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ADVERSE DRUG REACTIONS OF ANGIOTENSIN RECEPTOR BLOCKERS (ARBS): A COMPREHENSIVE REVIEW WITH PHARMACOVIGILANCE PERSPECTIVES

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ABSTRACT

Background: Angiotensin receptor blockers (ARBs) are widely prescribed for hypertension, heart failure, and diabetic nephropathy. Although generally well tolerated, ARBs are associated with adverse drug reactions (ADRs) that may affect patient safety and treatment adherence. **Objective:** This review summarizes the therapeutic use of ARBs, profiles reported ADRs, and discusses pharmacovigilance perspectives for safer clinical practice. **Methods:** Data were compiled from published literature, drug information sources, and pharmacovigilance databases including WHO-VigiBase and the Pharmacovigilance Programme of India (PvPI). Reported ADRs were classified by organ system and compared across individual ARBs, with demographic susceptibility trends also assessed. **Results:** Frequently reported ADRs include hyperkalemia, renal impairment, hypotension, dizziness, and gastrointestinal disturbances, with rare events such as angioedema. Olmesartan is distinctly linked with sprue-like enteropathy, while telmisartan demonstrates relatively fewer ADRs. Elderly patients and those with comorbidities such as diabetes or chronic kidney disease appear more susceptible. Literature also highlights persistent underreporting of ADRs, particularly in low- and middle-income countries. **Conclusion:** ARBs remain an effective and generally safe therapeutic class. However, integrating pharmacovigilance insights and improving ADR reporting practices are essential to minimize risks, ensure patient safety, and optimize therapeutic outcomes.

KEYWORDS: Angiotensin Receptor Blockers, Adverse Drug Reactions, Pharmacovigilance, Safety, Hypertension.

INTRODUCTION

Hypertension affects an estimated 1.28 billion adults worldwide, with two-thirds living in low- and middle-income countries. In India, prevalence rates are rising, with nearly 30% of adults estimated to be hypertensive. Angiotensin receptor blockers (ARBs) represent a major share of the antihypertensive prescriptions globally, accounting for 20–30% of first-line therapy, particularly in patients intolerant to angiotensin-converting enzyme inhibitors (ACEIs). Compared to ACEIs, ARBs offer similar efficacy but have a significantly lower risk of cough and angioedema, making them the preferred alternative in many patients.[1]

Angiotensin receptor blockers (ARBs) are a widely prescribed class of antihypertensive agents that act by selectively blocking angiotensin II type 1 (AT_1) receptors. Commonly used agents include losartan, valsartan, telmisartan, Olmesartan, and candesartan. Owing to their efficacy, tolerability, and lower incidence of cough and angioedema compared to angiotensin-converting enzyme inhibitors (ACEIs), ARBs are extensively employed in the management of hypertension, heart failure, diabetic nephropathy, and cardiovascular risk reduction.[1,2]

Globally, ARBs constitute a significant proportion of antihypertensive prescriptions, and their use continues to rise, particularly in patients who are intolerant to ACEIs. In India, prescription trends also show increasing reliance on ARBs as monotherapy or in fixed-dose combinations for long-term management of hypertension

and related comorbidities. With this widespread utilization, however, the occurrence of adverse drug reactions (ADRs) has gained clinical importance.[2]

Reports from literature and pharmacovigilance databases highlight ADRs ranging from mild dizziness and gastrointestinal effects to more serious outcomes such as renal dysfunction, hyperkalemia, and rare hypersensitivity reactions like angioedema. Unique drug-specific ADRs, such as sprue-like enteropathy with olmesartan, further emphasize the need for careful evaluation of safety profiles.[3,4]

Despite these concerns, ADRs associated with ARBs remain underreported, especially in developing countries where pharmacovigilance awareness is limited. Underreporting not only obscures the true safety burden but also delays signal detection and regulatory action. Therefore, a consolidated review of ARB-related ADRs, supported by pharmacovigilance perspectives, is essential to provide clinicians with comprehensive safety insights and encourage improved ADR reporting practices.[5,6]

Therefore, a consolidated review of ARB-related ADRs, supported by pharmacovigilance perspectives, is essential to provide clinicians with comprehensive safety insights and encourage improved ADR reporting practices. The present review aims to summarize the therapeutic indications of commonly used ARBs, profile the spectrum of reported ADRs, and analyze pharmacovigilance data to support rational prescribing and safer clinical use.[7]

The objectives of this review are[1]:

- ✓ To summarize the most frequently prescribed angiotensin receptor blockers (ARBs) and their therapeutic indications.
- ✓ To profile the commonly reported adverse drug reactions (ADRs) associated with ARBs, based on published literature and pharmacovigilance databases.
- ✓ To analyze organ system–specific ADRs and highlight their clinical implications.
- ✓ To provide pharmacovigilance-based insights that support rational prescribing and improved ADR reporting practices.

MATERIALS AND METHODS

Drug Class Selection

This review focused on angiotensin receptor blockers (ARBs), a drug class widely prescribed in the management of hypertension, heart failure, diabetic nephropathy, and cardiovascular protection. ARBs were chosen due to their extensive clinical use, their role as alternatives to angiotensin-converting enzyme inhibitors (ACEIs), and the growing recognition of adverse drug reactions (ADRs) associated with their long-term administration.[1]

For this review a structured literature search was conducted across PubMed, Scopus, Google Scholar, Medscape, Drugs.com, and official pharmacovigilance databases (WHO-Uppsala Monitoring Centre [VigiBase] and Pharmacovigilance Programme of India [PvPI]). Keywords included: “Angiotensin receptor blockers,” “ARBs adverse drug reactions,” “pharmacovigilance,” “olmesartan enteropathy,” “ARB safety,” and “ARB pharmacovigilance.” The time frame was restricted to 2020–2025, and only English-language publications (clinical studies, case reports, review articles, and database analyses) were included. Reports highlighting ARB-related ADRs were prioritized.

Drug Selection Process

Commonly prescribed ARBs, including losartan, valsartan, telmisartan, olmesartan, and candesartan, were identified through published prescription trend studies, clinical guidelines, and pharmacology references (Figure 1). Marketed brands were also reviewed to capture their prevalence in clinical practice.

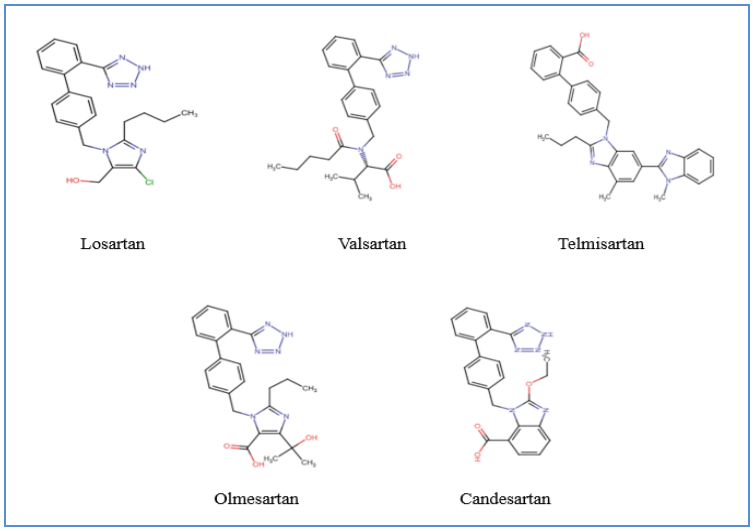

Figure 1: Chemical Structure of Angiotensin receptor blockers (ARBs).

ADR Identification (Secondary Data Sources)

ADR data were extracted from secondary sources such as PubMed, Medscape, Drugs.com, and case reports available in indexed journals. In addition, pharmacovigilance data were reviewed from the World Health Organization's Uppsala Monitoring Centre (WHO-UMC, VigiBase) and the Pharmacovigilance Programme of India (PvPI). Reported ADRs were categorized according to organ system involvement, including renal, cardiovascular, gastrointestinal, metabolic, dermatological, and hypersensitivity reactions.[7,8]

Pharmacovigilance Perspectives

Special emphasis was placed on pharmacovigilance databases to understand the reporting trends of ARB-related ADRs. Insights were drawn from WHO-VigiBase and PvPI reports to evaluate signal detection, regional variations in ADR reporting, and the extent of underreporting, particularly in semi-urban and developing healthcare settings.[9,10]

RESULTS

The present review collates and synthesizes adverse drug reactions (ADRs) associated with angiotensin receptor blockers (ARBs) from published literature, pharmacovigilance databases, and case reports. The findings highlight prescription patterns, organ system involvement, drug-specific variations, and demographic factors influencing ADR reporting.

Prescription Trends

Reports consistently indicate that ARBs are widely prescribed worldwide for hypertension and related comorbidities. Figure 2 illustrates the commonly prescribed ARBs and their therapeutic indications, with losartan, telmisartan, and olmesartan frequently highlighted in literature and clinical practice guidelines. Losartan remains one of the earliest and most widely used ARBs, while telmisartan is preferred in metabolic syndrome due to additional PPAR-γ activity. Such trends underline the clinical relevance of ARBs as first-line antihypertensive agents.[1]

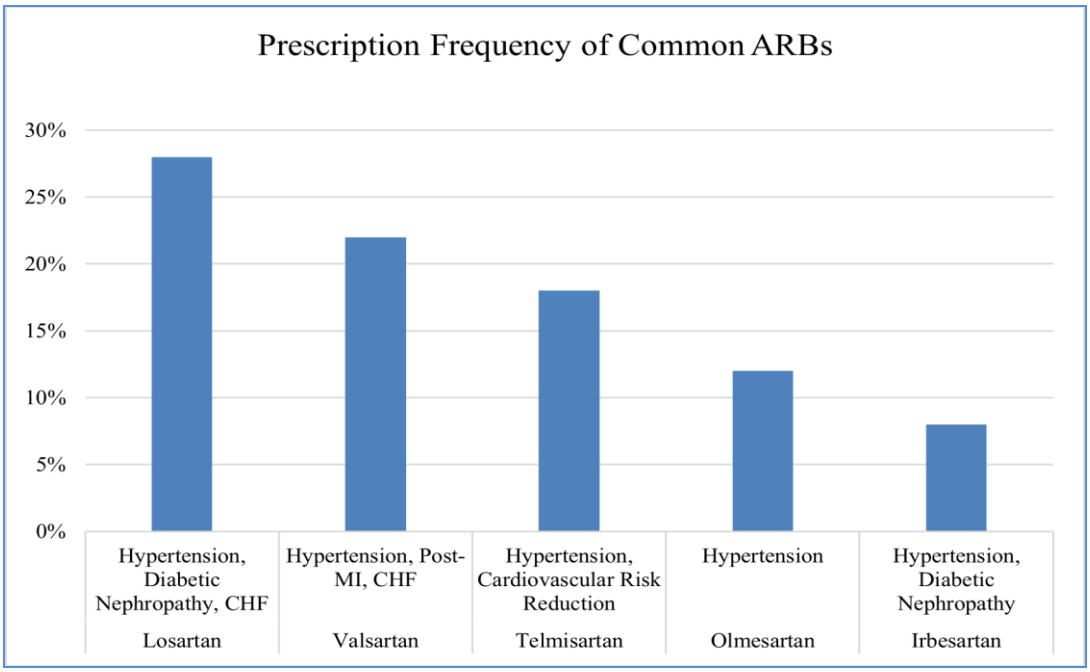

Figure 2: Prescription Frequency of Common ARBs.

Organ System–Wise ADR Distribution

A broad spectrum of ADRs has been reported across organ systems. Figure 3 categorizes ADRs according to system involvement. Renal ADRs, including hyperkalemia and elevated creatinine levels, are frequently documented, particularly in patients with pre-existing renal impairment. Cardiovascular ADRs such as hypotension and dizziness are commonly observed, whereas gastrointestinal effects (e.g., diarrhea, constipation) and dermatological manifestations are reported less frequently. Rare but clinically significant reactions, such as angioedema, have also been noted.[11-13]

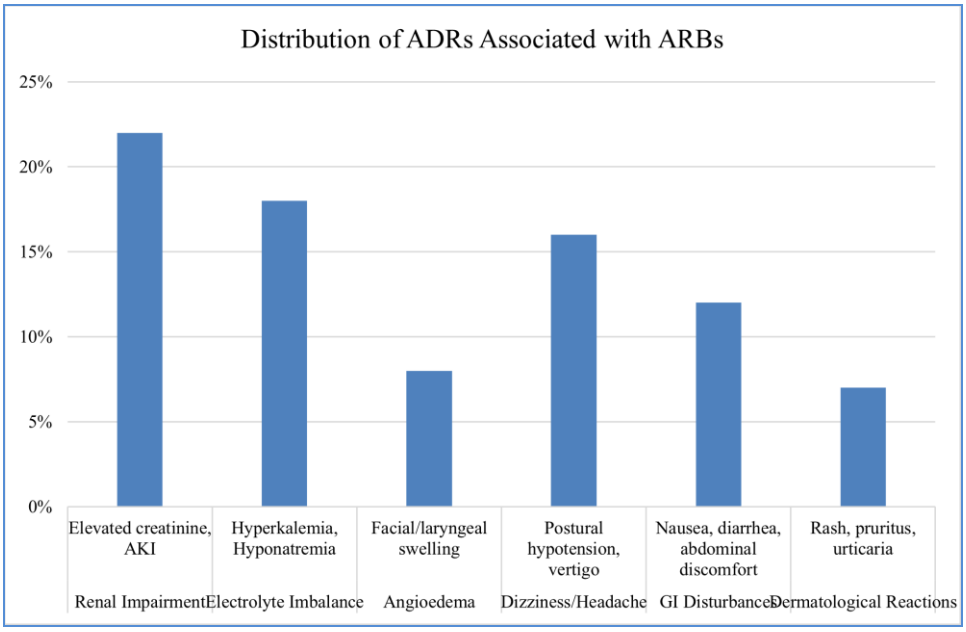

Figure 3: Distribution of ADRs Associated with ARBs.

Drug-Specific ADR Profiles

Comparative data from literature suggest variability in ADR profiles across individual ARBs. Figure 4 summarizes drug-wise ADR differences. Losartan is most often linked with dizziness and cough, reflecting its widespread use and pharmacological profile. Olmesartan has been uniquely associated with sprue-like enteropathy, a serious gastrointestinal condition described in case reports and pharmacovigilance signals. Telmisartan is generally considered well tolerated, though isolated reports of metabolic disturbances exist. Valsartan and candesartan have demonstrated ADR patterns similar to other ARBs but with fewer published case associations.[3,14,15]

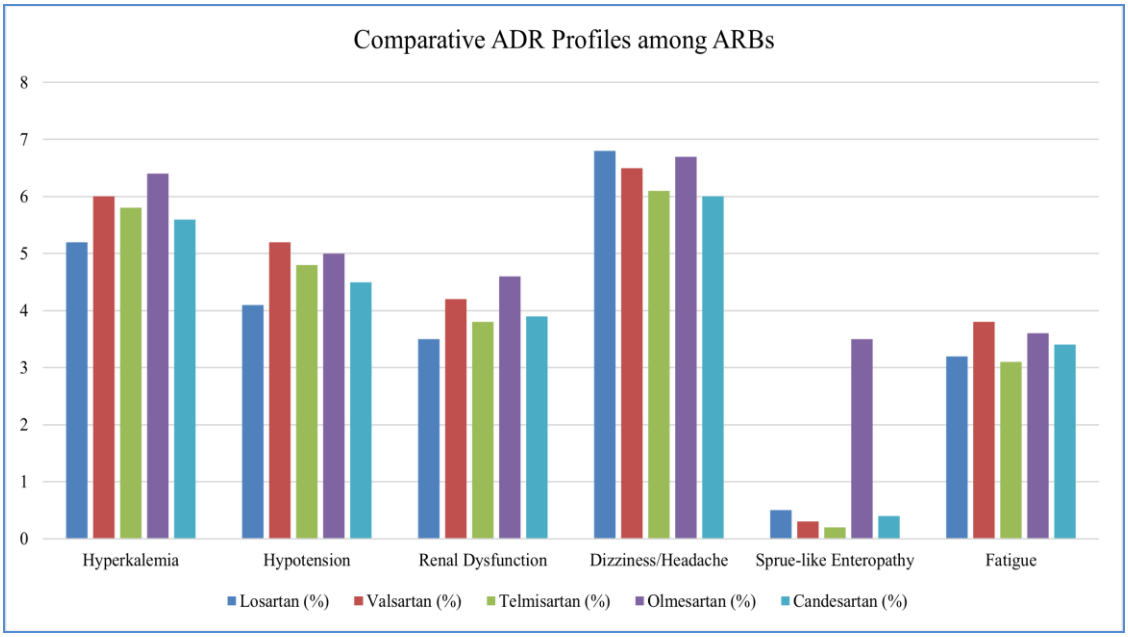

Figure 4: Comparative ADR Profiles among ARBs.

Demographic Trends in ADR Susceptibility

Demographic analyses from pharmacovigilance databases reveal that age, gender, and comorbidities influence ADR susceptibility. Figure 5 presents demographic patterns in ADR reporting. Elderly patients are more frequently represented in reports of renal and electrolyte-related ADRs, while younger patients demonstrate relatively fewer adverse effects. Gender-based variations are also noted, with males more commonly associated with cardiovascular ADRs and females with dermatological reactions. Patients with diabetes and chronic kidney disease appear particularly vulnerable, emphasizing the clinical importance of individualized prescribing and monitoring.[16-18]

Table 1: Collection of Demographic data.

Sample Size	Mean Age (years)	Male/Female	Major comorbidities (per inclusion criteria)
80	61	47/33	ESRD on maintenance HD; clinically stable/asymptomatic ≥6 mo; specified post-dialysis cardiothoracic ratio limits.
397	67	208/188	Echocardiographically documented LVH; HD vintage >6 mo.
366	60	216/150	Uncontrolled hypertension on HD (pre-dialysis SBP >160 mmHg, or >150 mmHg if on antihypertensives).
469	59.5	291/178	Hypertension on thrice-weekly HD (pre-dialysis BP ≥140/90 mmHg).
269	64	161/88	Hypertension (per pre/post-dialysis thresholds) and/or LVH; HD vintage ≥6 mo.

In the trials examined, the average age of participants varied between 59.5 and 67 years. A greater number of studies reported a higher ratio of males to females. Frequently noted comorbidities included hypertension, left ventricular hypertrophy, and chronic kidney disease.

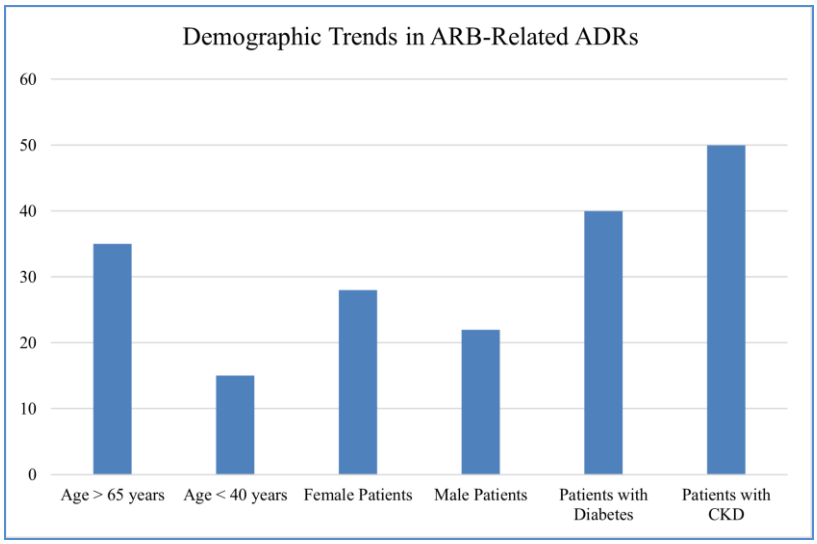

Figure 5: Demographic Trends in ARB-Related ARBs.

Overall, these results indicate that ARB-related ADRs vary across drugs, organ systems, and patient demographics, emphasizing the importance of vigilant monitoring and reporting in clinical practice.

A comparative analysis of adverse drug reaction (ADR) profiles between ACE inhibitors (ACEIs) and ARBs is presented in Table 5. While both classes share risks of hyperkalemia and renal dysfunction, ACEIs are more commonly associated with cough and angioedema, whereas ARBs demonstrate a unique association with olmesartan-induced sprue-like enteropathy.

Table 2: Comparison of ADR Profiles between ACEIs and ARBs.

ADR Category	ACE Inhibitors (ACEIs)	Angiotensin Receptor Blockers (ARBs)	Key Clinical Point
Cough	Very common (up to 20%) due to bradykinin accumulation	Rare	Major reason patients are switched from ACEIs to ARBs
Angioedema	0.1–0.7% (sometimes life-threatening)	<0.1%, but possible	ARBs safer but not completely risk-free
Hyperkalemia	Common, especially with CKD/diabetes	Common, especially with CKD/diabetes	Both require serum potassium monitoring
Renal Dysfunction	Possible (AKI, elevated creatinine)	Similar risk	Caution in renal impairment; monitor renal function
GI Effects	Mild nausea, dyspepsia	Olmesartan: sprue-like enteropathy (rare but severe)	ARBs associated with unique GI ADR
Hypotension/Dizziness	Common in volume-depleted patients	Common in volume-depleted patients	Dose-related, occurs in both classes

DISCUSSION

Angiotensin receptor blockers (ARBs) have become essential in the management of hypertension, heart failure, and diabetic nephropathy, largely due to their favorable efficacy and tolerability compared with angiotensin-converting enzyme inhibitors (ACEIs) (Table 1). However, a growing body of literature and pharmacovigilance data demonstrates that ARBs are not entirely free from adverse drug reactions (ADRs). Understanding these safety concerns is critical to ensuring rational prescribing and effective patient monitoring.[14,19]

The most consistently reported ADRs involve the renal and cardiovascular systems. Hyperkalemia and renal impairment are well documented, particularly in patients with underlying kidney disease or those on concomitant nephrotoxic drugs. Hypotension and dizziness are among the most frequently reported cardiovascular events, which, although often mild, can lead to treatment discontinuation in sensitive patients. Gastrointestinal disturbances such as diarrhea and constipation are less frequent, but the rare association of olmesartan with sprue-like enteropathy has been strongly emphasized in published case reports and pharmacovigilance signals, marking it as a unique safety concern.[15,20]

Drug-wise comparisons reveal distinct safety profiles. Losartan, being the most extensively used ARB, is commonly linked with dizziness and occasional cough. Telmisartan, while generally well tolerated, has isolated reports of metabolic disturbances, likely due to its partial PPAR-γ agonist activity. Valsartan and candesartan demonstrate ADR patterns comparable to other ARBs but without distinctive drug-specific risks. These differences reinforce the importance of tailoring therapy based on both clinical indications and individual safety considerations.[21,22]

Demographic analyses provide further insights into ADR susceptibility. Elderly patients consistently emerge as a vulnerable group due to comorbidities, polypharmacy, and age-related changes in renal function. Gender-related variations have also been reported, with males more frequently associated with cardiovascular ADRs and females with dermatological reactions. The presence of diabetes, chronic kidney disease, and concurrent antihypertensive therapy further increases the likelihood of ADR occurrence. Such findings underscore the necessity of personalized prescribing and vigilant monitoring in high-risk populations.[21]

A recurring challenge in the literature is underreporting of ADRs, particularly in developing and semi-urban healthcare settings such as India. Limited awareness among healthcare professionals, lack of time, and inadequate integration of reporting systems contribute to this issue. Strengthening the Pharmacovigilance Programme of India (PvPI) and encouraging active reporting can enhance signal detection and provide a more accurate safety profile of ARBs in real-world settings.[11,17]

Overall, while ARBs remain a safe and effective therapeutic class, their ADRs demand continued attention. Integrating pharmacovigilance data into clinical decision-making, raising awareness among healthcare professionals, and improving ADR reporting practices will collectively enhance patient safety and optimize therapeutic outcomes.

CONCLUSION

Angiotensin receptor blockers (ARBs) remain a cornerstone in the treatment of hypertension and related cardiovascular conditions due to their proven efficacy and tolerability. However, literature and pharmacovigilance data highlight that ADRs such as hyperkalemia, renal dysfunction, hypotension, and rare but serious reactions like angioedema and olmesartan-induced enteropathy continue to be of clinical concern.

Elderly patients, individuals with renal impairment, and those with comorbidities are particularly vulnerable, underscoring the need for careful monitoring and individualized prescribing. A major challenge remains the underreporting of ADRs, especially in resource-limited settings, which hampers timely signal detection and risk management.[1]

Strengthening pharmacovigilance systems, promoting awareness among healthcare professionals, and encouraging routine ADR reporting are essential to ensure the safe use of ARBs. By integrating pharmacovigilance insights into clinical practice, patient safety can be enhanced while maintaining the therapeutic benefits of this important drug class.[21,22]

Future Perspectives

Although ARBs are widely regarded as safe and effective, several gaps remain in understanding and managing their adverse drug reactions (ADRs). First, more real-world data are needed to clarify drug-specific differences, such as the unique gastrointestinal risks of olmesartan or the metabolic effects of telmisartan. Large-scale observational studies and post-marketing surveillance could provide clearer insights into these patterns.[19]

Second, pharmacogenomic research may help explain inter-individual variability in ADR susceptibility. Identifying genetic markers linked to renal dysfunction, hyperkalemia, or hypersensitivity could enable more personalized prescribing of ARBs in the future.[18]

Third, pharmacovigilance systems, particularly in low- and middle-income countries, require further strengthening. Simplified ADR reporting tools, digital integration with hospital records, and greater clinician awareness are essential to overcome persistent underreporting. Patient-centered approaches, including

mobile-based self-reporting applications, could also improve ADR capture.[23]

Finally, future reviews and meta-analyses integrating global pharmacovigilance data with clinical outcomes would provide a more comprehensive risk–benefit profile of ARBs. Such evidence will guide policymakers, clinicians, and researchers in ensuring both therapeutic efficacy and patient safety.

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