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Determinants of Adherence to Anti-retroviral therapy in HIV Positive patients, Nampula, Mozambique, 2014.

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ABSTRACT

Background and objective: *the HIV epidemic in Mozambique is a public health problem. The Mozambican National Health Service expanded treatment with Antiretroviral therapy (ART) to all districts of the country in 2009. Unfortunately the expansion of ART was followed by a high rate of ART non-compliance thought to be due to inadequate food intake and difficulty accessing health centres due to transport and resource availability issues. Causes of non-compliance with treatment have not been well researched. Our research evaluates ART adherence rates in Nampula Province and treatment non-compliance reasons.*

Methods: *a quantitative cohort study was undertaken in 5 health centres in areas of Nampula Province. Surveys were done with patients on treatment and patients who are non-compliant with therapy. Patient information documents (clinical files, pharmacy and statistical records) were also consulted.*

Results: *ART non adherence rates attained 40%. We surveyed 208 patients who were ART adherent and 86 patients who were non-compliant with therapy, 70% were female, between 18 and 62 years of age. The main reason for treatment non-compliance (36%) was the stigma attached to having HIV; 58% of all people do not have enough food, 37% suffer from depressive ideation and 18% abuse substances, mainly alcohol. ART adherence (>95% of pills are taken for the last three months) is 69%, but 36% of people who are adherent have a CD4 count under 350 and 63% are not following the Health Ministry recommended treatment protocol.*

Discussion: *families and local communities percept stigma of having HIV is considered the main reason for ART non-adherence, but food insecurity and depression are also important determinants. Although poor health services occupy the last position in ART cessation causes, many patients are not following the recommended treatment protocol due to Health Centre deficits. ART adherence rate of 69% explains the high incidence of opportunistic infections (27%).*

Conclusion*: ART non-adherence in Nampula is a serious and complex problem due to individual, social and health system factors. It will be necessary to develop an interdisciplinary*

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intervention with patients and their families, health professionals and traditional healers, to reverse this situation and improve the long term outcome of HIV patients.

KEY WORDS: ART non-compliance, ART non-adherence, Nampula, Mozambique.

1. INTRODUCTION

Worldwide in 2010 about 34 million people were living with Human Immunodeficiency Virus (HIV) and almost half (47%, 6.6 million) of 14.2 million people eligible for treatment had access to antiretroviral treatment (ART).[1]

The United Nations General Assembly (2011) Political Declaration on HIV and Acquired Immune Deficiency Syndrome (AIDS), made the following findings:

- "The International Drug Purchase Facility based on innovative financing and focused on access, quality and reduction of prices of antiretroviral medicines (ARV) allowed the expansion of access to ART.
- Access to safe, effective, affordable, good-quality medicines and commodities in the context of epidemics such as HIV is fundamental to the full realization of the right of everyone to enjoy the highest attainable standard of physical and mental health."[2]

Adherence to ART is the key factor in determining the degree and duration of viral suppression[3]. A study in Spain showed that inadequate social and family environments diminish the adherence rate to ART[4]. Another study in Uganda found that "in patients on ART, routine laboratory monitoring is associated with better health and survival compared with clinical follow-up alone".[5]

The Mozambican population has suffered a significant negative impact due to HIV infection in terms of morbidity an mortality. One of the challenges is the increasing burden on the health system, which suffers a general lack of health professionals, especially in rural areas. In 2011 Mozambique had a HIV prevalence of 11,5% prevalence and about 46% on ART[6] compared to 3,500 patients receiving treatment in 2003, attesting to the effectiveness of the Health Ministry's efforts to bring ART to all the country's districts.

Professional experience over six years in HIV clinics in Mozambican Zambezia and Nampula provinces and other health professionals' testimonies underline food insecurity and low accessibility to health services as the two main difficulties for ART expansion in Mozambique.

In the last three years treatment withdrawals numbers have increased significantly, causing a new public health challenge, due to the danger of quickly developing resistance to ARV's if therapy is interrupted. In Nampula province, HIV infection prevalence rate is below 10% (national average 16%).[7] However ART non-compliance can cause the spread of resistant viruses and increase mortality.

Thus the HIV problem is still worrying and faced with this situation, Lúrio University Health Sciences Faculty (HSF) did the following: 1) planned knowledge translation programme necessary for the development of local communities; 2) acquired financing from the Institutional Development Fund of the Ministry Education to fund this project. Another reason to study ART adherence[8] and ART

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cessation determinants in Nampula, is the absence of systematic knowledge regarding these determinants[9] [10]. Having a clear idea of these determinants will allow the researchers to implement actions to reduce this public health problem.

The research two main objectives are: 1) evaluate ART adherence[11] [12] in Nampula province health centres (HC); 2) identify ART cessation main factors in these patients.

2. METHODOLOGY

Descriptive cohort study using quantitative and qualitative methods[13].

Study population: patients seeking care in five HC in Nampula province during 2014 and enrolled to take ART, including those who are adherent and those who are non-compliant with ART or ceased ART.

Sample: the number of patients to be surveyed in each district (in treatment and who ceased therapy) was calculated using the formula ($n = pq \varepsilon^2 / i$) where (n = sample number of subjects, $\varepsilon = 1.96$, p = ART last dropout rate prevalence in the HC, $q = 1 - p$, considering a confidence range = 98%, $i = 0.02$ error limit). It was added a margin of 10% for occasional losses or dropouts, and calculated 165 patients on ART and 165 patients who are non-adherent to meet the above parameters. The subjects on ART were randomly chosen, according to a random date of query to ART service. It was used a snowball sampling to find people who were non-compliant with therapy (with active search, AS, and individual availability signing an informed consent form).

Inclusion criteria: districts with prevalence of HIV and ART's cessation rate higher than the provincial average, and an ART program that is implemented in a HC with accurate statistical data including geographic location, and evidence of voluntary participation.

Non-inclusion criteria: patient who does not sign an informed consent form.

Exclusion criteria: patients with acute illness or intoxication, or who wished to withdraw from the study.

Variables: district, gender, age, on ART, adherence, education, time in treatment, number of doses and pills per day, depression, consumption of psychotropic substances, family support, membership in Community Adherence Support Group (CASG), use of traditional medicine, knowledge about risks of poor adherence, attendance for ARV pharmacy refills in the last 3 months, food availability, Body Mass Index (BMI), medication intake failure over the last 72 hours and last month[14], last CD4 count level and date, alleged causes of ART non-compliance, occurrence of diarrhoea or vomiting in the last week and Tuberculosis (TB) in the last month.

ART dropout data were reviewed through the Nampula Provincial Health Directorate (NPHD) and statistical districts HC records. HC ART program leaders were interviewed. Seven questioners were selected (completed secondary education, fluency in the local language, unrelated to the health care system, unknown to respondents), trained and signed ethical commitment term for undertaking the active search (patients who had abandoned ART) within a HC pedestrian radius (five kilometres), being paid 100 meticais (2.5 euro) per survey.

The study followed five phases: 1) districts and HC selection: documental analysis and geographical criteria: HC 25 September, Nampula City - urban; Nacaroa HC - corridor; Lalaua HC - rural; Murrupula HC - corridor; Mossuril HC - coast (see Annex Table III); 2) target groups identification: patients on ART, patients who dropped out ART; documental analysis (HC statistics and medical records, see Annex Table IV); 3) references about dropout causes in ART services were searched and reviewed; 4) patients surveys[15], review of Pharmacy ARV dispensing registers and interviews with health professionals in charge of HC ART program[16]; 5) data introduction in Statistical Package for Social Sciences 21, data processing, inferential (bivariate) analysis and interpretation of results[17].

The following risks were considered and prevention methods applied to avoid bias: institutional risks – statistical indicators health records low reliability controlled by gathering information locally at HC; poor individual medical records, controlled by patients clinical examination; target group risks - reliability of survey responses, controlled by triangulation questions, records in clinical files and HC pharmacy.

The research protocol was approved by the Lúrio University Institutional Bioethics Committee for Health and by NPHD and the research complied with all Helsinki Declaration recommendations (2013).

3. RESULTS

ART cessation rates collected in district HC monthly statistics vary from 40% (Nacaroa) to 7% (Nampula), with an average of 11%. Were surveyed 295 subjects (208 on ART surpassing the calculated sample and 86 cessations, lower than expected due to missing or incorrect information in medical records for their location by the inquirers in the AS), 70% were female, between 18 to 62 years old. ART cessation rates were inversely proportional to age and 81% of patients have an inadequate level of education (illiterate or primary level) and had limited comprehension and expression of Portuguese which is the official language of the country. The following table shows patients reported causes for ART cessation.

Table I: patients reported ART cessation causes (86).

Causes	% Respondents
Fear of society (stigma and discrimination, rejection and divorce)	36%
Travel (with temporary change of residence)	27%
ARV Side effects[18]	26%
HC Poor care	13%

Depression[19] signs or symptoms are or were present in 37% of the group (295) but the majority (82%) said they do not consume psychotropic substances[20] (alcohol consumption[21] [22] was seen in 15%); 58% consider that they lack sufficient food; severe under nutrition (BMI <18.5) is present in 12%.

Table II: risk factors for ART cessation (295)

Risk factors	Patients on ART (208)	Patients who left ART (86)	p
Time on ART	90% between 4 months and more than 4 years	71% between less than 3 months and a year	p = 0,000
Number of daily doses	One (50%)	More than one (72%)	p = 0,000
Lack of family support[23]	55%	67%	p = 0,012
Do not know CASG	63%	91%	p = 0,000
Belong to CASG	14%	0%	p = 0,01
Think CASG facilitates ART	45%	4%	p = 0,000
Relies on traditional medicine	24%	37%	p = 0,18
Know poor adherence risks	51%	41%	p = 0,000

In ART patients (208) 27% missed taking at least one dose over the last 3 days and 33% failed at least once in the previous month[24] (failure of two or more doses was observed in 23%); 26% did not regularly pick up ARV in HC Pharmacy during last 3 months[25] (ARV refill for these patients is limited to HC Pharmacy). ART adherence (> 95% doses taken[26] in the last three months) estimated average in 5 districts stands at 69% but 36% had a low CD4 count (<350) and 63% do not comply with ART monitoring protocol (CD4 count every 6 months). The occurrence of diarrhoea or vomiting in the last week was reported by 18% and the incidence of tuberculosis in the last month was reported by 9%.

4. DISCUSSION

The researchers were initially challenged by insufficient and unreliable information at central level (NPHD) and in the HC, including that in clinical files that did not allow the AS for absentees and cessations. ART cessation rates are underestimated in districts HC HIV programme indicators statistics. ART cessation main reason pointed by patients, stigma and discrimination, as also pointed out by other authors[27], is confirmed by the significant lack of family support. The low level of education, also confirmed by the literature[28], could explain the second cessation cause, travelling, because patients did not change residence but did not make the documentation transfer for benefiting ART at the new HC. Depression diagnosis suspicion is quite prevalent in the group and confirms other studies[29] [30] but does not appear in clinical records (and the majority of HC has no antidepressant drugs). Food insecurity[31] is highly prevalent in this group and yet not reported by patients as a cessation cause. Although HC poor health service occupies the last place in cessation causes, the number of doses and tablets[32] (higher than stipulated in the ART program), the last CD4 blood collection date (more than 6 months) and the patients' lack of knowledge about poor

adherence risks, reveal that many patients are not following the recommended ART protocol due to a deficit in HC services quality. Still CASG are weakly set in all districts, their role to support these patients is insignificant and even unsure. Patients on ART adherence (> 95% of dose[33]) estimated average in 5 districts for the last three months stands at 69%, below other studies in Africa[34], what may explain the poor results in CD4 count (< 350) and the occurrence of opportunistic infections (27%).

5. CONCLUSION

The ART non adherence rate in Nampula, depends mainly on patient's food insecurity and social stigma. It is a serious and complex public health problem, resulting from individual factors (patient's educational and economic low level[35,36]), social determinants (stigma, discrimination, lack of family support[37]) and health system inadequacy. The ART adherence rate is less than the regional average, increasing the risk of resistant HIV. The researchers think it is necessary to improve clinical file management and health information systems and develop a regular, systematically reviewed interdisciplinary approach among patients[38] and families (health information and education, CASGs design and training, rural extension), health professionals (referral to CASGs, home visits, poor adherence prevention strategies[39 40 41]) and traditional healers (healthy diet, chronic diseases, CASGs management), to reverse this situation[42] and reduce the incidence, morbidity and mortality caused by HIV.

ANNEXURES

Table III: HIV / ART Program District indicators (provided by NPHD).

Indicators ***February 2014***

N.	District	N⁰ People HIV + 2014	N⁰ Total on ART 2014	% HIV+ on ART	HIV Prevalence 2014 (% pregnancies)	HIV Prevalence 2014 (% District Population)	N⁰ ART Cessation	Cessation Rates (% ART)
1	Angoche	1526	1239	81	6.1	0.5	85	6.9
2	Erati	4639	3461	75	5.1	1.5	1	0.0
3	Ilha de Moçambique	1114	1277	115	7.7	2.0	102	8.0
4	Lalaua	1355	422	31	2.1	1.6	80	19.0
5	Malema	3845	1401	36	2.3	2.0	50	3.6
6	Meconta	2272	1672	74	2.4	1.2	130	7.8
7	Mecuburi	1342	1042	78	5.7	0.7	6	0.6
8	Memba	1654	554	33	1.9	0.6	44	7.9
9	Mogincual	690	925	134	1.8	0.4	37	4.0
10	Mogovolas	1703	1409	83	1.6	0.4	200	14.2
11	Moma	3091	2993	97	5.1	0.9	156	5.2
12	Monapo	2081	1499	72	2.4	0.6	138	9.2
13	Mossuril	894	581	65	5.1	0.7	77	13.3
14	Muecate	840	1329	158	6	0.8	43	3.2
15	Murrupula	2031	1125	55	3	1.2	0	0.0
16	Nacala a Velha	855	801	94	6.8	0.7	67	8.4
17	Nacala Porto	5691	7857	138	5.8	2.4	358	4.6

18	Nacaroa	1358	959	71	3	1.1	197	20.5
19	Nampula Cidade	18354	16331	89	9.8	3.0	507	3.1
20	Nampula Distrito	965	964	100	2.8	0.4	22	2.3
21	Ribaue	1196	860	72	5.1	0.5	27	3.1
	Total	57496	48701		91.6	23.2	2327	
	Average	2738	2319	85	4	1	111	5

Table IV: HIV / ART Program District Indicators (collected in HC October 2014).

	District	HC Population	N^0 HIV + Persons 2014	N^0 Total on ART 2014	% HIV + on ART	HIV Prevalence 2014 (% pregnancies)	HIV Prevalence 2014 (% District Population)	N^0 ART Cessations	Cessation rate (% on ART)	Deaths N^0 on ART	Mortality Rate (% ART)
1	Lalaua	43106	978	494	51	2	10.1	85	17.2	23	4.7
2	Mossuril	25102	519	269	52	4.6	2.4	80	29.7	53	10.7
3	Murrupula	57824	2024	1149	57	15.1	2.5	46	4.0	26	9.7
4	Nacaroa	35246	1402	688	49	6.1	8.4	278	40.4	54	4.7
5	Nampula	103404	13071	5651	43	4.9	25.0	406	7.2	79	11.5
	Total	264682	17994	8251		32.7	48.4	895	10.8	235	2.8
	Average	52936	3599	1650	46	7	10	179		47	

Note: the total number of cessations in Murrupula and Nampula HC far exceeds the monthly statistics and it is not possible to find a large number of clinical files, so we do not exactly know the ART cessation rate in these HC.

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