani			Lubumbashi	Likasi	Bukavu	Means % DRC-East
		2002Δ [6] (n=23)	2006 [**31**] (n=83)	**Means Kisangani (%)**	2002Δ [6] (n=144)	2004° [**30**] (n=27, n'=11)	2007 [**31**] (n=83)	
M	**A**	8 (34,75%)	39 (47,0%)	40,875 [34,75-47,0]	57 (39,6%)	5 (45,45%)	44 (53,0%)	44,73 [39,6-53,0]
	B	0	4 (4,8%)	2,4 [0-4,8]	0	0	1 (1,2%)	0,9 [0-4,8]
	C	1 (4,35%)	1 (1,2%)	2,78 [1,2-4,35]	14 (9,7%)	2 (18,2%)	15 (18,1%)	12,20 [1,2-18,2]
	D	4 (17,4%)	6 (7,2%)	12,3 [7,2-17,4]	20 (13,9%)	1 (9,1%)	1 (1,2%)	9,12 [1,2-17,4]
	F	1 (4,35%)	3 (3,6%)	3,98 [3,6-4,35]	2 (1,4%)	0	4 (4,8%)	2,54 [0-4,8]
	G	5 (21,7%)	18 (21,7%)	21,7	15 (10,4%)	1 (9,1%)	4 (4,8%)	11,5 [4,8-21,7]
	H	3 (13,0%)	0	6,5 [0-13,0]	9 (6,25%)	0	1 (1,2%)	3,49 [0-13,0]
	J	0	2 (2,4%)	1,2 [0-2,4]	2 (1,4%)	2 (18,2%)	0	5,2 [0-18,2]
	K	0	0	0	4 (2,8%)	0	0	0,7 [0-2,8]
	CRF01-AE	0	0	0	4 (2,8%)	0	0	0,7 [0-2,8]
	CRF02-AG	0	0	0	3 (2,1%)	1 (9,1%)	0	2,8 [0-9,1]
	CRF05-DF	0	0	0	2 (1,4%)	0	0	0,35 [0-1,4]
	CRF11-cpx	0	0	0	1 (0,7%)	0	0	0,175 [0-0,7]
	U	1 (4,35%)	10 (12,0%)	8,18 [4,35-12,0]	11 (7,6%)	0	11 (13,2%)	7,24 [0-13,2]

ΔIdentification by sequencing the genome part env
No identification by sequencing of env and pol part of the genome
* ID by sequencing part of the gag and env genome
+ Identification by sequencing the pol part of the genome
n 'match phylogenetic
Different averages are expressed in "% Average [% extremes]"

Table 2: Variants circulating in the **Central** share (Bwamanda Mbuji Mayi)

Types/Sous-types/CRFs		Bwamanda	Mbuji Mayi			Means % DRC-Central
		1997Δ [4] (n=45)	1997Δ [4] (n=60)	2002Δ [6] (n=43)	**Means Mbuji Mayi (%)**	
M	**A**	31 (68,9%)	34 (56,7%)	24 (55,8%)	56,25 [55.8-56.7]	62,57 [55.8-68.9]
	B	1 (2,2%)	0	0	0	1,1 [0-2,2]
	C	0	15 (25,0%)	7 (16,3%)	20,65 [16.3-25.0]	10,32 [0-25.0]
	D	0	4 (6,6%)	4 (9,3%)	7,95 [6.6-9.3]	3,97 [0-9.3]
	E	3 (6,7%)	0	0	0	3,35 [0-6.7]
	F	1 (2,2%)	1 (1,7%)	0	0,85 [0-1.7]	1,53 [0-2.2]
	G	0	2 (3,3%)	1 (2,3%)	2,8 [2.3-3.3]	1,4 [0-3.3]
	H	4 (8,9%)	0	1 (2,3%)	1,15 [0-2.3]	5,02 [0-8.9]
	J	0	2 (3,3%)	3 (7,0%)	5,15 [3.3-7.0]	2,58 [0-7.0]
	K	2 (4,4%)	1 (1,7%)	0	0,85 [0-1.7]	2,63 [0-4.4]
	CRF01-AE	--	--	0	0	0
	CRF02-AG	--	--	2 (4,65%)	2,33 [0-4.65]	1,16 [0-4.65]
	CRF05-DF	--	--	0	0	0
	CRF11-cpx	--	--	0	0	0
	CRF13-cpx	--	--	0	0	0
	CRF26-A5U	--	--	--	0	0
	U	3 (6,6%)	1 (1,7%)	1 (2,33%)	2,01 [1.7-2.33]	4,3 [1.7-6.6]

ΔIdentification by sequencing the genome part env
No identification by sequencing of env and pol part of the genome
* ID by sequencing part of the gag and env genome
+ Identification by sequencing the pol part of the genome
Different averages are expressed in "% Average [% extremes]"

Table 3: Variants circulating in the **Western** part (Kinshasa, Kimpese)

Types/Sous-types/CRFs		Kinshasa						Kimpese	Means % DRC-West
		1985-86*[7] (n=24, n'=16)	1997Δ [4] (n=142)	1999-2000*[7] (n=83, n'=44)	2002Δ [6] (n=144)	2007+ [10] (n=94)	Means Kinshasa (%)	1988-94g [5] (n=70)	
M	**A**	5 (31,2%)	62 (43,7%)	15 (34,1%)	57 (39,6%)	22 (23,0%)	34,32 [23.0-43.7]	29 (47,5%)	40,91 [23.0-47.5]
	B	0	0	0	0	0	0	0	0
	C	0	3 (2,2%)	5 (11,4%)	14 (9,7%)	13 (13,8%)	7,42 [2.2-13.8]	1 (1,6%)	4,51 [1.6-13.8]
	D	1 (6,2%)	19 (13,4%)	8 (18,2%)	20 (13,9%)	4 (4,3%)	11,2 [4.3-18.2]	6 (9,8%)	10,5 [4.3-18.2]
	E	0	1 (0,7%)	0	0	0	0,14 [0-0.7]	2 (3,2%)	1,67 [0-3.2]
	F	2 (12,5%)	8 (5,6%)	2 (4,5%)	2 (1,4%)	0	4,8 [0-12.5]	4 (6,5%)	5,65 [0-12.5]
	G	6 (37,5%)	15 (10,5%)	10 (22,7%)	15 (10,4%)	5 (5,3%)	17,28 [5.3-37.5]	13 (21,3%)	19,29 [5.3-37.5]
	H	0	14 (9,8%)	1 (2,3%)	9 (6,25%)	1 (1,1%)	3,89 [0-9.8]	3 (4,9%)	4,4 [0-9.8]
	J	0	5 (3,5%)	1 (2,3%)	2 (1,4%)	1 (1,1%)	1,66 [0-3.5]	0	0,83 [0-3.5]
	K	0	4 (2,8%)	0	4 (2,8%)	0	1,12 [0-2.8]	0	0,56 [0-2.8]
	CRF01-AE	2 (12,5%)	0	2 (4,5%)	4 (2,8%)	‡	4,95 [0-12.5]	0	2,47 [0-12.5]
	CRF02-AG	0	0	0	3 (2,1%)	‡	0,52 [0-2.1]	0	0,26 [0-2.1]
	CRF05-DF	0	0	0	2 (1,4%)	‡	0,35 [0-1.4]	0	0,17 [0-1.4]
	CRF11-cpx	0	0	0	1 (0,7%)	‡	0,17 [0-0.7]	0	0,08 [0-0.7]
	U	0	11 (7,7%)	0	11 (7,6%)	2 (2,1%)	3,48 [0-7.7]	0	1,74 [0-7.7]

ΔIdentification by sequencing the genome part env
No identification by sequencing of env and pol part of the genome
* ID by sequencing part of the gag and env genome
+ Identification by sequencing the pol part of the genome
gIdentification by sequencing the portion of the genome gag
n 'match phylogenetic
‡ 15% CRFs (01_AE, 02_AG, 11_cpx, 13_cpx, 25_cpx, 26_A5U, 37_cpx, 43_02G and 45_cpx)
Different averages are expressed in "% Average [% extremes]"

Table 4 : Variants circulating in The **Democratic Republic of Congo**

Types/Sous-types/CRFs		RDC N=247 [8] en %	**Means DRC-East en %**	**Means DRC-Central en %**	**Means DRC-West en %**	**Means DRC* en %**
M	A	51,4	44,73 [39,6-53,0]	62,57 [55,8-68,9]	40,91 [23,0-47,5]	49,40 [23,0-68,9]
	B	0,4	0,9 [0-4,8]	1,1 [0-2,2]	0	0,67 [0-4,8]
	C	7,3	12,20 [1,2-18,2]	10,32 [0-25,0]	4,51 [1,6-13,8]	9,01 [0-18,2]
	D	9,3	9,12 [1,2-17,4]	3,97 [0-9,3]	10,5 [4,3-18,2]	7,86 [0-18,2]
	E	0	0	3,35 [0-6,7]	1,67 [0-3,2]	1,67 [0-6,7]
	F	4,1	2,54 [0-4,8]	1,53 [0-2,2]	5,65 [0-12,5]	3,24 [0-12,5]
	G	6,9	11,5 [4,8-21,7]	1,4 [0-3,3]	19,29 [5,3-37,5]	10,73 [0-37,5]
	H	7,3	3,49 [0-13,0]	5,02 [0-8,9]	4,4 [0-9,8]	4,30 [0-13,0]
	J	2,8	5,2 [0-18,2]	2,58 [0-7,0]	0,83 [0-3,5]	2,87 [0-18,2]
	K	3,2	0,7 [0-2,8]	2,63 [0-4,4]	0,56 [0-2,8]	1,30 [0-4,4]
	CRF01-AE	1,6	0,7 [0-2,8]	0	2,47 [0-12,5]	1,06 [0-12,5]
	CRF02-AG	2,55	2,8 [0-9,1]	1,16 [0-4,65]	0,26 [0-2,1]	1,41 [0-9,1]
	CRF05-DF	--	0,35 [0-1,4]	0	0,17 [0-1,4]	0,17 [0-1,4]
	CRF11-cpx	--	0,175 [0-0,7]	0	0,08 [0-0,7]	0,085 [0-0,7]
	CRF13-cpx	--	0	0	0	0
	CRF26-A5U	0	0	0	0	0
	U	6,0	7,24 [0-13,2]	4,3 [1,7-6,6]	1,74 [0-7,7]	4,43 [0-13,2]

* According to literature review