04. Renal Adverse Events Associated with Clozapine: A FAERS Disproportionality Analysis

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BACKGROUND: Clozapine is classed as an atypical antipsychotic and is used mainly in treatment-resistant schizophrenia. It is associated with multiple serious adverse effects which require medical monitoring. The cardiotoxic and hematologic toxicities of this drug are well recognized and monitored, however, the renal adverse events are less extensively monitored, primarily being represented by smaller observational studies or case reports. This study aimed to identify and analyze reporting patterns of renal adverse events associated with clozapine, in addition to assessing for potential disproportionality signals using data from the United States Food and Drug Administration Adverse Event Reporting System (FAERS) database. **METHODS:** This study analyzed data from the United States Food and Drug Administration Adverse Event Reporting System (FAERS) through January 1989 to December 2025. The drug analyzed in the study was clozapine. Renal adverse events were identified using the Medical Dictionary for Regulatory Activities (MedDRA) preferred terms "Acute Kidney Injury," "Renal Injury," "Renal Failure," "Renal Impairment," "Renal Disorder," "Chronic Kidney Disease," "End stage renal disease," "Nephropathy," "Nephrolithiasis," "Tubulointerstitial Nephritis," and "Nephritis." The disproportionality analysis was performed using reporting odds ratio (ROR) and proportional reporting ratio (PRR) with 95% confidence intervals, using all other drugs in the FAERS database as the control group. **RESULTS:** Among the renal adverse events which were evaluated, acute kidney injury was the most frequently reported event involving clozapine, totaling 928 reported cases. Other reported events included renal failure (576 cases), renal impairment (377 cases), chronic kidney disease (203 cases), tubulointerstitial nephritis (147 cases), renal disorder (141 cases), and nephropathy (38 cases). The disproportionality analysis was unable to identify statistically significant signals for the majority of evaluated renal adverse events. Acute kidney injury demonstrated a ROR of approximately 0.99, while renal impairment demonstrated a ROR of 0.92. Additionally, chronic kidney disease, renal disorder, nephropathy, and renal failure did not exhibit evidence of disproportionate reporting comparative to the overall FAERS database. The highest disproportionality estimates among the evaluated renal adverse events were demonstrated by tubulointerstitial nephritis, with a ROR of approximately 1.6 and nephritis with a ROR of 1.28, despite having the lowest case count (28) among the included terms. No statistically notable signal was identified based on the study criteria. **CONCLUSION:** This FAERS pharmacovigilance study detected multiple reports of renal adverse events involving the use of clozapine within the database. Acute kidney injury represented the most frequently reported event. However, the disproportionality analysis could not identify a statistically significant safety signal for the renal adverse events assessed. Tubulointerstitial nephritis and nephritis demonstrated the highest disproportionality estimates with no signal, which may further necessitate an investigation in future studies. The importance of continued clinical awareness and renal monitoring in patients receiving clozapine is emphasized by the findings in this study. Additional observational studies to further evaluate potential renal adverse effects associated with this medication are also recommended, due to limitations of the database such as lacking denominator data or data quality inaccuracies from potential masking effects, underreporting and double entries.

Key Words: Clozapine, Acute Kidney Injury, Data Analysis, Pharmacovigilance

Table 1. Reporting frequency and disproportionality analysis of renal adverse events associated with clozapine in FAERS

Adverse Event	Reported Cases	ROR	PRR	Statistical Signal
Acute Kidney Injury	928	0.9956083506	0.9956358432	No
Renal Failure	576	0.862971786	0.8635042288	No
Renal Impairment	377	0.9183095399	0.9185172957	No
Chronic Kidney Disease	203	0.5405285039	0.5411577131	No
Tubulointerstitial Nephritis	147	1.577002102	1.576429918	No
Renal Disorder	141	0.6296153123	0.6299676122	No
Nephrolithiasis	51	0.2438399628	0.2441001132	
Nephropathy	38	0.8783729498	0.8784041283	No
Renal Injury	34	0.2514538648	0.251625552	No
End Stage Renal Disease	32	0.3667559938	0.3668926916	No
Nephritis	28	1.281397171	1.281344021	No

Abbreviations: FAERS = FDA Adverse Event Reporting System; ROR = Reporting Odds Ratio; PRR = Proportional Reporting Ratio