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Advantages of Rivaroxaban as an Anticoagulant: Strategies for Effective Use and Adverse Effect Management in Tertiary Care Hospitals

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Abstract

Background: Anticoagulants are the cornerstone therapy for thromboembolism prevention and treatment. Rivaroxabanis the an oral anticoagulant drug .It needs high-quality anticoagulation monitoring with frequent international normalization ratio (INR) testing. **Objective:** The study aimed to assess anticoagulation management with Rivaroxaban among adult outpatients and acess its adverse effect management produced in the tertiary care hospital .

Methods: A hospital-based retrospective study design that enrolled 374 patients receiving Rivaroxaban was taken in the study conducted at two centres i.e,Jinnah Postgraduate medical centre and Abbasi shaheed hospital. The time in the therapeutic range (TTR) was calculated using the Rosendaal method.

Results: The mean age of the patients was 57 years, and 218 (58.3%) participants were females. Out of 3384 INR tests, 1562 (46.5%) were within the therapeutic range and the mean percentage of TTR was 47.24%. Only 25.67% of the patients spent their TTR ≥ 65%. The present study revealed that dose adjustments were required 1764 times. In non-therapeutic INR values of 1764 that required Rivaroxaban dose adjustment, 59.7% of the doses were adjusted. About 262

(70.1%) of co-prescribed medications had drug interaction . Sixty-four patients (17.11%) experienced bleeding events.
Conclusion: Anticoagulation management with Rivaroxaban was suboptimal .INR values was not minimal, and many patients encountered bleeding during their course of therapy.

Introduction

Rivaroxaban is a direct oral anticoagulant (DOAC) that inhibits Factor Xa, a key enzyme in the coagulation cascade. It is used to prevent and treat thromboembolic disorders, including stroke prevention in non-valvular atrial fibrillation, deep vein thrombosis (DVT), and pulmonary embolism (PE)[1-4]. The international normalized ratio (INR) is a laboratory measure used to assess the effectiveness of therapy. Maintaining an INR within a narrow therapeutic range is crucial to prevent thromboembolic events while minimizing the risk of bleeding complications. Factors such as medication interactions, dietary changes, and comorbidities can impact INR levels, making regular monitoring essentia5,6]l. The time in therapeutic range (TTR) is a key indicator of anticoagulation control, with a minimum TTR of 65% recommended for effective Rivaroxaban therapy[7].

Achieving optimal INR control can be challenging in real-world settings, highlighting the need for careful patient management and education. Healthcare providers must balance the benefits and risks of therapy, taking into account individual patient characteristics and needs[8,9]. Effective anticoagulation management with therapy requires a multidisciplinary approach, involving healthcare providers, patients, and caregivers. By understanding the complexities of Rivaroxaban therapy and the importance of INR monitoring, healthcare providers can optimize patient outcomes and reduce the risk of adverse events.

Rivaroxaban offers several advantages over traditional anticoagulants like Rivaroxaban, including predictable pharmacokinetics, rapid onset of action, and fewer dietary restrictions. One of the key benefits of rivaroxaban is its convenient dosing regimen, which eliminates the need for routine coagulation monitoring[10-13]. This makes it an attractive option for patients who require long-term anticoagulation therapy. Additionally, rivaroxaban has a lower risk of food and drug interactions compared to other anticoagulants, which can simplify treatment management[14].

However, rivaroxaban is not without risks, and bleeding is a potential adverse effect. Patients taking rivaroxaban should be aware of the signs and symptoms of bleeding and seek medical attention if they experience any unusual bleeding or bruising[15-19]. Despite these risks, rivaroxaban has been shown to be effective in preventing thromboembolic events and has become a popular choice for many patients who require anticoagulation therapy.

In comparison to other anticoagulants ,Rivaroxaban, offers a more predictable and stable anticoagulant effect, which can reduce the risk of thromboembolic events and bleeding complications. However, the lack of routine monitoring can make it challenging to assess adherence and adjust dosing in certain situations[20]. Overall, rivaroxaban is a valuable treatment option for patients who require anticoagulation therapy, offering a convenient and effective alternative to traditional anticoagulants .

The study highlighted the benefits and risks of rivaroxaban and implementing effective strategies for use and adverse effect management, healthcare providers can improve patient outcomes and reduce the risk of thromboembolic and bleeding complications.

Objectives

The study's objectives are to assess the effectiveness of anticoagulation management with Rivaroxaban among adult outpatients and evaluate its adverse effects. Specifically, the

study aims to determine the incidence of bleeding complications, identify potential risk factors for adverse effects, and assess the impact of Rivaroxaban on patient outcomes, including thromboembolic events and quality of life. By achieving these objectives, the study seeks to provide valuable insights into the safe and effective use of rivaroxaban in clinical practice.

Methodology

This retrospective study was conducted at two centres i.e,Jinnah Postgraduate medical centre and Abbasi shaheed hospital .The study population consisted of adult patients receiving rivoraxoban therapy for 3 months or more for various indications. Patients' data were retrieved from medical records, and those with follow-up visits at the study centers were included in the analysis. The study aimed to evaluate the anticoagulation management and adverse effects of rivoraxoban therapy in these patients. A total of 1683 patients receiving rivoraxoban therapy were identified during the study period, and their data were reviewed to assess the quality of anticoagulation control, incidence of adverse effects, and other relevant outcomes.

Data collection involved a comprehensive instrument prepared after reviewing relevant literature. The data was collected by reviewing medical records. The data included demographic characteristics, anticoagulation indications, comorbidities, concomitant medications, and INR results. To ensure accuracy, the data abstraction tool was pretested on 5% of the study participants, and necessary amendments were made. The Rosendaal method was used to calculate the percentage of time in therapeutic range (TTR)

Statistical Analysis

The data was analysed by using SPSS version 21.0 . Descriptive statistics summarized socio-demographic and clinical characteristics, and Micromedex Healthcare Series database identified potential drug interactions with rivoraxoban therapy.

Results

The study analyzed the anticoagulation management of 374 patients receiving Rivaroxaban, with a mean age of 57±18 years and a female predominance (58.3%). Heart failure (36.89%) and hypertension (17.2%) were the most common comorbidities, and polypharmacy was prevalent in 51.34% of patients. Atrial fibrillation was the primary indication for Rivaroxaban therapy, followed by chronic rheumatic valvular heart disease.

Table 1 Socio-Demographic and Clinical Characteristics of Patients

Variables	Category	JPMC	Abbasi hosp	Total
		n(%)	**n(%)**	n(%)
Age in years	18–40	29(15.5)	38(20.3)	**67(17.91)**
	41–64	78(41.7)	74(39.6)	**152(40.64)**
	65–74	48(25.7)	51(27.3)	**99(26.47)**
	≥75	32(17.1)	24(12.8)	**56(14.97)**
Sex	Female	110(58.8)	108(57.8)	**218(58.3)**
	Male	77(41.2)	79(42.2)	**156(41.7)**
Comorbid conditions	Heart failure	65(34.8)	69(36.89)	**134(35.83)**
	Hypertension	32(17.2)	29(15.5)	**61(16.3)**

	Hypertension+ hyperthyroidism	14(7.5)	12(6.4)	**26(6.95)**
	Diabetic mellitus	9(4.8)	5(2.7)	**14(3.74)**
	Hypertension + heart failure	8(4.3)	4(2.1)	**12(3.2)**
	Hypertension + chronic renal failure	6(3.2)	2(1.1)	**8(2.14)**
	Hyperthyroidism	5(2.7)	4(2.1)	**9(2.4)**
	Hypertension+ diabetic mellitus + heart failure	5(2.7)	6(3.2)	**11(2.94)**
	Chronic renal failure	4(2.1)	3(1.6)	**7(1.87)**
	Hypertension + heart failure + hyperthyroidism	4(2.1)	3(1.6)	**7(1.87)**
	Hypertension+ diabetic mellitus + heart failure+ hyperthyroidism	3(1.6)	2(1.1)	**5(1.34)**
	Others*	12(6.4)	18(9.62)	**30(8.02)**
Number of medications prescribed per patient	1–2	18(9.6)	24(12.1)	**42(11.23)**
	3–4	54(28.9)	86(43.4)	**140(37.43)**
	≥5	**115(61.5)**	**77(38.1)**	**192(51.34)**

The patients had a target INR range of 2-3 (88.51%) or 2.5-3.5 (11.49%), with an average of 4 INR tests per patient. The mean percentage of time in therapeutic range (TTR) was 47.24%, indicating suboptimal anticoagulation control. Notably, only 25.67% of patients achieved a TTR above 65%. In this study, 64 (17.11%) patients encountered minor and major bleeding events.

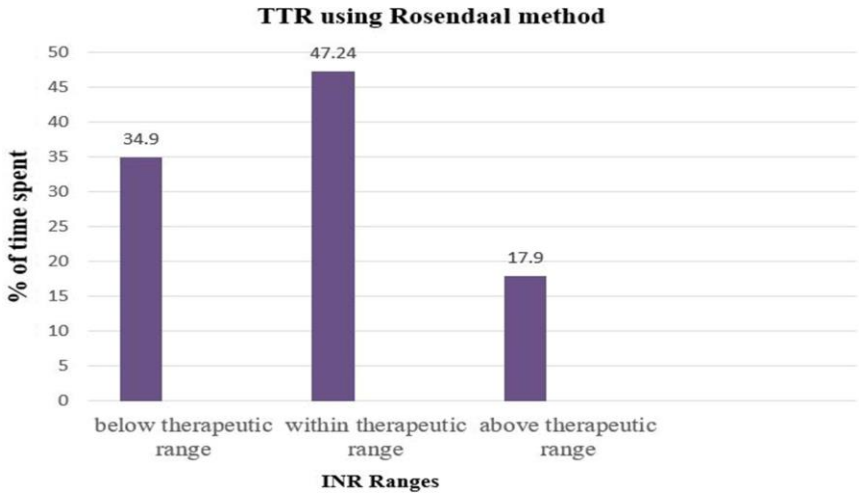

Figure 1 Time period of different INR ranges in patients taking Rivaroxaban.

Of these, 42 patients experienced minor bleeding events (nasal and vaginal bleeding) with therapeutic INR value. Seven patients had INR values of 3.1–4.99, while 11 patients had INR values greater than 5, and 4 patients experienced intracranial hemorrhages with an INR value of >5.

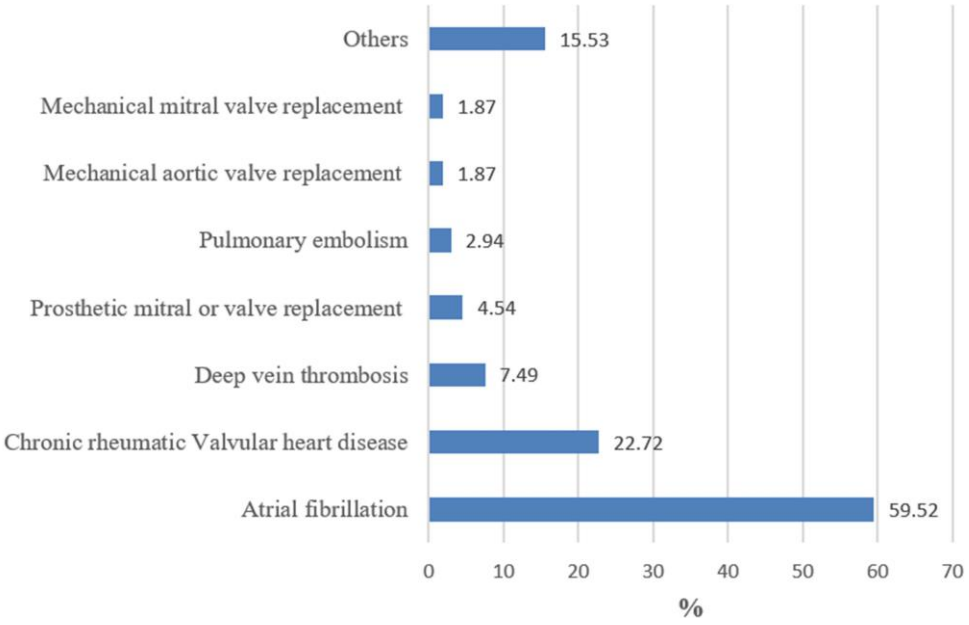

Figure 2 showed the indication of rivaroxaban in patients

In the context of anticoagulation management, rivaroxaban may offer advantages over other anticoagulant, such as predictable pharmacokinetics and reduced need for routine monitoring. Studies have shown that rivaroxaban can provide effective stroke prevention with a lower risk of bleeding complications compared to warfarin.

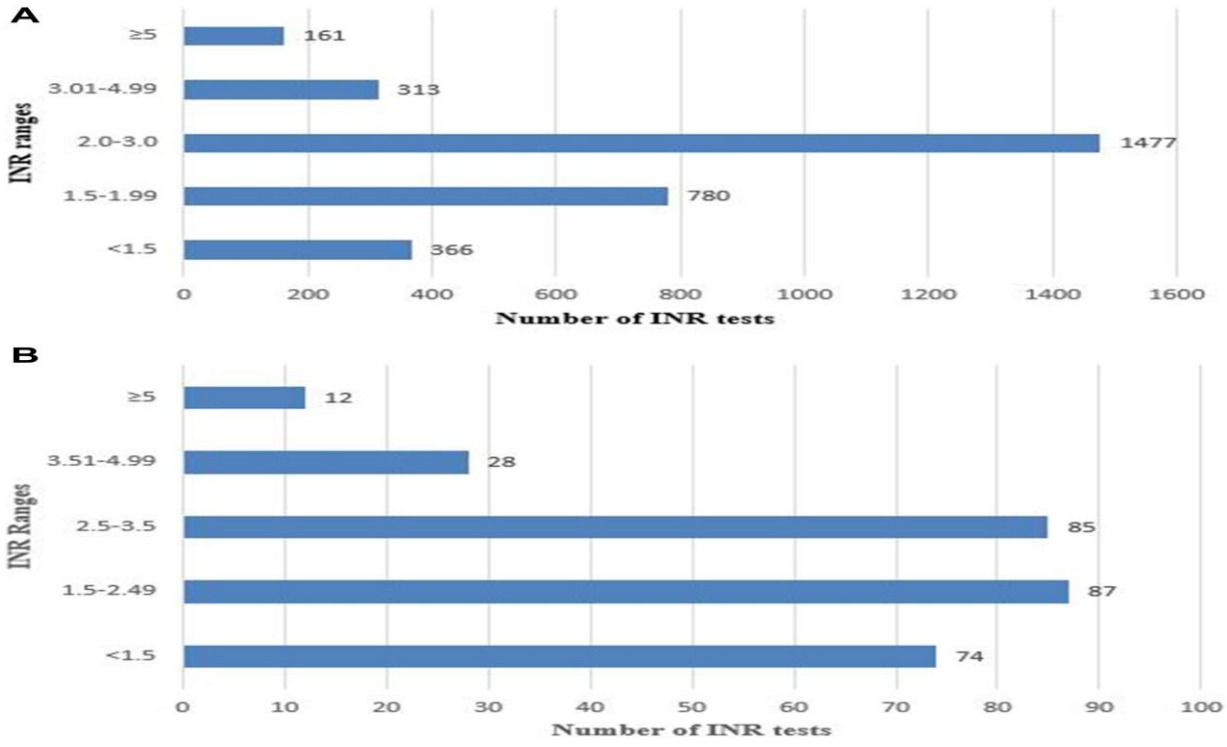

Fig 3 showed the INR values distributions within different intervals among patients taking rivaroxaban for achieving target ranges (A :2.0−3.0, B: 2.5−3.5).

By understanding the challenges of managing Rivaroxaban therapy, clinicians can better appreciate the potential benefits of alternative anticoagulants like rivaroxaban in achieving optimal anticoagulation control and improving patient outcomes.

Discusssion

This study aimed to assess anticoagulation management with rivaroxaban at two tertiary care hospityals. The majority of the study participants (58.3%) were females, and the mean age was 57 years. Atrial fibrillation (43.85%) was the commonest indication for rivaroxaban therapy in the current study[21-23].

The duration of time a patient is on oral anticoagulant influences the stability of INR. Moreover, dietary habits and the presence of drug interaction may alter INR levels associated with rivaroxaban treatment[24]. This study revealed that the mean frequency of INR monitoring per patient was every 47.85 days. The frequency of INR monitoring obtained in this study (every 47.85 days) was more infrequent when compared with the previous study, where most patients (84%) had INR determined every month. In addition, a study from Kenya showed that the median frequency of INR monitoring was 18.5 days. Another study reported the interval between two INR tests was 35 days[25]. These disparities could probably be linked to the difference in the patient size population and specific trends in the management of patients receiving rivaroxaban therapy in the study settings, which can affect their capacity to monitor INR frequently. Furthermore, it is also noticed that rivaroxaban monitoring is patient-tailored. However, current guidelines suggest that at least a 4-week monitoring is essential[26-29]. This time should be reduced to a few days on several occasions including in the case of frequent non-therapeutic INRs and the occurrence of bleeding and thrombotic events[30].

This difference could probably be the higher level of health care in developing countries that had better anticoagulation monitoring services[31,32]. In addition, this poor TTR in the study setting may be due to infrequent INR monitoring and a lack of separate anticoagulation clinics. The present study showed that 1764 INR tests were rivaroxaban therapy deemed to have dose adjustment. Nonetheless, doses were adjusted in only 1053 (59.69%) values[33]. This can probably be linked to physicians' adherence problems, lack of functionaldose adjustment algorithm, rivaroxaban drug–drug interaction, and drug–food interactions that affect warfarin serum levels. However, in the study settings, the management of nontherapeutic (sub-therapeutic) although the management of nontherapeutic INR value was not satisfactory.

The most commonly prescribed rivaroxaban -interacting drugs were furosemide, followed by spironolactone and meto- prolol succinate in the study settings. The prevalence of drug–drug interactions with warfarin was found to be 70%. This result was comparable with a study conducted previously that identified 71% warfarin drug interaction[34,35].This high percentage of drug–drug interaction with rivaroxaban therapy may be justified by the high prevalence of co-prescribed interacting medications.

The most common complication of rivaroxaban therapy was bleeding. This study reveals 64 (17.11%) minor and major (intracranial hemorrhage) bleeding events, which were lower in incidence as compared with previous studies. However, a retrospective study in Brazil reported comparable bleeding events (4.2% major and 10.3% minor bleeding episodes) with the present study.

Conclusion

The study highlights the challenges of rivaroxaban therapy in patients with atrial fibrillation and other cardiovascular conditions. The findings indicate suboptimal anticoagulation control, with a mean time in therapeutic range (TTR) of 47.24% and only 25.67% of patients achieving a TTR above 65%. The study also reveals opportunities for improvement in Rivaroxaban dose adjustment and monitoring. Given the complexities of

warfarin therapy, alternative anticoagulants like rivaroxaban may offer advantages in terms of predictability and reduced monitoring requirements. Clinicians should consider these findings when selecting anticoagulation therapy for patients and strive to optimize anticoagulation control to reduce the risk of thromboembolic and bleeding complications.

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