Programme Case Studies

1. Adverse effect reports - Nigeria
2. Change from d4T to ZDV - Cambodia
3. Change from d4T to TDF - Zambia
A CASE STUDY: “AN INVESTIGATION INTO ADVERSE DRUG REACTIONS (ADRs) OF ANTI-RETROVIRAL DRUGS EXPERIENCED BY HIV/AIDS PATIENTS IN SELECTED HEALTH CARE INSTITUTIONS IN THE FEDERAL CAPITAL TERRITORY (FCT), ABUJA, NIGERIA”

A PRESENTATION BY
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AT THE
WHO ANTIRETROVIRAL PHARMACOVIGILANCE TRAINING COURSE
DAR-ES-SALAAM, TANZANIA
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AIMS & OBJECTIVES

• To find out what adverse drug reactions patients on ARVs in some HIV/AIDS treatment centres in FCT are experiencing

• To identify the commonly reported ADRs due to ARVs in FCT

• To find out whether patients modifying treatment due to ARV toxicities in FCT, Abuja
Inspiration for the research:

• Provide evidence-based information to healthcare practitioners to sensitize them to report ADRs.

• Serves as a viable platform for further research

• Serves as a reference document in the national safety information database
Methodology

• This study was conducted at selected antiretrovirals therapy (ART) implementing centres such as 2nd, 3rd institutions, NGOs & FBOs.

• Using a structured questionnaire as a guide, Physicians screened pts’ files, interviewed the patients and then filled the questionnaires.

• The study was proposed to cover a total of 10 HIV/AIDS Treatment Centres in FCT but was scaled down to 5 sites. Scale up of this study is highly recommended.
SAMPLE QUESTIONNAIRE

• QUESTIONNAIRES

Sex: M F Age------ DOB: ---/----/---- Weight (kg):---- Height :( cm):-------

• ADRs:

Do you have many patients who come in complaining of ADRs due to ARVs?
• Yes No

What do you do when a patient comes in with such complain?
• ii) Just treat
• ii) Fill ADR & treat

Do you have ADR reporting forms readily available on your desk for reporting?
• Yes No

Please indicate if of your patients had experienced any of the following ART-related adverse reaction(s)/event(s)? Please tick as appropriate.

a) Hypersensitivity yes no
b) Severe reactions body/itching yes no
c) Lipodystrophy yes no
d) Hepatitis yes no

) Neuropathy yes no
e) Lactic acidosis yes no
f) Pancreatitis yes no
f) Nephrotoxicity yes no
g) CNS toxicity (dizziness) yes no
h) Anaemia yes no

Please give brief description of the ADR due to ARVs and the outcome of the event

• ARV Medicines Daily dose Date begun Date stopped

• 1.
• 2.
• 3.
• 4.

Did you stop the medication/treatment switches?

• Reasons for stopping the ARV medicines/treatment switches

• Poor compliance ADR too serious death others---------
Findings:

- Results from this study observed that 39 out of 70 respondents (56%) complained of ADRs due to ARVs. This confirms that ADRs due to ARVs occur in FCT.

- The existence of serious ADRs due to antiretrovirals is further corroborated by this analysis on table 3 and 4 (chart 1).

- Hence the importance for detection and reporting of ADRs due to antiretrovirals by healthcare professionals in FCT.
Findings cont’d

• Study further revealed that the 5 most commonly reported ADRs in Federal Capital Territory (FCT) are rash, CNS toxicity, neuropathy, lipodystrophy and liver toxicity.

• Also, switch in medication due to ARV toxicities ARVs occur in FCT, hence the need to monitor therapy very closely.
Whether pts complain of ADRs due to ARVs (Chart one)

No of Pts that complain of ADRs due to ARVs

- 56% complain about ADRs due to ARVs
- 44% no complaint about ADRs due to ARVs
Prevalence of ADRs due to ARVs in FCT
Abuja Nigeria (Chart Two)

% of ADRs due to ARVs in selected ART centres in FCT

- Severe Body Reaction/Itching: 30%
- CNS toxicity (dizziness): 26%
- Neuropathy: 16%
- Lipodystrophy: 9%
- Hepatitis: 7%
- Nephrotoxicity: 6%
- Lactic Acidosis: 5%
- Severe Anaemia: 1%
- Pancreatitis: 0%
Reasons for changing medications (Chart 3)

No of Pts that switched medications or not

- Serious ADRs: 36%
- Lack of efficacy: 56%
- Lack of adherence: 4%
- Medication error: 1%
- No switches: 3%

(Chart 3)
Lesson learn from the study

From the foregoing, it is important to note that a successful ARV programme requires more than just an adequate budget. Besides the development of clinical protocols, training curricula, logistic plans etc towards HIV/AIDS programmes, it is also crucial as shown by this pilot project to adopt a concrete policy on Drug Safety Monitoring (pharmacovigilance) to enhance detection and reporting of ADRs especially those of antiretrovirals by health care practitioners.
CONCLUSION

This study has demonstrated that

- Patients experience ADRs due to ARVs in the Federal capital Territory (FCT), Abuja
- The 5 most commonly reported ADRs in FCT are rash, CNS toxicity, peripheral neuropathy, lipodystrophy and liver toxicity.
- Significant number of patients experience ARV toxicities requiring treatment modification in FCT Abuja, hence the need to monitor therapy very closely.
Thank you for listening

as we monitor ARVs for toxicities to reduce additional burden on HIV/AIDS patients.
Programme Case Studies II

Change from d4T to ZDV
Tolerability of first-line regimens

![Graph showing proportion of patients having drug substituted over time on individual drugs, with data for AZT, EFV, NVP, and d4T.]

<table>
<thead>
<tr>
<th>Drug</th>
<th>n</th>
<th>0-1 year</th>
<th>1-2 years</th>
<th>2-3 years</th>
<th>Changed by 36 months, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZT</td>
<td>676</td>
<td>469</td>
<td>295</td>
<td>126</td>
<td>7.8 (5.9–10.3)</td>
</tr>
<tr>
<td>EFV</td>
<td>1,613</td>
<td>858</td>
<td>334</td>
<td>74</td>
<td>1.9 (1.3–2.8)</td>
</tr>
<tr>
<td>NVP</td>
<td>1,062</td>
<td>376</td>
<td>75</td>
<td>44</td>
<td>7.6 (5.3–10.9)</td>
</tr>
<tr>
<td>d4T</td>
<td>1,996</td>
<td>782</td>
<td>137</td>
<td>15</td>
<td>20.8 (16.2–26.5)</td>
</tr>
</tbody>
</table>

*Antiviral Therapy* 12:753–760
PEPFAR programs that have replaced d4T

<table>
<thead>
<tr>
<th>Preferred NRTI</th>
<th>Number of Countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>D4T/3TC</td>
<td>5</td>
</tr>
<tr>
<td>AZT/3TC</td>
<td>6</td>
</tr>
<tr>
<td>D4T or AZT/3TC</td>
<td>1</td>
</tr>
<tr>
<td>TDF/FTC</td>
<td>3</td>
</tr>
</tbody>
</table>
**Switch from d4T to AZT**

**Routine switch to AZT**
- 527 patients systematically switched from d4T to AZT
- Median time on d4T 18 months
- Within one year
  - 21.9% anaemia (grade 1-4)
  - 7.1% severe anaemia (Gd. 3/4)

**Chance of any anaemia over 2 years ~40%**

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Isaakidis P et al. JAIDS vol 49, number 1, Sept 2008
Program Considerations

PROGRAM STAFF
• revised drug forecasting and procurement
• more blood tests
• more blood transfusions
• extra consultations

PATIENTS
• more appointments
• increased absenteeism from work
• increased transportation costs

Isaakidis P et al. JAIDS vol 49, number 1, Sept 2008
Programme Case Studies III

Change from d4T to TDF - Zambia
Roll-Out of Tenofovir in Zambia

25,249 patients on TDF/FTC regimens

Mwango A, 2008 HIV/AIDS Implementers meeting Uganda
# Roll-Out of Tenofovir in Zambia

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Cost per Patient per Year (US$)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>OLD STANDARD TREATMENT GUIDELINES</strong></td>
<td></td>
</tr>
<tr>
<td>d4T + 3TC + NVP (30/150/200mg) (Triomune 30)</td>
<td>96</td>
</tr>
<tr>
<td>d4T + 3TC + EFV (30/150/600mg) (Coviro 30 + Efavirenz)</td>
<td>215</td>
</tr>
<tr>
<td><strong>NEW STANDARD TREATMENT GUIDELINES</strong></td>
<td></td>
</tr>
<tr>
<td>TDF + FTC + NVP (Truvada + Nevirapine)</td>
<td>343</td>
</tr>
<tr>
<td>TDF + FTC + EFV (Truvada + Efavirenz)</td>
<td>430</td>
</tr>
</tbody>
</table>

Mwango A, 2008 HIV/AIDS Implementers meeting Uganda
Monitoring renal function

- Renal impairment including acute renal failure reported
- Calculated creatinine clearance prior to initiating therapy
- “Clinically appropriate” during therapy
- Routine monitoring of CrCl and serum phosphorus
  - at risk for renal impairment
- CrCl <50 ml/min
  - dose reduction of TDF to 300mg every second day
25,249 patients initiating ART in Zambia
Program Considerations

• Safer 1\textsuperscript{st} line ART

• Higher cost

• ? Renal function monitoring

• Use in 1\textsuperscript{st} line impacts on 2\textsuperscript{nd} line drug choices