ENHANCING THE QUALITY OF ADVERSE DRUG REACTION REPORTS IN NEPAL

Sushil Nepal[1], Umanga Tipathee[2], Shyam Shah[1], Dr. Birna Trap[1], Dr. Andy Stergachis[3]

1. USAID Medicines Technologies and Pharmaceutical Services Program (MTaPS)Management Sciences for Health (MSH) (Sept 2019-Feb 2024)
2. Department of Drug Administration
3. University of Washington

Tenth National Summit of Health and Population Scientists in Nepal

10-12 April, 2024

BACKGROUND

- Pharmacovigilance (PV) is science and activities related to the detection, evaluation, understanding, and prevention of adverse drug reactions" [1]
- In 2014, the Uppsala Monitoring Center found only 13% of the complete reports [2]
- A large number of low-quality ADE reports can produce erroneous signal correlations and greatly affect data availability for any regulatory actions[3]
- In September 2021, MTaPS conducted a situational analysis of Nepal's PV system using USAID's Indicator-Based PV Assessment Tool4 and WHO's Global Benchmarking Tool[5]

BACKGROUND

- The analysis noted
  - underreporting and sub-optimal quality of ADE reports;
  - lack of a national safety and advisory committee;
  - weak functioning of both the DDA as the national PV center and the regional PV centers;
  - limited resources, including human resources;
  - lack of health care professionals' awareness of PV;
  - PV's exclusion from the current Drug Act (1978): insufficient guidance documents; and
  - the need for greater stakeholder coordination and engagement in Nepal[6]

- Despite these problems, stakeholders believe that ADE reporting is necessary in the country and an ADE monitoring system should be established and strengthened[7] .

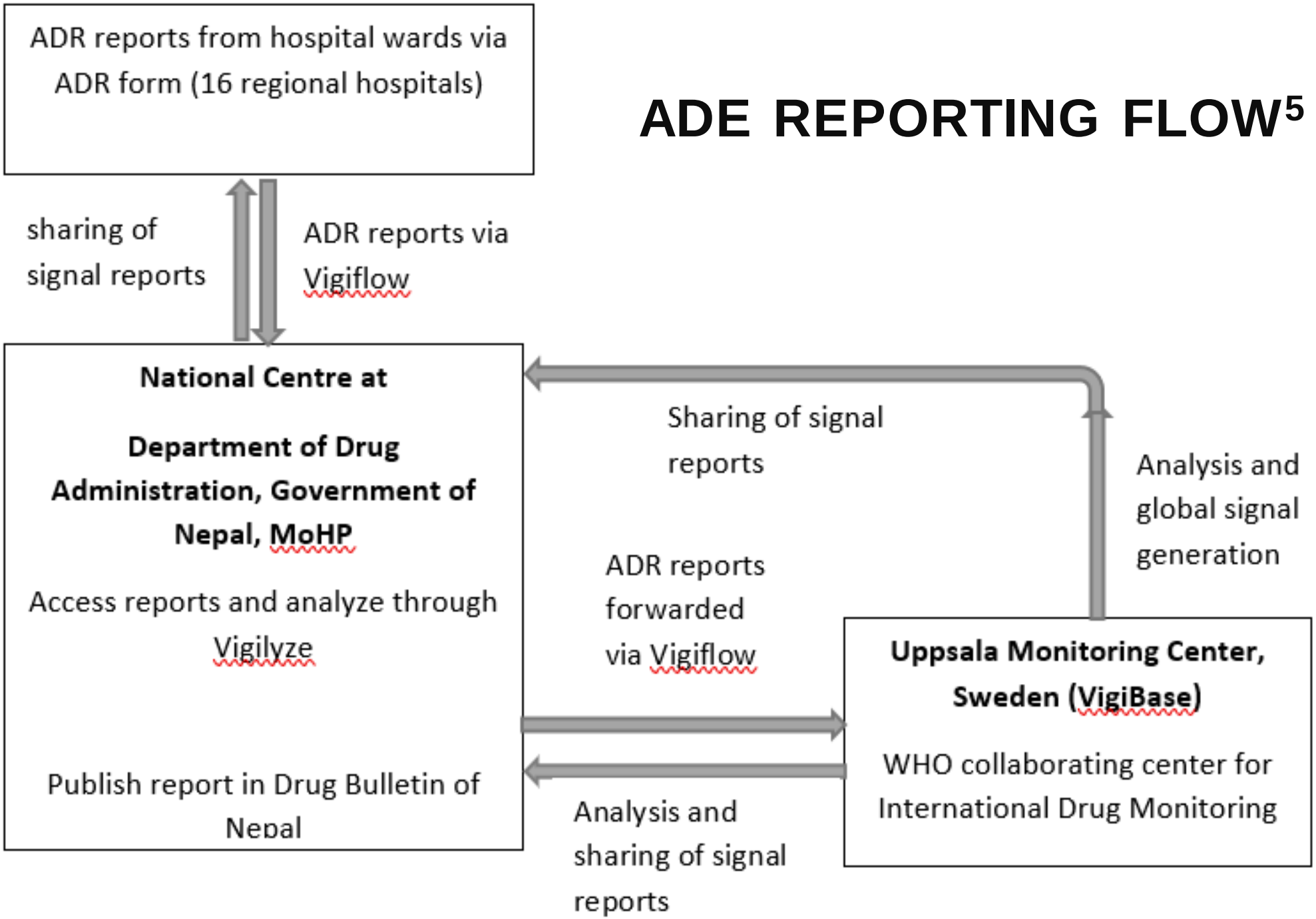
BACKGROUND

- High-quality ADE reports provide the information necessary to protect public health by preventing, detecting, and assessing adverse events related to medicinal products on the market. [8]
- Quality parameters include authenticity, completeness, accuracy, timeliness, severity, and outcomes.
- High-quality ADE reports generate signals that can prompt regulatory actions and therefore form the basis of drug safety monitoring and effective data use.
- They are needed to quickly identify risks to enable scientific conclusions to be drawn and risk management strategies to be formed.

BACKGROUND

- The degree of completion of a spontaneous report (SR) is an important quality parameter.[9]
- According to Good Pharmacovigilance Practices an ADR report is valid if it includes:
  (1) one or more identifiable notifiers;
  (2) an identifiable user (characterized by initials, date of birth, gender, or age);
  (3) one or more suspicious drugs; and
  (4) one or more suspected adverse reactions.
- In addition to these mandatory data, a well-documented SR should also contain information on
  - basic medical conditions,
  - comorbidities,
  - concomitant medication,
  - the patient's clinical evolution,
  - the therapy used to treat the ADR,
  - complementary means of diagnosis, and
  - information on the response to suspension and reintroduction of the drug.[10, 11]

ADE REPORTING FLOW[5]



OBJECTIVES

- To evaluate the characteristics and quality of ADE reports
- Identify potential factors contributing to low-quality reports

METHODS

- ADR reports received by the National PV Center
  - January 2020- November 2022 pre-training phase
  - January -April 2023 as the post-training phase

- The capacity building plan was developed and implemented in December 2022 for 60 health care professionals from 15 regional centers and 10 hospitals
- The reports were scored using a pre-validated AQUA-12 tool4.
- Scores of 1-9 indicated low quality, and scores of 10-12 indicated high quality
- The data were subjected to Fisher's exact and chi-square tests in R version 4.1.2.

RESULTS (Quality of ADR reports before and after training)

Quality of reports	Scores pre-training (N=57) (%)	Scores post-training (N=29) (%)	P-value
High quality (AQUA-12 score 10-12)	9 (15.8)	21 (72.4)	0.00000a
Low quality (AQUA-12 score 1-9)	48 (84.2)	8 (27.5)	

a Fisher's exact test

RESULTS (COMPONENTS)

Components fully completed	Pre (N=57) (%)	Post (N=29) (%)
Previous ADR history	24 (42)	26 (90)
Actual reaction	16 (28)	25 (86)
Description of key events	10 (18)	23 (80)
Suspected medications	14 (25)	18 (62)
Timeline relevant to ADR	18 (32)	21 (73)
Management of reaction	31 (54)	23 (80)
Outcome/sequelae	29 (51)	25 (86)
The average percentage of the complete report (100-Average incomplete%)	**36**	**80**

RESULTS

	High quality	Low quality	p-value [a]
Reporter characteristics	**N (%)**	**N (%)**	**0.01355**
Pharmacist	14 (25.92)	17 (56.66)	
Physicians	32 (59.25)	12 (40.00)	
Others	8 (14.81)	1 (3.33)	
ADR severity	**N (%)**	**N (%)**	**0.47500**
Caused/prolonged hospitalization	14 (87.50)	8 (66.66)	
Congenital abnormality/birth defect	0	0	
Disabling/incapacitating	1 (6.25)	1 (8.33)	
Life-threatening	1 (6.25)	1 (8.33)	
Other medically important conditions	0	0	
Results in death	0	2 (16.66)	
ADR outcomes	**N (%)**	**N (%)**	**0.05741**
Recovered/Resolved	22 (59.45)	18 62.06)	
Recovering/Resolving	8 (21.62)	9 (31.03)	
Not Recovered/Not Resolved/ Ongoing	5 (13.51)	0	
Recovered/Resolved with Sequalae	0	0	
Fatal	0	2 (6.89)	
Unknown	2 (5.40)	0	
Gender of reporter	**N (%)**	**N (%)**	**0.2281**
Male	32 (57.14)	20 (66.66)	
Female	1 (1.78)	2 (6.66)	
Unknown	23 (41.07)	8 (26.66)	

a Fisher Exact test

CONCLUSION AND TAKE AWAY

- Education and training appear to have a significant influence on reporting

- Other improvement measures include providing feedback to the reporters, information through regular newsletters and awareness materials.

- To long-term sustainable PV strengthening, the Ministry of Health and Population and DDA should develop a PV framework that calls for the institutionalization of PV within the different health programs

ACKNOWLEDGMENTS

- Department of Drug Administration
  - Narayan Prasad Dhakal, Director General;
  - Pramod KC, Senior Drug Administrator
  - Kiran Bajracharya, Drug Administrator,

- USAID MTaPS program

REFERENCES

1. https://www.who.int/teams/regulation-prequalification/regulation-and-safety/pharmacovigilance accessed 10th April 2023
2. Bergvall T, G N N, Lindquist M. vigiGrade: a tool to identify well-documented individual case reports and highlight systematic data quality issues. Drug Saf. 2014;37:65–77.
3. Rui Niu, Yufang Xiang, Tingting Wu, Zhi Zhang, Yue Chen & Bianling Feng (2019) The quality of spontaneous adverse drug reaction reports from the pharmacovigilance centre in western China, Expert Opinion on Drug Safety, 18:1, 51-58, DOI: 10.1080/14740338.2019.1559812
4. Indicator-based pharmacovigilance assessment tool: Manual for conducting assessments in developing countries, Accessed 2023-may-04, available at https://pdf.usaid.gov/pdf_docs/PNADS167.pdf
5. Situational analysis on pharmacovigilance in Nepal, SWOT Analysis, GBT-IDP, and Public Health Programs by the Department of Drug Administration, Nov 2021
6. Jha N, Palaian S, Shankar PR, Santosh KC, Kshetry PB. Situation analysis of the pharmacovigilance system in Nepal using the indicator-based pharmacovigilance assessment tool (IPAT), Journal of Pharmaceutical Health Services Research, Volume 12, Issue 4, November 2021:485–491, https://doi.org/10.1093/jphsr/rmab054.
7. Danekhu K, Shrestha S, Aryal S, Shankar PR. Health-care Professionals' Knowledge and Perception of Adverse Drug Reaction Reporting and Pharmacovigilance in a Tertiary Care Teaching Hospital of Nepal. Hosp Pharm. 2021 Jun;56(3):178-186. doi: 10.1177/0018578719883796. Epub 2019 Nov 5. PMID: 34024926; PMCID: PMC8114297.
8. https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:32010L0084&from=PT accessed 10th April 2023
9. Durrieu G, Jacquot J, Mège M, Bondon-Guitton E, Rousseau V, Montastruc F, Montastruc JL. Completeness of Spontaneous Adverse Drug Reaction Reports Sent by General Practitioners to a Regional Pharmacovigilance Centre: A Descriptive Study. Drug Saf. 2016 Dec;39(12):1189-1195. doi: 10.1007/s40264-016-0463-4. PMID: 27688025.
10. Bailey C, Peddie D, Wickham ME, Badke K, Small SS, Doyle-Waters MM, Balka E, Hohl CM. Adverse drug event reporting systems: a systematic review. Br J Clin Pharmacol. 2016 Jul;82(1):17-29. doi: 10.1111/bcp.12944. Epub 2016 May 9. PMID: 27016266; PMCID: PMC4917803.
11. https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/guideline-good-pharmacovigilance-practices-gvp-module-vi-collection-management-submission-reports_en.pdf10th April 2023

Photo Credit: MSH Staff

Thank You

Questions?

SUSHIL NEPAL (BIO)

With over 10 years of diverse experience spanning from quantitative and qualitative health research to regulatory affairs, I bring a unique blend of skills as a Pharmacist, Epidemiologist, and Public Health Researcher. My expertise extends to health/pharmaceutical system strengthening, monitoring, evaluation, research, and learning (MERL), alongside proficiency in reporting documentation, knowledge management, and Data Quality Assessment.