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Research Article

Idiosyncratic Drug-Induced Agranulocytosis: Risk Clusters, Big Data and AI-Driven Innovations for Patient Care

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ABSTRACT

Idiosyncratic drug-induced agranulocytosis is a rare yet potentially life-threatening adverse reaction, characterized by an abrupt and profound depletion of neutrophils that predisposes patients to severe infections. Although its incidence is low, its unpredictable onset and the broad spectrum of implicated drugs make it a persistent clinical challenge. Current management hinges on prompt recognition and immediate withdrawal of the causative agent, but preventive strategies have traditionally been limited. Advances in pharmacogenomics have shed light on individual susceptibility, identifying specific HLA alleles and genetic polymorphisms as key risk factors. The concept of risk clusters—integrating genetic, demographic and clinical features—offers a foundation for more targeted prevention. Big data analytics and artificial intelligence (AI) now provide powerful tools for predictive modeling and real-time pharmacovigilance signal detection. In parallel, technological innovations such as telemedicine, wearable sensors and home-based blood cell monitoring enhance early detection and timely intervention, particularly in high-risk populations. Therapeutic patient education (TPE) is essential for fostering awareness, improving adherence to monitoring and empowering patients in self-management. This review outlines the convergence of scientific, clinical and technological advances that supports a shift toward a proactive, personalized and preventive approach to managing idiosyncratic drug-induced agranulocytosis in contemporary internal medicine.

Keywords: Drug-induced agranulocytosis, Risk clusters, Big data, Artificial intelligence, Telemedicine, Connected sensors, Therapeutic patient education, Prevention, Prediction

Introduction

Idiosyncratic drug-induced agranulocytosis (IDIA) is an uncommon but potentially fatal adverse drug reaction, defined by a profound neutrophil depletion that can precipitate severe infections and, in some cases, death. Its clinical management remains particularly challenging due to the abrupt and unpredictable onset, the broad spectrum of implicated drugs and the frequent absence of early warning signs. Although certain medications-such as antithyroid drugs, clozapine, sulfonamides and specific antibiotics-exhibit a stronger documented association with IDIA, the idiosyncratic nature of the reaction reflects a multifactorial pathogenesis, integrating genetic susceptibility, immune dysregulation, comorbid conditions and drug-specific pharmacological properties[1,2].

Despite its rarity, IDIA carries a substantial risk of morbidity and rapid clinical decline, making it a priority concern in internal medicine. The scarcity of reliable predictive biomarkers and the often-delayed symptom onset hinder early recognition; once agranulocytosis is established, prompt withdrawal of the causative drug and urgent supportive interventions are imperative[3,4]. A particular emphasis is placed on advancing innovative methodologies for precise risk stratification, early detection and continuous patient monitoring, with the ultimate objective of establishing a proactive, individualized framework for the prevention and management of IDIA that integrates emerging biomarkers and real-time clinical data[5,6].

This review aims to deliver a comprehensive synthesis of current evidence and emerging insights into IDIA. It emphasizes the transformative potential of pharmacogenomics, big data analytics, artificial intelligence (AI) and telemedicine in reshaping prevention and management strategies.

Idiosyncratic Drug-Induced Agranulocytosis

Idiosyncratic drug-induced cytopenias are characterized by a reduction in circulating blood cells, including, neutrophils (neutropenia). These events result from unpredictable reactions to drugs, independent of the administered dose or the known pharmacological properties of the agent. Neutropenia is defined as an abnormally low absolute neutrophil count (ANC), a key cell type in the defense against bacterial and fungal infections. It is classified according to severity: mild (1000–1500 cells/μL; 1–1.5 × 10^9/L), moderate (500–1000 cells/μL; 0.5–1 × 10^9/L) and severe (<500 cells/μL; <0.5 × 10^9/L), with infection risk rising sharply as counts decline[7]. Agranulocytosis represents a severe and often abrupt form of neutropenia, usually defined by ANC <500 cells/μL and frequently <100 cells/μL (0.1 × 10^9/L), leading to profound immune compromise[3].

IDIA is rare, with an estimated incidence of 6-10 cases per million inhabitants and arises from adverse drug reactions influenced by individual genetic predisposition, immune mechanisms or yet unidentified factors[1,2]. In contrast to other forms of neutropenia, agranulocytosis in IDIA most often results from drug-induced bone marrow suppression and is associated with a substantial risk of rapidly progressive, life-threatening infections. Reported mortality ranges from 5 % to 20 % in severe neutropenia or agranulocytosis[8]. Thus, early recognition of these drug-induced cytopenias is critical to promptly discontinue the offending medication and initiate appropriate supportive or targeted interventions[9]. Such vigilance is essential to minimize complications and improve patient outcomes.

IDIA can result from exposure to a remarkably broad spectrum of medications, reflecting its inherently unpredictable and idiosyncratic pathophysiology. Historically, well-recognized causative agents include certain antimicrobials (e.g., trimethoprim–sulfamethoxazole, selected cephalosporins), nonsteroidal anti-inflammatory drugs (NSAIDs) such as phenylbutazone (with far rarer associations involving newer NSAIDs), antithyroid agents (e.g., methimazole, propylthiouracil) and the antipsychotic clozapine, which is associated with a particularly elevated risk and is subject to mandatory blood monitoring programs in many countries[10,11]. Additional frequently implicated drug classes comprise anticonvulsants (e.g., carbamazepine), antiarrhythmics (e.g., procainamide) and various chemotherapeutic agents-although the latter more typically induce predictable, dose-dependent myelosuppression rather than true idiosyncratic agranulocytosis[12,13].

More recently, emerging therapeutic modalities have been linked to isolated cases, including selected biologics (e.g., specific monoclonal antibodies) and, on rare occasions, advanced interventions such as gene therapy, cell-based therapies and CAR T-cell therapy[14,15]. The continuously expanding spectrum of potentially causative agents emphasizes the critical importance of comprehensive medication history taking and robust pharmacovigilance systems to detect novel associations and refine estimates of drug-specific risk[16,17].

Understanding Risk: The Concept of Risk Clusters in Idiosyncratic Drug-Induced Agranulocytosis

The conventional approach to drug-induced agranulocytosis has historically emphasized associations with individual drugs. While informative, this perspective is limited, as susceptibility to IDIA is likely multifactorial. A more comprehensive framework involves the identification of risk clusters-integrated profiles combining patient characteristics, genetic predispositions, comorbid conditions and medication patterns that, when present together, substantially elevate the likelihood of developing IDIA.

Genetic predisposition

Specific HLA alleles and polymorphisms in genes governing drug metabolism and immune regulation have been increasingly implicated in IDIA pathogenesis[18,19]. Variants influencing xenobiotic processing or immune tolerance can predispose individuals to aberrant immune responses. Incorporating genetic screening into clinical workflows may help identify patients at highest risk when exposed to certain high-risk drugs.

Age and sex

Epidemiological studies indicate that older age and female sex confer a higher risk of IDIA with selected medications[20,21]. Contributing factors include age-related pharmacokinetic changes, altered immune surveillance and hormonal influences on immune modulation. Slower drug clearance in elderly patients may result in prolonged exposure, whereas immune response differences in females may increase susceptibility to immune-mediated reactions.

Comorbidities

Autoimmune diseases, chronic infections and hepatic or renal dysfunction can amplify risk[22]. Autoimmune disorders may prime aberrant immune activation; infections can transiently dysregulate immunity; and impaired hepatic or renal clearance may elevate systemic drug levels, increasing the probability of immune-mediated cytotoxicity.

Polypharmacy and drug combinations

Concomitant use of multiple medications can potentiate risk via pharmacokinetic or pharmacodynamic interactions[23,24]. Some drug combinations exert synergistic myelotoxic effects, while others unpredictably modulate immune responses. Systematic evaluation of drug–drug interaction patterns is needed to refine risk stratification models.

History of prior adverse drug reactions

Patients with previous idiosyncratic, particularly immune-mediated, reactions may be predisposed to subsequent events[25]. Immune sensitization from prior exposures could trigger amplified responses to structurally or mechanistically related drugs.

Identifying such risk clusters through large-scale, integrative data analyses is crucial for enhancing prediction and prevention **(Table 1)**[18-25]. A precision medicine approach-integrating genetic, clinical and pharmacological data-could enable tailored treatment regimens, targeted monitoring and early intervention for high-risk patients, thereby reducing the incidence and severity of this potentially fatal condition.

Table 1: Risk clusters for idiosyncratic drug-induced-agranulocytosis (IDIA) (18-25).

Risk Factor	Description	Impact on Risk of IDIA
Genetic Predisposition	Specific HLA alleles and polymorphisms in genes involved in drug metabolism and immune regulation Genetic testing could help identify individuals at high risk	Genetic variations affect how the body processes drugs and respond to them, increasing susceptibility to IDIA
Age and Sex	Older individuals and females are more likely to develop IDIA Age-related changes in metabolism and immune function and hormonal differences, contribute to this increased risk	Older patients may have slower drug metabolism, while hormonal differences in females could influence immune responses
Co-morbidities	Autoimmune diseases, infections and hepatic/renal impairment can increase the risk These conditions may influence immune regulation and drug metabolism	Co-existing diseases may exacerbate immune responses, alter drug metabolism and make the body more prone to IDIA
Polypharmacy and Specific Drug Combinations	The use of multiple medications increases the likelihood of interactions, which can either heighten or reduce the risk of agranulocytosis Some combinations may have synergistic effects	Drug-drug interactions could amplify or alter the impact on the hematopoietic system, increasing the likelihood of IDIA
Previous Adverse Drug Reaction History	Individuals with a history of immune-mediated adverse drug reactions are at a higher risk for developing IDIA due to immune system sensitization	A prior sensitization to medications may lead to an exaggerated immune response, elevating the risk of future ADRs

The Power of Big Data and Artificial Intelligence in Idiosyncratic Drug-Induced Agranulocytosis Research

The enormous volume of data generated from sources such as electronic health records (EHRs), pharmacovigilance databases, genomic research and even social media offers unprecedented opportunities to deepen our understanding of the complex mechanisms underlying drug-induced agranulocytosis (IDIA). The application of big data analytics in conjunction with artificial intelligence (AI) algorithms markedly enhances our capacity to predict, detect and manage IDIA risk in clinical practice. These advanced technologies enable the extraction of insights that remain largely inaccessible through traditional analytical approaches. Key advances enabled by big data and AI include the following factors.

Identification of novel risk factors and drug associations

Machine learning techniques excel at processing vast, heterogeneous datasets to detect hidden patterns that conventional analyses may overlook. By mining extensive EHRs, pharmacovigilance reports and genomic datasets, AI can reveal previously unrecognized risk factors and drug-drug interactions that increase susceptibility to IDIA, especially within defined patient subpopulations[26,27]. For instance, AI may identify specific medication combinations or genetic polymorphisms that predispose individuals to agranulocytosis, thereby refining risk stratification.

Development of predictive models

AI models trained on retrospective clinical and genetic data can estimate an individual's probability of developing IDIA based on their composite risk profile, incorporating genetic predisposition, demographics (age, sex), co-morbidities and current pharmacotherapy. Such predictive algorithms facilitate preemptive identification of patients at elevated risk prior to initiating drugs associated with agranulocytosis[27,28]. These models support evidence-based, personalized prescribing and enable enhanced surveillance of high-risk patients.

Enhanced signal detection in pharmacovigilance

AI-powered tools improve pharmacovigilance by analyzing spontaneous adverse drug reaction reports collected from diverse sources, including clinical practice databases, patient registries and social media platforms. By efficiently processing large-scale data and identifying subtle signals, AI enables earlier detection of potential IDIA-related safety concerns compared to traditional methods[29,30]. Early signal recognition promotes timely regulatory action such as risk warnings or further drug safety investigations, ultimately reducing adverse outcomes.

Personalized risk assessment

One of AI's greatest strengths lies in integrating multifaceted data streams-genomic markers, clinical history, medication profiles and social determinants of health-to deliver individualized risk assessments for IDIA[31,32]. This precision approach empowers clinicians to anticipate patient-specific risks before prescribing potentially agranulocytosis-inducing drugs, fostering informed decision-making and minimizing harm.

The integration of big data analytics and AI into IDIA research and clinical management holds transformative potential for enhancing drug safety and patient outcomes[33]. Through identification of novel risk factors, predictive modeling, improved pharmacovigilance and personalized risk stratification **(Table 2)**, these technologies promise to revolutionize our ability to predict, detect and prevent this severe adverse drug reaction, paving the way toward safer and more effective therapeutic strategies.

Table 2: Key opportunities provided by big data analytics and artificial intelligence (AI) in the context of idiosyncratic drug-induced agranulocytosis (IDIA)[26-33].

Opportunity	Description	Impact on IDIA Management
Identify Novel Risk Factors and Drug Associations	Machine-learning algorithms can process vast datasets from electronic health records, pharmacovigilance databases and genomic studies to uncover hidden patterns, such as drug-drug interactions and genetic variants	AI can reveal new risk factors and drug associations, allowing for more accurate identification of at-risk patient groups
Develop Predictive Models	AI models can be trained on historical data to predict an individual's likelihood of developing IDIA based on their risk cluster profile, such as genetic predisposition and co-morbidities	Predictive models can help foresee which patients are most likely to develop IDIA, enabling proactive risk management
Improve Signal Detection in Pharmacovigilance	AI-powered tools can analyze adverse drug reaction reports from diverse sources, including clinical practice, patient registries and social media, to detect subtle patterns and signals faster	Early detection of IDIA signals leads to quicker regulatory responses, reducing the time to intervention and preventing harm
Personalize Risk Assessment	AI can integrate data from various sources, including genetic markers, medication history and social determinants of health, to create a personalized IDIA risk profile for each patient	Personalized risk assessments allow healthcare providers to tailor treatment and monitoring plans based on individual patient risks

Innovations in Biological Understanding

Recent advancements in biology are providing deeper insights into the complex mechanisms underlying drug-induced agranulocytosis. These innovations are essential for improving prevention, diagnosis and treatment strategies.

Pharmacogenomics

Ongoing research into genetic markers associated with susceptibility to IDIA is refining our understanding of individual risk profiles[34,35]. As this field progresses, it may lead to pre-prescription genetic testing for patients taking medications known to carry a high risk of agranulocytosis, ensuring more personalized and safer prescribing practices.

Immunopathogenesis

Investigating the immune mechanisms involved in IDIA, such as the formation of drug-dependent antibodies and the activation of cytotoxic T cells against neutrophils, is critical for developing targeted therapies. By understanding how the immune system responds to certain drugs, researchers can design interventions that block or modulate these harmful immune responses, potentially reducing the incidence and severity of agranulocytosis[35,36].

Neutrophil biology

Recent breakthroughs in understanding the development, survival and clearance mechanisms of neutrophils-the white blood cells primarily affected by agranulocytosis-are opening up new avenues for intervention[37,38]. These insights may lead to novel therapeutic targets aimed at mitigating the severity and duration of agranulocytosis, enhancing the body's ability to recover from neutrophil depletion.

Biomarkers

The identification of early biomarkers that precede the onset of agranulocytosis would be invaluable for proactive monitoring and timely intervention. Ongoing research is focused on identifying such biomarkers in peripheral blood or bone marrow, which could help healthcare providers detect early warning signs of agranulocytosis before the condition becomes severe, allowing for earlier treatment and improved patient outcomes[39,40].

These biological innovations are crucial for advancing our understanding of IDIA and paving the way for more effective strategies in managing and preventing this serious adverse drug reaction[41].

Integrating Telemedicine and Connected Sensors for Enhanced Monitoring

Telemedicine and connected sensors represent promising innovations for enhancing patient monitoring, particularly during the early detection phase of drug-induced agranulocytosis. These tools can enable more proactive, personalized care by facilitating real-time health tracking and faster response to warning signs.

Remote symptom monitoring

Telehealth platforms allow patients to regularly report symptoms from home, such as fever, fatigue or sore throat-early signs that may indicate infection, a critical and potentially life-threatening complication of agranulocytosis[42,43]. This continuous symptom tracking supports earlier recognition of concerning developments and enables clinicians to respond more quickly.

Wearable sensors

Devices capable of continuously monitoring vital signs-such as body temperature, heart rate and possibly oxygen saturation-offer an added layer of protection for patients at risk. Abnormal readings can trigger automated alerts to healthcare providers, prompting further evaluation[44,45]. These early warnings may allow for swift intervention before complications progress, potentially improving outcomes and reducing the need for hospitalization.

Home-based blood cell counts

Emerging point-of-care testing (POCT) technologies that allow for home-based white blood cell (WBC) monitoring are particularly valuable in the context of IDIA. These devices are being designed to be user-friendly, affordable and reliable, enabling high-risk individuals to check their blood counts more frequently without visiting a clinical laboratory. This is especially beneficial for patients who have recently started medications known to be associated with IDIA or who belong to identified risk clusters[46,47]. Early detection of a declining neutrophil count at home could drastically reduce the time to diagnosis and treatment, ultimately preventing severe complications.

These innovations support a shift toward patient-centered care, enabling earlier diagnosis, timely treatment and potentially better clinical outcomes for individuals at risk of this serious adverse drug reaction **(Table 3)**[48,49].

Table 3: Role of telemedicine and connected sensors in enhancing the monitoring of drug-induced agranulocytosis (DIA)[42-49].

Innovation	Functionality	Impact on DIA Monitoring
Remote Symptom Monitoring	Patients use telehealth platforms to report early symptoms (e.g., fever, sore throat, fatigue) from home	Enables earlier recognition of potential infections and faster clinical response
Wearable Sensors	Continuous tracking of vital signs such as temperature, heart rate and possibly oxygen saturation. Alerts can be sent to providers when abnormalities are detected	Facilitates real-time monitoring and allows rapid intervention before complications worsen
Home-Based Blood Cell Counts	Point-of-care testing (POCT) devices enable patients to check white blood cell counts at home, particularly neutrophils	Supports early detection of neutropenia, reduces diagnostic delay and prevents severe outcomes in high-risk patients

The Crucial Role of Therapeutic Patient Education

Therapeutic patient education (TPE) plays a crucial role in mitigating the risks associated with drug-induced agranulocytosis **(Table 4)**. By equipping patients with knowledge and self-management tools, TPE not only promotes safer medication use but also enhances early detection and timely intervention, both of which are essential in preventing severe complications.

Medication awareness

One of the foundational goals of TPE is to ensure that patients are fully informed about the medications they are prescribed, particularly those associated with a known risk of IDIA[50,51]. This includes educating them on the potential side effects-especially the risk of agranulocytosis-and emphasizing the importance of reporting any unusual or early symptoms, such as fever, sore throat or mouth ulcers, as these could indicate the onset of neutropenia or infection.

Early symptom recognition

TPE empowers patients to recognize the early clinical signs of agranulocytosis. By understanding what symptoms to look out for and the seriousness of a delayed response, patients are more likely to seek immediate medical attention when warning signs appear. This can lead to earlier diagnosis and a better chance of recovery[52,53].

Adherence to monitoring protocols

For patients on medications known to carry a risk of IDIA, adherence to routine blood monitoring is critical. TPE can improve compliance with scheduled white blood cell (WBC) counts and follow-up appointments by helping patients understand the purpose of these tests and the potential consequences of missing them[54,55].

Self-management strategies

TPE also supports preventive behavior. Teaching patients' effective infection prevention techniques, such as maintaining proper hand hygiene, avoiding crowded places during neutropenic episodes and recognizing signs of infection, can help reduce the risk of complications associated with low neutrophil counts[56].

Importantly, tailored TPE programs-especially those delivered through digital platforms and mobile applications-can enhance patient engagement and long-term knowledge retention. These tools offer flexible, accessible and interactive learning experiences that can be customized to each patient's literacy level, risk profile and personal preferences[57-59]. Features like symptom trackers, medication reminders, educational videos and real-time chat with healthcare providers can significantly improve patient involvement in their own care.

Table 4: Key roles and benefits of therapeutic patient education (TPE) in preventing and managing drug-induced agranulocytosis (IDIA)[50-59].

TPE Aspect	Objectives / Content	Expected Benefits	Possible Tools / Supports
Medication Awareness	Inform patients about medications associated with IDIA risk and their side effects, especially agranulocytosis	Increased vigilance regarding side effects and prompt reporting of symptoms	Brochures, educational sessions, explanatory videos
Early Symptom Recognition	Teach patients to recognize early signs (fever, sore (throat, mouth ulcers	Faster medical consultation, early diagnosis, improved outcomes	Mobile apps, symptom checklists, SMS alerts
Adherence to Monitoring Protocols	Encourage compliance with routine blood tests (WBC counts) and follow-up visits	Early detection of abnormalities, prevention of severe complications	SMS/app reminders, shared calendar
Self-Management .7.4 Strategies	Teach preventive measures (hand hygiene, avoiding .crowds, infection vigilance	Reduced infection risk, improved quality of life during neutropenic periods	Video tutorials, practical guides, online support groups
Personalization via Digital Platforms	Tailor education to patient literacy, needs and profiles using interactive tools	Enhanced engagement, long-term knowledge retention, active patient involvement	Mobile apps, real-time chat, interactive videos

Prevention and Prediction: Towards a Proactive Approach

The ultimate goal in managing drug-induced agranulocytosis is its prevention. Achieving this requires a comprehensive, multi-pronged strategy that integrates clinical vigilance, technological innovation and patient and public engagement. The following key components are essential to a preventive approach.

Evidence-based prescribing

Clinicians must evaluate the risk-benefit profile of medications, especially those known to be associated with IDIA[60,61]. In patients identified as high risk-based on genetic, clinical or pharmacological factors-safer alternatives should be prioritized whenever available. This careful selection of therapy is a crucial first step in reducing preventable cases of agranulocytosis.

Targeted monitoring strategies

Effective prevention also relies on risk-stratified monitoring protocols, tailored to individual patient risk cluster profiles. For high-risk patients, this may include more frequent blood count assessments, supported by innovations such as telemedicine and connected sensors[62,63]. These technologies enable remote tracking of symptoms and vital signs, allowing for earlier detection of neutropenia and rapid clinical response.

Pre-prescription risk assessment

The use of AI-powered predictive models offers a transformative tool for risk prevention. By analyzing genetic data, comorbidities, medication history and other relevant factors, these models can estimate a patient's likelihood of developing IDIA before initiating therapy[64,65]. This facilitates personalized prescribing decisions and customized monitoring plans, reducing the risk of adverse outcomes.

Pharmacovigilance enhancement

Strengthening pharmacovigilance systems is essential for real-time detection and evaluation of IDIA cases. Integrating big data analytics and AI into these systems can improve signal detection, enabling earlier identification of emerging drug safety concerns and more timely regulatory interventions[66,67]. Enhanced reporting and analysis mechanisms also contribute to a more accurate understanding of IDIA incidence and risk factors.

Public awareness campaigns

Educating both healthcare professionals and the public is critical to prevention efforts. Campaigns should focus on increasing awareness of IDIA risks, promoting early symptom recognition and emphasizing the importance of prompt reporting. Ensuring that clinicians and patients are informed can lead to faster diagnosis, discontinuation of the offending drug and initiation of appropriate treatment[68].

In conclusion, preventing IDIA requires a coordinated approach that spans clinical decision-making, patient engagement, technological support and public health communication. By aligning these efforts, healthcare systems can significantly reduce the incidence and impact of this serious adverse drug reaction **(Table 5)**, ultimately improving safety and outcomes for patients[69-70].

Table 5: Key points from prevention and prediction for drug-induced agranulocytosis (IDIA)[60-70].

Prevention & Prediction Component	Description	Benefits / Impact	Tools / Approaches
Evidence-based prescribing	Assess risk-benefit of drugs; prioritize safer alternatives in high-risk patients based on genetic/clinical factors	Reduce preventable IDIA cases through careful drug selection	Clinical guidelines, genetic testing, risk profiling
Targeted monitoring strategies	Implement risk-stratified blood monitoring tailored to patient risk clusters, enhanced by telemedicine and sensors	Early detection of neutropenia, faster clinical intervention	Frequent blood counts, remote monitoring devices, telehealth
Pre-prescription risk assessment	Use AI predictive models analyzing genetics, comorbidities and history to estimate IDIA risk before starting therapy	Personalized prescribing and monitoring plans, reducing adverse outcomes	AI algorithms, predictive analytics platforms
Pharmacovigilance enhancement	Strengthen real-time detection of IDIA cases using big data and AI to improve signal detection and regulatory response	Faster identification of safety signals and more effective drug safety oversight	Big data analytics, AI in pharmacovigilance databases
Public awareness campaigns	Educate healthcare providers and the public on IDIA risks, symptom recognition and prompt reporting	Increased early diagnosis, quicker drug discontinuation, timely treatment	Awareness campaigns, educational materials, professional training

Conclusion

IDIA remains a significant clinical challenge due to its unpredictable nature, potential severity and wide range of implicated medications. However, the convergence of advancements across multiple disciplines offers a transformative opportunity to shift from reactive to proactive care.

Progress in the identification of risk clusters-through the analysis of genetic predispositions, patient characteristics, comorbidities and medication profiles-has laid the groundwork for more targeted prevention strategies. At the same time, the integration of big data analytics and AI is enabling the development of sophisticated predictive models that can estimate an individual's risk of IDIA before exposure to high-risk drugs. These models offer the potential for personalized prescribing and monitoring protocols, reducing the likelihood of adverse outcomes.

Innovations in biological research, including advances in pharmacogenomics, neutrophil biology and immunopathogenesis, are deepening our understanding of the mechanisms underlying IDIA. These insights may lead to the development of targeted therapies and biomarkers for early detection. Meanwhile, connected health technologies-such as wearable sensors, telemedicine platforms and home-based blood monitoring devices-are revolutionizing how patients at risk are monitored, enabling earlier intervention and reducing the burden on healthcare systems.

By embracing this multidisciplinary toolkit, we can move toward a more personalized, predictive and preventative approach to managing IDIA, with the ultimate goal of improving patient safety and clinical outcomes in internal medicine.

However, further research is critical to fully realize these advancements. This includes the validation of risk clusters in diverse populations, the refinement and clinical validation of AI-driven predictive tools and the assessment of the real-world utility of connected monitoring technologies. Only through rigorous study and careful implementation can we translate scientific and technological progress into tangible benefits for patients at risk of this rare but serious adverse drug reaction.

Conflict of Interest

The authors declare no conflict of interest.

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Key points of the present paper

Key Point	Summary
Nature of IDIA	Rare, potentially life-threatening neutrophil depletion causing severe infections with unpredictable onset.
Clinical challenge	Low incidence but broad drug spectrum and unpredictability complicate management.
Current management	Prompt recognition and immediate withdrawal of offending drug remain essential.
Pharmacogenomics insights	Identification of genetic risk factors like specific HLA alleles and polymorphisms enhances understanding of susceptibility.
Risk clusters concept	Integration of genetic, demographic and clinical data allows targeted prevention strategies.
Big data & AI applications	Enable predictive modeling and real-time pharmacovigilance for earlier detection and risk assessment.
Technological innovations	Telemedicine, wearable sensors and home blood monitoring improve early detection and timely intervention.
Therapeutic patient education (TPE)	Essential for patient awareness, monitoring adherence and empowering self-management.
Shift in approach	From reactive to proactive, personalized and preventive management in internal medicine.

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