

# MACHINE LEARNING-DRIVEN EARLY PREDICTION OF VORICONAZOLE PLASMA LEVELS: ENHANCING PRECISION DOSING AND PATIENT SAFETY IN ANTIFUNGAL THERAPY

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## BACKGROUND

Voriconazole, a second-generation triazole, is essential for treating invasive fungal infections. However, its non-linear pharmacokinetics, high interpatient variability, and narrow therapeutic window complicate dosing. Subtherapeutic levels risk treatment failure, while elevated levels increase toxicity. Many hospitals lack routine therapeutic drug monitoring (TDM), making precise dosing challenging. Machine learning (ML) offers a promising solution to optimize early dosing and improve patient safety.

## OBJECTIVES

Develop an ML model to classify patients into subtherapeutic, therapeutic, or toxic voriconazole plasma levels early in therapy, allowing individualized dosing and reducing risks.

## MATERIAL & METHODS

**Study Design:** Retrospective, single-center study (May 2021 – June 2024, Hospital Universitario Central de Asturias, Spain).

**Data Collected:** Demographic, clinical, and pharmacokinetic data, including liver and kidney function, serum albumin, comorbidities, and voriconazole plasma concentration (Architect Abbot®), were collected.

**ML Approach:** Extreme Gradient Boosting (XGB) vs. K-nearest neighbors (KNN), support vector machines (SVM), Bayesian linear discriminant analysis (BLDA), Gaussian naïve Bayes (GNB), and decision trees (DT).

**Validation:** 70% training / 30% validation, 5-fold cross-validation.



## RESULTS

128 patients included.

XGB outperformed all models with 97% accuracy.

**Key Metrics:** AUC 0.96, MCC 85.85%, Kappa 86.14%, demonstrating robust classification performance.

Model	Accuracy (%)	AUC	MCC (%)	Kappa Index (%)	F1 Score (%)	Sensitivity (%)	Specificity (%)
XGB	97	0.96	85.85	86.14	96.5	95.8	96.9
KNN	89	0.91	75.42	76.05	87.2	86.4	88.1
SVM	86	0.88	72.18	73.12	85.1	83.9	86.7
BLDA	81	0.83	65.32	66.88	80.5	79.2	81.7
GNB	80	0.81	62.75	63.95	78.9	77.5	80.2
DT	84	0.85	68.1	69.72	83.2	82.5	84.3

## CONCLUSION

- ML enables **early, precise voriconazole dosing**, addressing the limitations of traditional methods—especially in hospitals without routine TDM.
- XGB's superior performance** makes it a valuable tool for enhancing patient safety and treatment efficacy.

