603: Increase in HIV Primary Drug Resistance in a Demographic Surveillance Area in Rural KwaZulu-Natal South Africa

Justen Manasa; Siva Danaviah; Frank Tanser; Sureshnee Pillay; Hloniphile Mthiyane; Eduan Wilkinson; Deenan Pillay; Tulio de Oliveira
Africa Centre for Health and Population Studies, University of KwaZulu-Natal, Durban, South Africa

Background: Antiretroviral therapy (ART) has been associated with significant reduction in HIV and AIDS morbidity and mortality as well as incidence.

As more patients access antiretroviral therapy (ART), higher proportions of newly infected patients may be infected with drug-resistant viruses.

Recent results suggest an increase of transmitted drug resistance in East Africa as well as some parts of southern African countries with older public treatment programmes.

There is need for close surveillance of the transmission of drug resistance in southern Africa where high rates of transmission persist despite rapid expansion of ART.

Methods: The study used samples collected from a population-based HIV surveillance conducted in 2010, 2011 and 2012.

The surveillance is conducted in the rural district of uMkhanyakude in northern KwaZulu-Natal, which had an adult (15-49 years) HIV prevalence of 29% in 2011.

With a crude HIV incidence of 2.63 per 100 person years between 2004 and 2011 for all adults >15 years of age, this area has one of the highest incidence rates in South Africa.

Antiretroviral therapy is most accessed through a 10 year old rapidly expanding and devolving public treatment programme.

Figure 1: The Africa Centre demographic surveillance area is a 438 km² area on the east coast of South Africa between a national high way (N2) and a game reserve. The area has a population of approximately 95000 people, of which about 24% are HIV infected and about 25000 are accessing antiretroviral therapy through the public treatment programme.

More info: bioafrica.net | africacentre.ac.za

Methods: Dry Blood Spot (DBS) samples with a viral load ≥ 10,000 c/ml were genotyped using the SATuRN-Life Technologies genotyping protocol.

The 2009 Surveillance of Drug resistance mutation list was used to assess for drug resistance in treatment naïve participants.

Detailed participants' testing and treatment history and demographic data were obtained the surveillance database.

The participants were grouped into recently infected and chronically infected based on their testing histories. Three threshold for recent infection were assessed, ≤12, ≤24 and ≤36 months.

Proportions of samples with any SDRM were compared for the years 2010, 2011 and 2012, using the Chi-squared test for trend, to see if there was any trend in transmitted drug resistance

Results: Data from 701 participants were used. Table 1 shows the distribution of the participants by year and their demographics.

36 (5.1%) of the 701 participants had ≥1 SDRM.

32 (4.6%) of the participants had non-nucleoside reverse-transcriptase inhibitor SDRM. The K103N mutation was the most common, occurring in 27 (3.8%).

10 (1.4%) of the participants had nucleoside reverse-transcriptase inhibitor (NRTI) SDRM, of which 9 had a single NRTI mutation only.

7 (1.0%) participants had both NNRTI and NRTI resistance mutations; K103N + M184V being the most common combination.

No TDR was detected in 2010. 2011 and 2012 both had 18 participants with any SDRM, 4.7% and 7.1% respectively

The p-value for the X^2 trend test between 2010 and 2012 showed a statistically significant change in the percentage of participants with any SDRM (p = 0.0246) (Figure 2).

The proportions of patients with ≥1 SDRM were not significantly different between the participants classified as recently infected and chronically infected (Table 2).

		2010	2011	2012	Total
Participants, No		67	381	253	701
Men, n (%)		10 (15%)	93 (24%)	73 (29%)	176 (25%)
Age, mean (SD), y		29 (9)	34 (12)	34 (13)	34 (12)
Viral load, log_{10} copies/ml, Mean (SD)		-	5.0 (0.3)	5.1 (0.4)	5.1 (0.6)
#Estimated Duration of Infection, mean (SD), months		28 (16)	29 (20)	34 (26)	30 (21)
Proportion with recent infection according to different thresholds	≤12 months	25%	10%	10%	11%
	≤24 months	45%	18%	14%	19%
	≤36 months	66%	23%	17%	26%

Table 1: Summary of the characteristics of the surveillance participants included in the analysis from the three sampling years

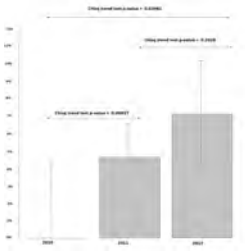

Figure 2: The percentage of participants whose samples had evidence of surveillance drug resistance mutations between 2010 and 2012. The p-value for the X^2 trend test between 2010 and 2012 showed a statistically significant change in the percentage of participants with any SDRM (p = 0.0246). There were no significant difference between 2010 and 2011 or 2011 and 2012. The X^2 trend test taking into account all three years had a p value of 0.0200.

Definition of recent infections		Recently infected, % (n)	Chronically infected, % (n)	p-value
≤12 months	All	10% (62)	3% (422)	0.1073
	2011	11% (37)	4% (263)	0.0584
	2012	8% (25)	6% (159)	0.7474
≤24 months	All	9% (104)	4% (380)	0.0939
	2011	9% (68)	3% (232)	0.0646
	2012	8% (36)	6% (148)	0.6235
≤36 months	All	7% (135)	5% (349)	0.2167
	2011	7% (91)	4% (209)	0.2965
	2012	9% (44)	6% (140)	0.4288

Table 2: Percentage of participants with surveillance drug resistance mutations according to three different definitions of recent infections.

Figure 3: Geographic map showing the Africa Centre demographic surveillance area and the approximate location of the household of individuals with any SDRM. The two main roads are marked in yellow (N2 and R618).

Conclusion: Our results suggest that levels of transmitted drug resistance are increasing in rural KwaZulu-Natal. With current levels of transmitted drug resistance, the current treatment recommendations are still effective. However, there is need for more vigilance in the surveillance of transmitted drug resistance in order to identify further increases that might impact on the choice of the recommended first-line regimens, this is specially important for a treatment as prevention trial (TasP) at Africa Centre.

Funding: This research has been fund by the South African Medical Research Council, and South Africa National Research Foundation. Africa Centre is funded by a strategic award of the Wellcome Trust.