

AN ANALYTICAL CROSS-SECTIONAL OBSERVATIONAL STUDY ON DRUG UTILIZATION AND EVALUATION OF NARROW THERAPEUTIC INDEX DRUGS IN A TERTIARY CARE HOSPITAL

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Article Received on 12 April 2026,
Article Revised on 01 May 2026,
Article Published on 04 May 2026,

<https://doi.org/10.5281/zenodo.19879923>

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How to cite this Article: Peddapally Bhargavi*¹, Fiza Firdous², Gudipally Susmitha³, Ryala Sri mani Chandana⁴, Dr. Fiaz⁵, Hajera Fatima⁶. (2026). An Analytical Cross-Sectional Observational Study on Drug Utilization and Evaluation of Narrow Therapeutic Index Drugs In A Tertiary Care Hospital. World Journal of Pharmaceutical Research, 15(10), 1056-1068.

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ABSTRACT

Narrow therapeutic index drugs (NTIDS) are medications that requires careful handling because even small changes in the dose or blood levels can make the medicine not work, cause harm, or lead to serious side effects. These drugs need to be prescribed correctly, monitored closely, and followed exactly as per clinical guidelines. This study focused on the use of NTIDS in a tertiary care hospital to understand how they are prescribed, whether they are used rationally, and what drug-related problems (DRPs) occur. The results showed that more than half of the prescriptions were irrational, and many patients experienced at least one DRP, showing major gaps in safe medications practices. One approach used was monotherapy, which was meant to reduce drug interactions. The high number of DRPs showed that there are still problems with prescribing and monitoring. NTID use was more common among women and people aged 18 to 39 years, with Heparin, Levothyroxine, and Amikacin being the most prescribed drugs. Many patients

also had other health conditions, like diabetes or hypertension, which made treatment more complicated. These findings highlight the need for standard treatment plans, ongoing

education for prescribers, and more involvement of clinical pharmacists. Making drug utilization evaluation a daily activity can help reduce errors, improve patient outcomes, and enhance the quality of healthcare.

KEYWORDS: Narrow therapeutic index, Drug-related problems, Drug utilization evaluation.

INTRODUCTION

Drug utilization evaluation (DUE), also known as drug utilization review (DUR) or Medication Utilization Evaluation (MUE), is a continuous process that looks at how medicines are prescribed by doctors, given by pharmacists, and used by patients. It plays a key role in maintaining quality in healthcare by making sure medicines are used correctly and for the right reasons. DUE includes checking prescriptions and medication details before, during, and after dispensing to ensure treatment decisions are appropriate, and patients get the best results. Even when medicines are prescribed correctly, involving a clinical pharmacist in patient care helps with proper treatment planning, spotting problems early, preventing harmful side effects, and improving overall patient safety and medication adherence.

The importance of Drug Utilization Evaluation becomes clear when considering rational pharmacotherapy. Rational pharmacotherapy means giving medicines that are suitable for a patient's condition, in doses that match their needs, for the right length of time, and at the lowest cost. This is especially important when it comes to Narrow Therapeutic Index Drugs (NTIDs). These drugs have a very small range between being beneficial and harmful. In many cases, the difference between the minimum effective concentration and the minimum toxic concentration is less than double. Some NTIDs also have unpredictable absorption, Bioavailability that depends on the product form, and large variations in how different people process them, which is why regular blood monitoring is needed. The therapeutic window refers to the dose range that provides the desired effect without causing serious side effects. Examples of drugs with a low therapeutic index include digoxin, lithium, warfarin, gentamicin, vancomycin, phenytoin, insulin, and tricyclic antidepressants.

Evaluating NTID use in a tertiary care hospital is crucial because these drugs have a high risk of toxicity or treatment guidelines to ensure safety. Using these drugs improperly can lead to serious side effects, longer hospital stays, and higher healthcare costs. A systematic review of NTID use helps identify prescribing patterns and errors, ensures rational drug use and

compliance with guidelines, supports pharmacovigilance efforts, reduces drug-related problems, and improves treatment outcomes. By examining how NTIDs are used, this study aims to improve patient care, lower risks, and help overall healthcare quality. NTIDs are high-risk drugs because the difference between the minimum effective concentration and the minimum toxic concentration is very small. This means even minor changes in dosage or blood levels can push the drug into an ineffective or toxic range. Both underdosing and overdosing can be dangerous. Underdosing can lead to treatment failure, like poor seizure control in patients on phenytoin or increased risk of blood clots when warfarin levels are too low. It can also make it seem like the patient isn't responding, which might lead to unnecessary dose increases or adding more medicines. Overdosing can cause life-threatening side effects, such as heart rhythm problems with digoxin, tremors or seizures with lithium toxicity, or severe bleeding due to high INR levels with warfarin. These situations often require hospitalization, intensive care, or stopping the drug entirely, which puts more strain on the healthcare system.

Certain groups of patients are more at risk when using NTIDs. Elderly patients, for example, are more vulnerable because kidney and liver function naturally decline with age, which affects how drugs are removed from the body. Changes in body composition, such as increased fat and less muscle, also affect how drugs are distributed. As a result, older patients are more likely to experience adverse drug reactions and drug interactions. Patients with kidney or liver disease are also at greater risk. Drugs like lithium, digoxin, and methotrexate are mainly removed through the kidneys, so impaired renal functions can lead to drug buildup and toxicity. Similarly, liver disease can slow the metabolism of drugs like warfarin and phenytoin, increasing the chance of harmful side effects. Because of all factors, it's important to closely monitor and properly assess narrow therapeutic index drugs (NTIDs) using drug utilization evaluation (DUE) to make sure patients are safe and get the best possible treatment.

AIM OF THE STUDY

To look at how narrow therapeutic index drugs are used, understand their clinical effects, and ensure they are used in a smart, safe, and effective way in a large hospital setting.

OBJECTIVES

1. To check how doses of narrow therapeutic index drugs are adjusted for patients.
2. To find out the risk ratio for these drugs.

3. To look at how these drugs are used and find out any issues related to drug use, like wrong dosing, side effects, or treatment not working.
4. To check how well these drugs are used in line with clinical guidelines, how well they work, and how safe their use is.

METHODOLOGY

Place of study: The study was done at Apollo Institute of Medical Sciences and Research, Jubilee Hills, Hyderabad.

Duration of study: The study took six months to complete.

Study Design: This was an analytical cross-sectional observational study.

Data was collected both from past and current patient records over six months.

Inclusion criteria

1. Patients of all ages.
2. Patients of both genders.
3. Inpatients who were given any narrow therapeutic index drug in any department.

Exclusion criteria

1. Pregnant and breastfeeding women.
2. Patients with allergies.

Study population: 149 patients.

METHOD AND COLLECTION OF DATA

We got permission from the medical director to collect data. A special form was designed for this study. Patient data was gathered from the hospital's electronic records, medical records, medical records department, clinical case sheets, and progress notes.

Study parameters

1. Age and gender of patients using NTI drugs.
2. Vital signs and lab results.
3. Reasons for using NTI drugs.
4. Other health conditions.
5. How often and in what way the drugs were prescribed.
6. How doses were given and adjusted.
7. Whether patients had acute or chronic conditions.

8. How NTI drugs were used in different departments.
9. Which NTI drugs were most commonly prescribed.

RESULTS

A total of 149 participants were included in the study, with 84 females (50%) being more common than 65 males (39%), as shown in figure 1.

Among different age groups, the use of narrow therapeutic index (NTI) drugs was most common in adults aged 18 to 60 years, as seen in table 1.

Hypothyroidism was the most frequent comorbid condition among the 149 patients, followed by hypertension and diabetes mellitus.

Based on the distribution of diagnoses, diseases related to the heart were most common, affecting 50 patients (33.5%), followed by respiratory issues in 17 patients (11.4%). The severity of the illness was categorized into acute (108 patients, 72.8%) and chronic (41 patients, 27.5%).

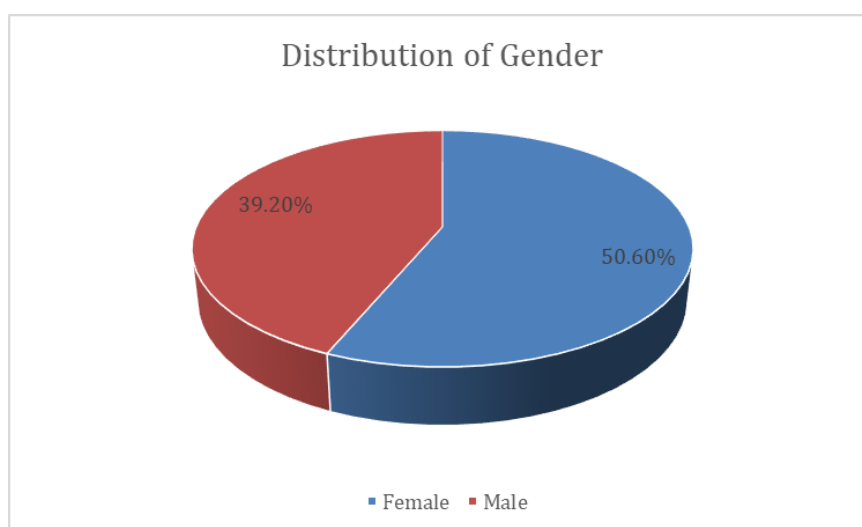


Fig. 1: Distribution based on Gender.

Table 1: Distribution Based on Age.

Age in years	Age group	Count	Percentage
0-1	Neonates and infants	16	10.70
2-12	paediatrics	8	5.36
13-18	Adolescents	2	1.30
18-60	Adults	96	64.40
60-100	Geriatrics	27	18.10

Table 2: Distribution of comorbid Conditions.

Comorbid conditions	Count	Percentage
Diabetes Mellitus	38	25.50
Hypertension	54	36.20
Coronary Artery Disease	6	4.02
Cerebrovascular Accident	4	2.68
Thyroids	55	36.90
Seizures	6	4.02
Tuberculosis	4	2.68
Chronic Kidney Disease	3	2.01
Asthma	2	1.34
Retroviral Disease	2	1.34
Poliomyelitis	2	1.34
COPD	1	0.67
CHRD	1	0.67
Anaemia	1	0.67

Table: 3 Distribution based on Diagnosis.

Diagnosis categorization	Count	Percentage
Cardiac system	50	33.55
Respiratory system	17	11.40
CNS	16	10.73
Infection	13	8.72
Surgery	9	6.04
Digestive system	8	5.36
Cancer	3	2.01
Circulatory system	1	0.67
Endocrine system	3	2.01
ENT	2	1.34
Drug induced condition	1	0.67
Gastro intestinal	4	2.68
Haematology	4	2.68
Hepatic portal system	2	1.34
Immune system	6	4.02
Labor	4	2.68
Musculo-skeletal system	5	3.35
Toxicity	1	0.67
Total	149	100

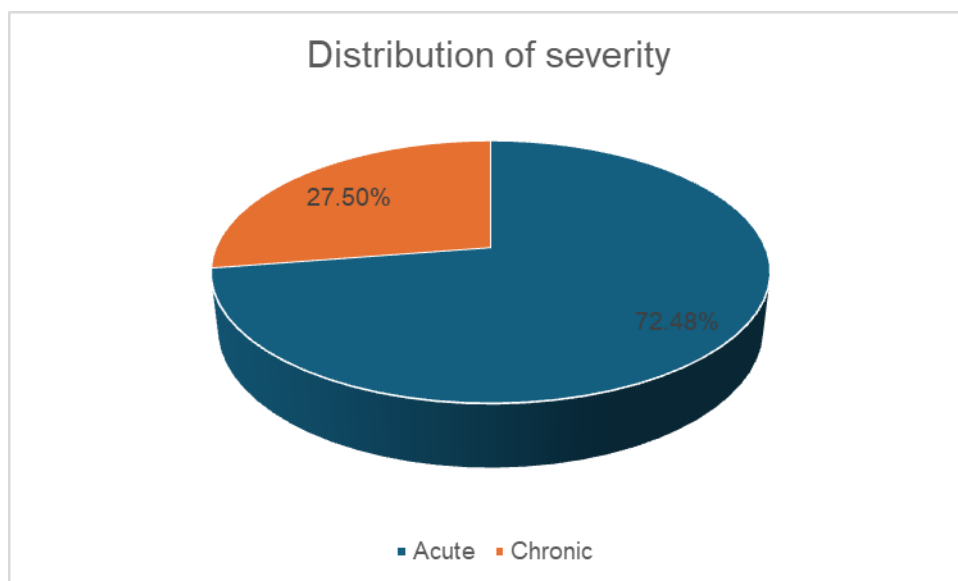


Fig. 2: Distribution based on Severity.

Out of 149 patients, 14 NTI drugs were identified in 166 prescriptions. The most commonly prescribed NTI drug was levothyroxine, with 73 prescriptions (43.9%), followed by heparin (30 prescriptions, 18.07%) and amikacin (24 prescriptions, 14.45%). The analysis of frequency and route of administration revealed that most prescriptions were given once a day (OD) in 114 cases, taken orally (PO) in 94 cases, and administered intravenously in 70 cases.

Table 4: Distribution of Narrow Therapeutic Index Drugs.

Distribution of NTI drugs	Count	Percentage
Carbamazepine	2	1.20
Amikacin	24	14.45
Amiodarone	6	3.61
Gentamicin	1	0.60
Heparin	30	18.07
Tobramycin	1	0.60
Vancomycin	11	6.62
Digoxin	7	4.21
Lithium Carbonate	1	0.60
Phenytoin	2	1.20
Sodium Valproate	2	1.20
Theophylline	2	1.20
Warfarin	4	2.40
Levothyroxine	73	43.90
Total	166	100

Table 5: Distribution based on Frequency.

Frequency	Count	Percentage
0.9ml OD	1	0.6
1.7ml/hr.	1	0.6
24 Hourly	1	0.6
8q	3	1.8
BD	17	10.2
OD	115	77.18
Onflow	4	2.4
QID	9	5.4
STAT	4	2.4
Thrice week	1	0.6
TID	9	5.4
Weekly Once	1	0.6
Total	166	100.0

Table 6: Distribution based on Route of Administration.

Route	Count	Percentage
IM	1	0.6
IV	70	42.2
PO	94	63.08
RT	1	0.6
Total	166	100.0

The most common reason for prescribing NTI drugs was hypothyroidism, which suggests that levothyroxine is widely used in this study.

Second was anti-coagulant therapy, with 39 prescriptions (23.4%), indicating that anti-coagulants are frequently used in cardiovascular and blood clot-related conditions.

Table 7: Distribution based on Indication.

Indication	Count	Percentage
Aminoglycoside Antibiotic	26	15.7
Anti-Arrhythmias	6	3.6
Anti-coagulant	39	23.4
Anti-manic	1	0.6
Cardiac Glycoside	7	4.2
Glycopeptide Antibiotics	11	6.6
Hypothyroidism	74	44.5
Xanthine	2	1.2
Total	166	100.0

The standard prescribing details, such as frequency, dosage form, route, and dose, were analysed to assess medication compliance.

In most cases, patients followed their prescribed medication, but a small percentage did not, which could have serious consequences for their health.

Table 8: Distribution of Medication Compliance.

Medication Compliance	Count	Percentage
Compliance	136	81.9
Non-Compliance	30	18.1
Total	166	100.0

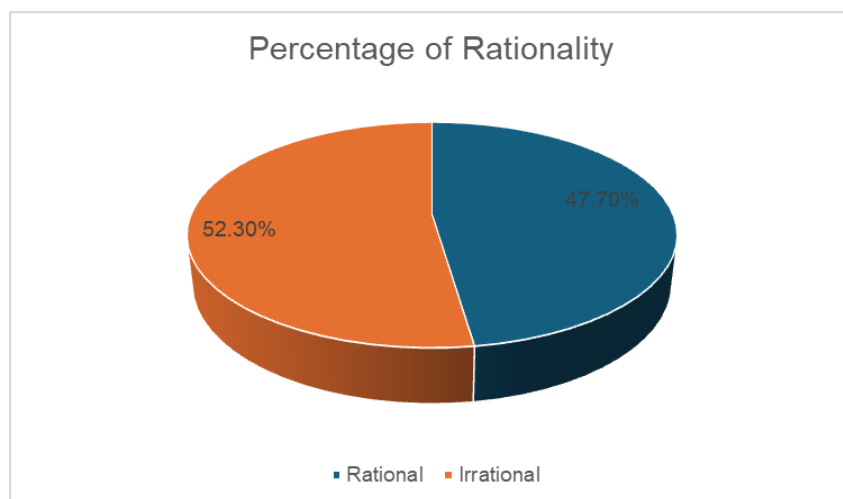


Fig. 3: Percentage of Rationality.

Table 9: Drug-Risk Ratio of Narrow Therapeutic Index Drugs.

Drug	Drug Risk Ratio	Count	Female	Male	Percentage
Carbamazepine	0.5	Count	1	1	2
		% within NTIDRUG	100.0%	100.0%	100.0%
		% within GENDER	1.2%	1.5%	1.3%
Amikacin	1.29	Count	9	15	24
		% within NTIDRUG	33.3%	62.5%	100.0%
		% within GENDER	9.4%	23.4%	16.1%
Gentamicin	1	Count	1	0	1
		% within NTIDRUG	100.0%	0.0%	100.0%
		% within GENDER	1.2%	0.0%	0.7%
Heparin	0.40	Count	14	16	30
		% within NTIDRUG	46.6%	53.3%	100.0%
		% within GENDER	16.4%	25.0%	20.1%
Tobramycin	0	Count	1	0	1
		% within NTI DRUG	100.0%	0.0%	100.0%
		% within GENDER	1.2%	0.0%	0.7%
Vancomycin	0.91	Count	3	8	11
		% within NTIDRUG	27.2%	72.7%	100.0%
		% within GENDER	3.5%	12.5%	7.3%
Amiodarone	0.8	Count	0	6	6

		% within NTIDRUG	0.0%	100.0%	100.0%
		% within GENDER	0.0%	9.3%	4.0%
Digoxin	0.57	Count	3	4	7
		% within NTIDRUG	42.8%	57.1%	100.0%
		% within GENDER	3.5%	6.3%	4.7%
Lithium Carbonate	1	Count	0	1	1
		% within NTIDRUG	0.0%	100.0%	100.0%
		% within GENDER	0.0%	1.5%	0.7%
Phenytoin	1	Count	2	0	2
		% within NTIDRUG	100.0%	0.0%	100.0%
		% within GENDER	2.4%	0.0%	1.3%
Sodium Valproate	1	Count	1	1	2
		% within NTIDRUG	100.0%	100.0%	100.0%
		% within GENDER	1.2%	1.2%	1.3%
Theophylline	1	Count	0	2	2
		% within NTIDRUG	0.0%	100.0%	100.0%
		% within GENDER	0.0%	3.1%	1.3%
Levothyroxine sodium	0.7	Count	54	19	73
		% within NTIDRUG	73.9%	26.0%	100.0%
		% within GENDER	63.5%	29.6%	48.9%
warfarin	1	Count	1	3	4
		% within NTIDRUG	100.0%	75.0%	100.0%
		% within GENDER	1.2%	4.6%	2.7%
Total	Total	Count	85	64	149
		% within NTIDRUG	57.0%	43.0%	100.0%
		% within GENDER	100.0%	100.0%	100.0%

DISCUSSION

Our study found that women made up a slightly larger share of the group (50.6%) compared to men (39.2%), and there was a significant use of NTI drugs among adults aged 18 to 60 years (64.4%).

This trend is consistent with other studies, though some had a higher proportion of men. The high rates of hypothyroidism (36.9%) and hypertension (36.2%) in our group, along with a notable amount of heart-related conditions (33.5%), led to levothyroxine (43.9%) and heparin (18.07%) being the most commonly prescribed NTI drugs. This trend reflects the health conditions present in our patient population, a common occurrence in clinical settings where drug use often aligns with prevalent health problems.

We found that adherence to prescriptions was significantly lower in children compared to adults across various factors like dosing, duration, and treatment reason ($P < 0.01$).

Adults showed moderate adherence (30–61%), but children had high non-adherence rates,

ranging from 74.1% to 100%. This huge difference is concerning because children are more vulnerable when dealing with NTI drugs. This finding is similar to the work of Rezvani et al. (2022) regarding vancomycin, which also found significant differences from CDC and UpToDate guidelines, especially in terms of dose and length of treatment, and even noted 0% adherence in children. The ongoing issue of non-adherence, as our study and prior research indicate, points to the challenges in managing NTI drugs. This suggests that trial-and-error treatment methods and insufficient monitoring contribute to these problems, potentially leading to issues like antibiotic resistance.

Our study found that about half of the prescriptions (52.3%) were rational, while the other half (47.7%) were irrational, indicating room for improvement in prescribing practices.

This pattern of irrational prescribing is consistent with the findings of Yadav et al. (2018), who also noted a high rate of irrational prescriptions involving NTI drugs. Our analysis found that patients had an average of 2.74 drug-related problems (DRPs), with drug-drug interactions making up the majority (61%), followed by subtherapeutic dosing (18.26%) and adverse drug reactions (9.96%). This pattern matches other studies; Iyer et al. (2018) also found that drug interactions were the most common category of DRPs (63%), particularly involving NTI drugs such as digoxin, phenytoin, and aminoglycosides. Our identification of amikacin, vancomycin, and amiodarone as high-risk NTI drugs is in line with established knowledge about NTI drugs, where even small variations in dosing can lead to toxicity or reduced treatment effectiveness.

In line with the findings of Blix HS et al. (2010), our study confirmed that patients using NTI drugs face a much higher risk of DRPs compared to those not on these medications.

Our calculated NTI Drug Risk Ratio was 2.75 times higher than the 0.50 risk ratio reported by Blix et al. for NTI drugs. We identified several important factors that increase the likelihood of DRPs, including gender (Odds Ratio 2.65), existing health conditions (OR 2.947), using more than 11 medications (OR 3.987), and staying in the hospital for over 7 days (OR 1.087). The strong link between using multiple medications and DRPs (60% of DRPs occurred with more than 10 drugs versus 39.1% with ≤ 10 drugs, $p=0.006$) is a key insight that aligns with broader literature on medication safety. Blix HS et al. (2010) also noted that NTI users were often older and had more health conditions, making them more vulnerable to DRPs. However, our study found a higher rate of DRPs, possibly due to

different research methods or patient groups.

Our study highlights how NTI drugs are prescribed differently based on gender. Men were more often prescribed Levothyroxine sodium, while women received more of Amiodarone, Lithium Carbonate, Theophylline, Vancomycin, and Warfarin. These differences suggest there might be reasons related to health conditions or care practices that we need to explore further. For instance, we found that children receiving Vancomycin had zero dose adherence, which is a major concern. This finding matches what Rezvani *et al.* (2022) reported, showing a need for improved monitoring and possibly new guidelines specifically for children. Despite existing efforts to manage drug-related problems (DRPs), they still happen, which means we must keep being careful. Our findings, along with other research, point to the importance of having clinical pharmacists involved from the start to help identify and handle these issues, thus making sure patients are safer when it comes to NTI drugs.

CONCLUSION

Our study included 149 patients, with just over half being women. Most were adults aged between 18 and 60, and a large number had acute illnesses. Common comorbid conditions included thyroid issues, high blood pressure, and diabetes, which were often linked to heart problems or breathing issues. Levothyroxine sodium was the most commonly prescribed NTI drug, making up nearly 44% of all NTI prescriptions. It was usually given once a day and by mouth. Heparin and Amikacin were also commonly used. While 81.9% of patients followed their medication plans, the study found that 47.7% of NTI prescriptions were not appropriate, showing a big gap between patient adherence and correct prescribing for these high-risk drugs. Amikacin had the highest risk ratio at 1.29, indicating a high chance of adverse events or misuse, while Warfarin, with a ratio of 1, is at the point where it could be problematic and needs strict monitoring. Vancomycin and Amiodarone also showed moderate to high risk. Women received 57% of all NTI drugs, mainly due to conditions like hypothyroidism, which are more common in women.

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